In the name of God, the Beneficent, the Merciful.
To

My Sisters

Soraya, Sohaila and

Mahshid

and.............
In the Name of God, the Beneficent, the Merciful.
The work in this thesis was carried out by the author under the supervision of Dr. G. Jones.

Hamid Sheikh
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Abstract

Our aim was to identify the possible factors which controlled the photochemical reactions of benztropones or more widely, annulated tropones, by synthesising benztropones with electron-donating and electron-withdrawing substituents on the benzene ring. These substituents are far enough away to have no steric effects; thus, steric effects which might be important if there are substituent groups on the seven-membered ring are eliminated and only electronic effects which can be transmitted from the benzene ring are left.

The first chapter of this work reports a review of previous syntheses of annulated tropones, unsubstituted on the tropone ring.

The second chapter deals with the synthesis of the methoxybenztropones (38), (247), (234) and (268), and 5H-benzocyclohepten-5-one (1) and its substituted derivatives, such as 3-amino-, 3-nitro-, 3-acetamido-, 3-amino-2,4-dibromo- and 6,8-dinitro-5H-benzocyclohepten-5-one (270), (20), (21), (272), and (269). The syntheses of 1-methyl-3-phenylcyclohepta(b)pyrrolo-8-one (281), cyclohepta(b)indol-10(5H)-one (8) and its methyl and ethyl derivatives (289), (285), as well as 4H-cyclohepta(b)furan-4-one (9) were also reported.

The third chapter is a review of photochemistry of tropones and annulated tropones.

Finally the fourth chapter reports the photochemistry of the benztropone and its substituted derivatives as well as tropones with fused hetero rings.
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H. Sheikh
Nomenclature

Names, structures and numbering of the following compounds will be adopted according to the method used in Chemical Abstracts.

1. 5H-Benzocyclohepten-5-one

2. 7H-Benzocyclohepten-7-one

3. 3H-Cyclohepta(f)inden-5-one

4. 11H-Cyclohepta(a)naphthalen-11-one
(5) 8H-Cyclohepta(b)pyrrol-8-one

(6a) 6H-Cyclohepta(b)pyrrol-6-one

(7) 5H-Cyclohept(b)indol-6-one

(8) 5H-Cyclohept(b)indol-10-one

(9) 4H-Cyclohepta(b)furan
(10) $6H$-Cyclohepta(c)furan-6-one

(11a) $9H$-Cyclohepta(b)pyridin-9-one

(12a) $5H$-Cyclohepta(b)pyridin-5-one

(13a) $7H$-Cyclohepta(b)pyridin-7-one
Chapter 1

Introduction

A review of previous syntheses of benztropones together with the syntheses of annulated tropones unsubstituted on the tropone ring.
The syntheses of benztropolones and tropones have been a subject of interest and controversy, nevertheless less attention has been paid towards the synthesis of 5H-benzocyclohepten-5-one (I), specially with substituents on the benzene ring. An attempt has been made to include only those papers that relate to the substituted 5H-benzocyclohepten-5-ones and the tropones with fused hetero rings, which are significant to the present work and not include those which are related to the benztropolones.

The syntheses of benztropolones can be divided into the four groups:

(I)- From 9-hydroxy-5H-benzocyclohepten-5-one .

(II)- Those which start from conversion of the 6,7,8,9-tetrahydro-5H-benzocyclohepten-5-ones by bromination and dehydrobromination sequences.

(III)- Those which start from a direct oxidation of 5H-benzocycloheptene.

And finally (IV)- those which start from tetralones.
5H-Benzocyclohepten-5-one

In 1957 Rennhard and Eschenmoser \(^1\) reported the preparation of 5H-benzocyclohepten-5-one(1). The synthesis starts from 9-hydroxy-5H-benzocyclohepten-5-one(2a).

Treatment of the benztopolone (2a) with isobutyl alcohol gave 9-isobutoxy-5H-benzocyclohepten-5-one(3a). Subsequent reduction of the isobutyl ether(3a) with lithium aluminium hydride followed by treatment with sulfuric acid, yielded 5H-benzocyclohepten-5-one(1) (Scheme 1).

Scheme 1
The 9-hydroxy-5H-benzocyclohepten-5-one (2a) itself was first prepared by Buchanan. The synthesis starts from the condensation of diethyl phthalate with diethyl glutarate followed by hydrolysis and decarboxylation to give the benzocycloheptadione (4a). The diketone (4a) was converted into its bis-enol acetate (5a) by treatment with isopropenyl acetate. The diacetate (5a) was brominated with N-bromosuccinimide, and then was hydrolysed to give the 9-hydroxy-5H-benzocyclohepten-5-one (2a) (Scheme 2).

Scheme 2
A convenient synthesis of 5H-benzocyclohepten-5-one (1) has proceeded from 6,7,8,9-tetrahydro-5H-benzocyclohepten-5-one (6) by bromination and dehydrobromination sequences.

Three routes from the bicyclic ketone (6) were given by Buchanan and Lockhart.\textsuperscript{4,5}

The first and preferred route was by bromination using bromine in carbon tetrachloride to give 6-bromo-6,7,8,9-tetrahydro-5H-benzocyclohepten-5-one (7a) followed by further bromination at position nine by N-bromosuccinimide giving 6,9-dibromo-6,7,8,9-tetrahydro-5H-benzocyclohepten-5-one (8a). Dehydrobromination of the dibromo ketone (8a) with collidine afforded the 5H-benzocyclohepten-5-one (1).

The second route\textsuperscript{6} was by bromination using N-bromosuccinimide to give 9-bromo-6,7,8,9-tetrahydro-5H-benzocyclohepten-5-one (9a) followed by dehydrobromination with collidine to give the 6,7-dihydrocyclohepten-5-one (10a). Subsequent oxidation of compound (10a) with selenium dioxide gave 5H-benzocyclohepten-5-one (1).

The third route\textsuperscript{7} was by bromination of 6,7-dihydrocyclohepten-5-one (10a) with N-bromosuccinimide in carbon tetrachloride followed by dehydrobromination gave 5H-benzocyclohepten-5-one (1) (Scheme 3).
Scheme 3

\[
\begin{align*}
(6) & \xrightarrow{\text{NBS/CCl}_4} (9a) \xrightarrow{\text{Collidine -HBr}} (10a) \\
(6) & \xrightarrow{\text{Br}_2/\text{CCl}_4} (7a) \xrightarrow{\text{NBS/CCl}_4} (8a) \xrightarrow{\text{Collidine -2HBr}} (1a) \xrightarrow{\text{SeO}_2} (1)
\end{align*}
\]
In 1966 Proctor et al. reported the preparation of 2-acetoxy-5H-benzocyclohepten-5-one (14) from 2-methoxy-6,7,8,9-tetrahydrobenzocyclohepten-5-one (11). The compound (11) was demethylated in good yield by using aluminium bromide in refluxing benzene to give 2-hydroxy-6,7,8,9-tetrahydrobenzocyclohepten-5-one (12). The 2-hydroxy compound (12) was reacted with acetic anhydride to yield 2-acetoxy-6,7,8,9-tetrahydrobenzocyclohepten-5-one (13).

Bromination by N-bromosuccinimide and dehydrobromination by collidine was repeated twice to yield the 2-acetoxy-5H-benzocyclohepten-5-one (14) (Scheme 4).

![Scheme 4](image)
The most convenient synthesis of 5H-benzocyclohepten-5-one(1) was reported by Collington and G. Jones in 1968. They prepared a number of benzocyclohepten-5-ones(1, 20 and 21) from different 6,7,8,9-tetrahydro-5H-benzocyclohepten-5-ones (6, 15 and 16). The ketone(6) and 3-nitro compound(15) were brominated by bromine(2 Moles) in carbon tetrachloride to give the corresponding dibromoketones(17, 18). In the case of 3-acetamido compound(16), they used phenyltrimethylammonium tribromide(PTAB) to avoid nuclear bromination of aromatic ring. All three dibromoketones were dehydrobrominated by lithium chloride in boiling dimethylformamide(DMF) to give the corresponding 5H-benzocyclohepten-5-one(1, 20 and 21) (Scheme 5).

**Scheme 5**

\[
\begin{align*}
&\text{Br}_2/\text{CCl}_4 \\
&\text{R} = \text{H or NO}_2 \\
&\text{PTAB} \\
&\text{R} = \text{CH}_3\text{CONH}
\end{align*}
\]

\[
\begin{align*}
&(15) \text{R} = \text{NO}_2 \\
&(16) \text{R} = \text{CH}_3\text{CONH}
\end{align*}
\]

\[
\begin{align*}
&\text{LiCl/DMF} \\
&\text{R}
\end{align*}
\]

\[
\begin{align*}
&(1) \text{R} = \text{H} \\
&(20) \text{R} = \text{NO}_2 \\
&(21) \text{R} = \text{CH}_3\text{CONH}
\end{align*}
\]
In 1972 Srivastava and Dev\textsuperscript{8} observed a direct oxidation of 5H-benzocycloheptene\textsuperscript{(24)} by selenium dioxide in buffered aqueous dioxane to give the 5H-benzocyclohepten-5-one\textsuperscript{(1, 13\%)} and 7H-benzocyclohepten-7-one\textsuperscript{(2, 27\%).} The synthesis started from the ketone\textsuperscript{(6)}. The bicyclic ketone\textsuperscript{(6)} was reduced by lithium aluminium hydride to give the alcohol\textsuperscript{(22)} which was then dehydrated to the dihydro compound\textsuperscript{(23)}\textsuperscript{9}. Bromination with N-bromosuccinimide in carbon tetrachloride with subsequent elimination of hydrogen bromide gave 5H-benzocycloheptene\textsuperscript{(24)} (Scheme 6).

Scheme 6

\begin{center}
\begin{tikzpicture}
\node at (0,0) {\textbf{(6)}};
\node at (3,0) {\textbf{(22)}};
\node at (6,0) {\textbf{(24)}};
\node at (9,0) {\textbf{(23)}};
\node at (12,0) {\textbf{(1)} + \textbf{(2)}};
\draw [->] (0,0) -- (3,0) node[midway,above] {Li\textsubscript{3}AlH\textsubscript{4}};
\draw [->] (3,0) -- (6,0) node[midway,above] {p-TsOH Benzene};
\draw [->] (6,0) -- (9,0) node[midway,above] {NBS CCl\textsubscript{4}};
\draw [->] (9,0) -- (12,0) node[midway,above] {SeO\textsubscript{2}};
\end{tikzpicture}
\end{center}
The reaction of dibromocarbene and 1-methoxynaphthalene (25) has been reported to yield 6-bromo-5H-benzocyclohepten-5-one (27) as the major product, but in 1972 Moncur and Grutzner have repeated the reaction by refluxing 1-methoxynaphthalene (25) and phenyl(tribromomethyl)mercury in dry benzene. They have isolated 8-bromo-5H-benzocyclohepten-5-one (26) (Scheme 7).

Scheme 7

In agreement with this, Ebine et al. reported the reaction of 8-bromo-5H-benzocyclohepten-5-one (26) with maleic anhydride (140°C) to give an adduct, which was hydrolysed to diacid (28), whose n.m.r. spectrum is identical to that published. This product could rise from compound (26) but not from (27). These results indicated that dibromocarbene adds to 3,4 double bond of 1-methoxynaphthalene rather than 1,2 double bond.
The chemical behavior of difluorocyclopropyl acetates, generated by addition of difluorocarbene to enol acetate of aliphatic, alicyclic and aromatic ketones, has been investigated by Crabbe et al. in 1973. The difluorocyclopropane adducts of substituted tetralones were formed by addition of difluorocarbene to the enol acetates obtained from tetralones. Reaction of the acetoxydifluorocyclopropanes with 2% sodium hydroxide in methanol yields exclusively a 2:3 mixture of 1(or 2)-methoxy-6,6-difluoro-7,8,9-tetrahydro-5H-benzocyclohepten-5-ones and 1(or 2)-methoxy-5H-benzocyclohepten-5-ones respectively, thus making this sequence a new and efficient synthetic approach to the benztropone system. An attempt was made to isolate the crystalline intermediate by treatment of the difluoromethylene adduct with ammonium hydroxide in dioxane solution at room temperature. The fluoro enone is then converted quantitatively into tropone when exposed to a 2% methanolic sodium hydroxide solution. Various attempts (sodium hydroxide, lithium chloride, etc.) to convert the difluoro ketone into the benztropone were unsuccessful, thus showing the former not to be an intermediate in the conversion of the acetoxydifluorocyclopropane into the benztropone under these reaction conditions (Scheme 8).
Scheme 8

(29) $R^1=\text{OCH}_3$, $R^2=\text{H}$

(30) $R^1=\text{H}$, $R^2=\text{OCH}_3$

(31) $R^1=\text{OCH}_3$, $R^2=\text{H}$

(32) $R^1=\text{H}$, $R^2=\text{OCH}_3$

(33) $R^1=\text{OCH}_3$, $R^2=\text{H}$

(34) $R^1=\text{H}$, $R^2=\text{OCH}_3$

(35) $R^1=\text{OCH}_3$, $R^2=\text{H}$

(36) $R^1=\text{H}$, $R^2=\text{OCH}_3$

(37) $R^1=\text{OCH}_3$, $R^2=\text{H}$

(38) $R^1=\text{H}$, $R^2=\text{OCH}_3$
In 1975 Ebine et al. reported another method of synthesizing 5H-benzocyclohepten-5-one (1) from the easily available α-tetralone (40) by ring expansion of the six-membered ring compound. In the presence of an acid catalyst, α-tetralone (40) was converted with ethyl orthoformate into 1-ethoxy-3,4-dihydronaphthalene (41). The enol-ether (41) reacted with dihalocarbene to give dihalocarbene adduct (42). The adduct (42) was treated with aqueous silver tetrafluoroborate to give the 6-halo-ketone (43). The compound (43) was dehydrohalogenated with lithium chloride in dimethylformamide to give the 5H-benzocyclohepten-5-one (1) (Scheme 9).

Scheme 9
A similar route was adopted by Proctor et al.\(^\text{15}\) in 1979, in their synthesis of 3-acetoxy(or hydroxy)-2-methoxy-benzocyclohepten-5-one (46 or 47), to those via 6,6-dibromo-ketone, in this case compound (45).

Hydrogenation\(^\text{16}\) of 5-(4-hydroxy-3-methoxyphenyl)penta-2,4-dienoic acid, formed from the condensation of 4-benzyloxy-3-methoxybenzaldehyde\(^\text{17}\) with methyl crotonate, gave 5-(4-hydroxy-3-methoxyphenyl)valeric acid. The valeric acid was then cyclised with polyphosphoric acid to give 3-hydroxy-2-methoxy-6,7,8,9-tetrahydro-5H-benzocyclohepten-5-one, which was acetylated to acetoxy compound (44) with acetic anhydride. Bromination by bromine in carbon tetrachloride and dehydrobromination by lithium chloride in DMF gave the acetoxy compound (46) (Scheme 10).

**Scheme 10**

\[
\begin{align*}
&\text{AcO} \quad \text{Br}_2 / \text{CCl}_4 \quad \text{LiCl} / \text{DMF} \\
&\text{(44)} \quad \text{(45)} \quad \text{(46)} \quad \text{(47)}
\end{align*}
\]
Another report in the same year was given by Carpenter, Peesapati and Proctor. They studied the effect of replacing the hydroxyl group of compound (47) with a nitro group. This was achieved via 2-methoxy-6,7,8,9-tetrahydro-5H-benzocyclohepten-5-one (11), which was nitrated by cupric nitrate in acetic anhydride to give a mixture of the 2-methoxy-3-nitro compound (48) and the 2-methoxy-1-nitro compound (49). The nitro ketone (48) was separated by column chromatography and then brominated by bromine in carbon tetrachloride and dehydrobrominated with silver acetate in acetic acid to give 2-methoxy-3-nitro-5H-benzocyclohepten-5-one (50) (Scheme 11).

Scheme 11

\[
\text{CH}_3\text{O}\ \text{O}_2\text{N} \quad \text{CH}_3\text{O} \quad \text{CH}_3\text{O} \\
\text{Cu(NO}_3\text{)}_2 \quad \text{Ac}_2\text{O} \quad \text{AgOAc} \quad \text{AcOH} \\
\text{Br}_2/\text{CCl}_4 \quad \text{Br} \quad \text{O}_2\text{N} \\
\]

(11) \quad (48) \quad (49) \quad (50)
The first reported synthesis of 7H-benzocyclohepten-7-one(2) was in 1910 by Thiele and Weitz. Condensation of o-phthalaldehyde with acetonedicarboxylate gave 6,8-dicarbothoxy-7H-benzocyclohepten-7-one(51), which was subsequently hydrolysed and partially decarboxylated to monocarboxylic acid(52). The acid (52) heated with 5% HCl at 200 °C for five hours to give 7H-benzocyclohepten-7-one(2)(Scheme 12).

Scheme 12
In 1955 Eschenmoser et al.\textsuperscript{20} reported the conversion of 5H-benzocyclohepten-5-one to 7H-benzocyclohepten-7-one (2). The ketone (1) was reduced to the alcohol (52a) with lithium aluminium hydride followed by treatment with sulphuric acid to give the benztropylium salt (53). The salt (53) was treated with base and subsequent oxidation with chromium trioxide in pyridine yielded approximately a 1:1 ratio of 5H-benzocyclohepten-5-one (1) and 7H-benzocyclohepten-7-one (Scheme 13).

Scheme 13

As mentioned previously Srivastava and Dev\textsuperscript{8} reported that oxidation of 5H-benzocycloheptene (24) with selenium dioxide gave a mixture of 5H-benzocyclohepten-5-one (1) and 7H-benzocyclohepten-7-one (2) (Scheme 6).
In 1973 Battiste et al. developed a new method for synthesizing 7H-benzocyclohepten-7-one (2) from the benzyne-furan adduct (54). Treatment of this adduct with dichlorocarbene yielded the 2,3-benzobicyclo(4.1.0)heptane (55). The subsequent ring expansion of the dichlorocyclopropane adduct (55) to benzocyclohepten-6-ene (56) occurred, on boiling under reflux with nitrobenzene. The compound (56) was reduced by lithium hydride to give the chlorodiene (57). Treatment of the chlorodiene (57) with concentrated sulphuric acid gave the chlorobenzotropylium ion and subsequently 7H-benzocyclohepten-7-one (2) (Scheme 14).

Scheme 14

\[
\text{\begin{align*}
\text{CHCl}_3 / \text{NaOH} & \quad \text{PhCH}_2\text{N(Et)}_3 \\
\text{PhCH}_2\text{N(Et)}_3 & \quad \text{Cl}_1 \text{C}_1 \\
\text{LiAIH}_4 & \quad \text{Cl}_1 \text{C}_1 \\
\text{H}_2\text{SO}_4 & \quad \text{PhNO}_2 \\
\end{align*}}
\]

\[
\text{(54)} \quad \text{(55)} \quad \text{(56)} \quad \text{(57)} \quad \text{(2)}
\]
In 1975 Ewing and Paquette \(^{22}\) have focused on the fact that 7H-benzocyclohepten-7-one (2) is a bisdehydro derivative of 5,6,8,9-tetrahydro-7H-benzocyclohepten-7-one (60), and have gained simple access to the compound (60) in 51\% overall yield by bisalkylation of readily available o-xyylene dibromide \(^{23}\) (58) with lithio tert-butyl acetate and subsequent Dieckmann cyclization and then decarboxylation. Bromination of the tetrahydrotropone (60) with bromine in carbon tetrachloride gave the 6,8-dibromo ketone which was then dehydrobrominated by lithium chloride in boiling dimethylformamide to give the 7H-benzocyclohepten-7-one (2) (Scheme 15).

**Scheme 15**

\[
\begin{array}{c}
\text{CH}_2\text{Br} & \text{2 Li CH}_2\text{CO}_2\text{-t-Bu} \\
\text{THF , -78}^\circ\text{C} & \rightarrow \\
\text{CO}_2\text{-t-Bu} & \text{CO}_2\text{-t-Bu}
\end{array}
\]

(58) (59)

\[
\begin{array}{c}
\text{(i) NaH; Toluene} \\
\text{(ii) HCl; aq CH}_3\text{OH} \\
\rightarrow \\
\text{HCl; aq CH}_3\text{OH}
\end{array}
\]

(60)

\[
\begin{array}{c}
\text{(i) Br}_2/\text{CCl}_4 \\
\text{(ii) LiCl ; DMF} \\
\rightarrow \\
\text{Br}_2/\text{CCl}_4
\end{array}
\]

(2)
A direct conversion of o-phthalaldehyde to 7H-benzocyclohepten-7-one (2) was achieved by Walfe et al in 1976. Treatment of triphenylphosphineacetylmethylene (61) with 1.2 equivalents of n-butyllithium in tetrahydrofuran at -78 °C under a nitrogen atmosphere resulted in abstraction of a methyl proton to form the ylide anion, lithiotriphenylphosphineacetylmethylene (62). Reaction of o-phthalaldehyde with a tetrahydrofuran solution of ylide (62) afforded 7H-benzocyclohepten-7-one (2) (Scheme 16).

Scheme 16

\[
\begin{align*}
\text{(61)} & \quad \text{THF, } -78^\circ \text{C}, \text{N}_2 \\
(C_6H_5)_3P^+C^+\text{HCOCH}_3 & \xrightarrow{n-\text{Bu Li}} [\{(C_6H_5)_3P^+C^+\text{HCOC}^-\text{H}_2\} \text{Li}^+] \\
\text{(62)} & \quad \text{THF}
\end{align*}
\]
In 1978 Fohlish et al.\textsuperscript{25} reported some modification to the method of Thiele and Weitz. They hydrolysed the diester(51) by boiling it under reflux with aqueous sodium hydroxide. This gave a mixture of the dicarboxylic acid(63) and the monocarboxylic acid(64). Complete conversion to the monocarboxylic acid was achieved by heating the mixture of carboxylic acid in butanol until evolution of carbon dioxide ceased. Heating the acid(64) at 250°C with copper powder effected the decarboxylation giving the 7H-benzocyclohepten-7-one(2) in 57% yield (Scheme 17).

Scheme 17

\[
\begin{align*}
\text{(51)} & \quad \text{CO}_2\text{Et} \\
\text{CO}_2\text{Et} & \quad \text{CO}_2\text{Et} \\
\text{(63)} & \quad R = \text{CO}_2\text{H} \\
\text{(64)} & \quad R = \text{H} \\
\text{(2)} &
\end{align*}
\]
1H-2,3-Dihydro-cyclohept(f)inden-5-one and

3H-cyclohept(f)inden-5-one

In 1972 Patwardhan and Dev reported a method for synthesizing 3H-cyclohept(f)inden-5-one(3) which started from γ-(5-hydrindyl)-butyric acid. The acid cyclized by polyphosphoric acid to give 6,7-cyclopentano-1-tetralone(65). Conversion of the tetralone(65) to the enol-ether(66) was carried out using triethylorthoformate with Amberlyst-15 as a catalyst. The enol-ether(66) was reacted with dibromocarbene to give the dibromocarbene adduct(67). Dehydrobromination rearrangement of this carbene adduct(67) by heating with active alumina gave 1H-2,3-dihydro-cyclohept(f)inden-5-one(68). Bromination by N-bromosuccinimide gave the mono-bromotropone(69). Treatment of this compound (69) with silver nitrate in dimethylsulphoxide gave the 3H-cyclohept(f)inden-5-one(3) (Scheme 18).

Scheme 18
11H-Cyclohepta(a)naphthalen-11-one

The synthesis of 11H-cyclohepta(a)naphthalen-11-one (4) was reported by Elad and Ginsburg in 1957.

Catalytic reduction of the diketone (70) to the ketone (71) removed the carbonyl group conjugated the aromatic nucleus. Stepwise bromination by N-bromosuccinimide in carbon tetrachloride and dehydrobromination was repeated to yield the 11H-cyclohepta(a)naphthalen-11-one (4) (Scheme 19).

Scheme 19

![Chemical Structures](image-url)
7H-Cyclohepta(a)naphthalen-7-one

The synthesis of the naphthotropone(78) was reported by Julia et al. in 1956. Conversion of the ketone(72) to the ketal(73) was carried out using ethyl orthoformate. Subsequent reduction of the ester group with lithium aluminium hydride followed by acid hydrolysis gave ketol(74). Conversion of the ketol(74) with p-toluenesulphonyl chloride gave the tosylate(75), which was then cyclized to naphtho(1,2'')bicyclo(4,1,0)-hepten-3-one(76). The ketone(76) was then ring expanded to give 8,9-dihydro-7H-cyclohepta(a)naphthalen-7-one(77), which was subsequently oxidized with selenium dioxide to the naphthotropone(78) (Scheme 20).

Scheme 20
8H-Cyclohepta(b)naphthalen-8-one

Naville, Strauss and Heilbronner\(^{34}\) in 1960 reported the synthesis of 8H-cyclohepta(b)naphthalen-8-one (81). Condensation of naphthalene-2,3-dicarboxaldehyde (79) with diethyl acetone dicarboxylate gave 7,9-dicarbethoxy-8H-cyclohepta(b)naphthalen-8-one (80) which was subsequently hydrolysed and decarboxylated to 8H-cyclohepta(b)naphthalen-8-one (81) by refluxing with methanolic potassium hydroxide (Scheme 21).

**Scheme 21**

![Scheme 21 Image](image-url)
In 1979 Villessot and Lepage reported the syntheses of 1,2-diphenyl-7H-cyclohepta(f)-2-benzothiophen-7-one (86) and 1,2-diphenyl-7H-cyclohepta(f)-2-isobenzofuran-7-one (87). Reaction of benzo(c)thiophen dialdehyde (82) with acetone gave the thienobenzotropone (86). Under similar conditions, the isobenzofuran dialdehyde (83) gave only a poor yield of the isobenzofurotropone (87). The latter (87) was prepared by a two-step reaction sequence starting from the adduct (84). This adduct (84) readily obtained from compound (83) and N-phenylmaleimide which was subsequently condensed with acetone to give the adduct (85). Pyrolysis of the adduct (85) gave the isobenzofurotropone (87) (Scheme 22).

Scheme 22
Cycloheptapyrrolones

The syntheses of cycloheptapyrrolones can be divided into four groups.

(I) - Those which start from the conversion of cycloheptafuranones.

(II) - Those which start from 4-methoxybenzyl-2-aryl-N-alkylaminoacetonitriles.

(III) - Those which start from pyrrole moiety.

And finally (IV) - those which start from a tropone.

Conversion of cycloheptafuranones to cycloheptapyrrolones

N-Alkyl-2-methylcycloheptapyrrol-8-ones

The synthesis of N-alkyl-2-methylcycloheptapyrrol-8-one (89) was reported by Takeshita, Chisaka and Mametsuka in 1980. Conversion of 2-methylcyclohepta(b)furan-8-one (88) to N-alkyl-2-methylcycloheptapyrrol-8-one (89) was carried out by heating with alkylamines. When bulky amines were used, 2-alkylamino-3-(2-oxopropyl)tropones (90) were obtained as byproducts. However, compound (88) did not react with ammonia or t-butylamine under comparable conditions (Scheme 23).

Scheme 23

<table>
<thead>
<tr>
<th>R</th>
<th>Me</th>
<th>Et</th>
<th>((\text{CH}_2)_2\text{Me})</th>
<th>(\text{CHMe}_2)</th>
<th>Cyclohexyl</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yields of compound (89)</td>
<td>76%</td>
<td>70%</td>
<td>85%</td>
<td>45%</td>
<td>14%</td>
</tr>
<tr>
<td>Yields of compound (90)</td>
<td>0%</td>
<td>0%</td>
<td>4%</td>
<td>18%</td>
<td>12%</td>
</tr>
</tbody>
</table>
1-Methylcyclohepta(b)pyrrol-4-one

The synthesis of 1-methylcyclohepta(b)pyrrol-4-one (93) was reported by Crabbe et al.\textsuperscript{38} in 1980. Treatment of the 5,6,7,8-tetrahydrocyclohepta(b)furan-4-one (91) with methylamine in methanol under pressure afforded the 1-methyl-5,6,7,8-tetrahydrocyclohepta(b)pyrrol-4-one (92). The pyrrole (92) was then dehydrogenated with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone to give 1-methylcyclohepta(b)pyrrol-4-one (93) (Scheme 24).

Scheme 24

Conversion of N-4-methoxybenzyl- and N-3,4-dimethoxybenzyl-aminoacetonitriles to cycloheptapyrrolones

1-Aryl-N-methylcyclohepta(c)pyrrol-6-ones

In 1980 Waigh\textsuperscript{39} reported the synthesis of 2-aryl-N-methyl-cyclohepta(c)pyrrol-6-ones (97, 98 and 99). N-4-Methoxybenzyl- and N-3,4-dimethoxybenzylaminoacetonitriles (94, 95 and 96) with both
2-aryl and N-alkyl substituents undergo demethylation and rearrangement with elimination of ammonium ion in very strongly acidic conditions, such as concentrated sulphuric acid, to give 2-aryl-1-methylcyclohepta(c)pyrrolo-6-ones (97, 98 and 99) (Scheme 25).

Scheme 25

(94) R=H, Ar=Ph
(95) R=OMe, Ar=Ph
(96) R=OMe, Ar=DMP
(97) R=H, Ar=Ph
(98) R=Ome, Ar=Ph
(99) R=Ome, Ar=3,4-dimethoxyphenyl
Synthesis starting from a pyrrole

1,3-Dimethyl-2-phenylcyclohepta(c)pyrrol-6-one

The synthesis of 1,3-dimethyl-2-phenylcyclohepta(c)pyrrol-6-one (101) was reported by Ginesina, Kivokurtseva and El'tsov \(^\text{40} \) in 1969. The 3,4-diformyl-2,5-dimethyl-1-phenylpyrrole (100) could be condensed with acetone to afford 1,3-dimethyl-2-phenylcyclohepta(c)pyrrol-6-one (101) (Scheme 26).

Scheme 26

\[
\begin{align*}
\text{CHO} & \quad \text{CH}_3\text{COCH}_3 \\
\text{H}_3\text{C} & \quad \text{Ph} \\
\text{N} & \quad \text{H}_3\text{C} \\
\text{Ph} & \quad \text{Ph}
\end{align*}
\]

(100) \rightarrow (101)
The synthesis of 6H-2-methylcyclohepta(c)pyrrol-6-one (106) was reported by Duflo et al. in 1973. Reduction of 1-methyl-3,4-dicarboethoxypyrrole (102) gave diol (103) which was then oxidized to the dialdehyde (104) by using silver carbonate. Condensation of the dialdehyde with dimethyl 1,3-acetone-dicarboxylate gave the diester (105) which after hydrolysis and subsequent decarboxylation gave the 6H-2-methylcyclohepta(c)pyrrol-6-one (106) (Scheme 27).

Scheme 27
1-Methylcyclohepta(b)pyrrol-6-one

In another report also in 1973, Duflos et al. were able to synthesize 1-methylcyclohepta(b)pyrrol-6-one (112). The synthesis starts from 1-methyl-2,3-diformylpyrrole (109) which was prepared in four steps by the following route. The aldehyde function of methyl-2-formyl-1-methylpyrrole-3-carboxylate (107) was protected as an acetal enabling the ester to be reduced to an alcohol using lithium aluminium hydride. After hydrolysis of the acetal, the alcohol (108) was oxidized with silver carbonate to give 1-methyl-2,3-diformylpyrrole (109). Condensation of the pyrrole (109) with dimethyl acetylenedicarboxylate gave 6H-1-methyl-5,7-dicarbomethoxycyclohepta(b)pyrrol-6-one (110). The ester was hydrolysed to the acid (111) which was then decarboxylated to give the pyrrole (112) (Scheme 28).

Scheme 28
The synthesis of pyrroles (119 and 120) was reported by Kreher et al. in 1975. The $\alpha$-substituted heterocyclic dialdehyde (115, 116) required for the synthesis are accessible from 2,5-dimethyl- and 1,2,5-trimethylpyrrole (113, 114) by formylation with dimethylformamide and phosphorus oxychloride. Condensation of diethyl (or dimethyl) acetonedicarboxylate with both the pyrroles (115 and 116) occurred readily in the presence of triethylamine to give the diesters (117, 118) which with subsequent hydrolysis and decarboxylation gave the pyrrolotropones (119, 120). Condensation of acetone and 1,3-diphenylacetone with the trimethylpyrrole (116) could only be achieved under forcing conditions, such as morphine and potassium hydroxide, to give pyrrolotropones (120, 120a) (Scheme 29).

Scheme 29

\[
\begin{align*}
R\quad & \xrightarrow{\text{DMF/POCl}_3} \quad \text{OCH} \quad \text{CHO} \\
(113) R=H & \quad \text{CH}_3 & \quad \text{CH}_3 \\
(114) R=\text{CH}_3 & \\
(115) R=H & \\
(116) R=\text{CH}_3 & \\
\text{X} \quad & \xrightarrow{\text{XCH}_2\text{COCH}_2\text{X}} \\
(117) R=H, \quad \text{X}=\text{CO}_2\text{Et} & \\
(118) R=\text{CH}_3, \quad \text{X}=\text{CO}_2\text{Et} & \\
(119) R=H, \quad \text{X}=\text{H} & \\
(120) R=\text{CH}_3, \quad \text{X}=\text{H} & \\
(120a) R=\text{CH}_3, \quad \text{X}=\text{Ph} & 
\end{align*}
\]
In 1976 Jones and Santokh reported a similar synthesis of $2H$-1,3-dimethylcyclohepta(c)pyrrol-6-ones. Condensation of 3,4-diformyl-2,5-dimethylpyrrole (113) with acetone was carried out in aqueous methanol in the presence of sodium hydroxide at $25^\circ$C to give the $2H$-1,3-dimethylcyclohepta(c)pyrrol-6-one (119). A number of the 5,7-substituted-1,2-dimethylcyclohepta(c)pyrrol-6-ones (120-125) were also prepared in 60-65% yield by the base catalyzed condensation of the pyrroloaldehyde with 1,3-disubstituted acetones (Scheme 30).

Scheme 30

![Chemical Diagram]

(113) 

(119) $R^1=R^3=H$

(120-123) $R^1=R^3=\text{CH}_3$; Ph;

$\text{CO}_2\text{Me};\text{CO}_2\text{H}$.

(124-125) $R^1=\text{H};R^3=\text{Me or Ph}$.
Syntheses starting from tropones

**Substituted-1,8-dihydrocyclohepta(b)pyrrole-8-one**

An improved process for preparation of cyclohepta(b)pyrrol-8-ones\(^45\) is based on the treatment of substituted tropolones with ammonia or substituted amines or, alternatively, with amides and potassium carbonate. Thus, 5,7-dibromo-3-acetonyltropolone\((126)\) was mixed and stirred with formamide and potassium carbonate to give 5,7-dibromo-2-methyl-1,8-dihydrocyclohepta(b)pyrrole-8-one\((129)\).

The synthesis of substituted cycloheptapyrrole-8-one\((130-132)\) starting from 3-acetonyltropolone\((127)\) or also 3-phenacyltropolone\((128)\) was reported by Nakazawa et al\(^46\) in 1969. Reaction of 3-acetonyltropolone\((127)\) with liquid ammonia (or formamide) in the presence of potassium carbonate and also with methylamine (or N-methylformamide) gave 2-methyl or 1,2-dimethyl-1,8-dihydrocyclohepta(b)pyrrole-8-one\((130,132)\) respectively. Similarly, treatment of 3-phenacyltropolone\((128)\) with formamide gave 2-phenyl-1,8-dihydrocyclohepta(b)pyrrole-8-one\((131)\) (Scheme 31).

**Scheme 31**

\[
\begin{align*}
(126) \quad & R=CH_3, \ R^1=H, R^2=CH_3, R^3=Br \text{ (using HCONH}_2 \text{ or NH}_3) \quad (129) \\
(127) \quad & R=CH_3, \ R^1=H, R^2=CH_3, R^3=H \text{ (using HCONH}_2 \text{ or NH}_3) \quad (130) \\
(128) \quad & R=Ph, \ R^1=H, R^2=Ph, R^3=H \text{ (using HCONH}_2) \quad (131) \\
(127) \quad & R=CH_3, \ R^1=CH_3, R^2=CH_3, R^3=H \text{(using CH}_3\text{NH}_2 \text{ or HCONHCH}_3) (132)
\end{align*}
\]
The synthesis of $\text{6,7,8,9,10,11-Hexahydro-5H-dicyclohepta(b,d)pyrrol-5-one}$ (138) and $\text{2,3,4,5-Tetrahydro-1H-cyclohepta-(b)indol-6-one}$ (137) was reported by Yamane et al. in 1975. Reaction of cycloheptanone or cyclohexanone with 2-hydrazino-troponone (133) gave cycloheptanone 2-troponylhydrazone (135) and cyclohexanone 2-troponylhydrazone (134) respectively. Cyclization of the hydrazones (135,134) was effected by heating in dilute sulphuric acid to afford the pyrrolothropones (138,137). Similarly the 2-troponylhydrazone of $\text{N-benzyl-4-piperidone}$ (136) was easily converted to the $\text{2,3,4,5-tetrahydro-1H-2-(phenylmethyl)-cyclohepta(4,5)pyrrolo(3,2-c)pyridin-6-one}$ (139) (Scheme 32).

**Scheme 32**
3-Phenylcyclohepta(b)pyrrol-8-one

The synthesis of 3-phenylcyclohepta(b)pyrrol-8-one (141) was reported by Yamane, Fujimori, Sin and Nozoe\textsuperscript{48} in 1977. Condensation of 2-hydrazinotropane (133) with phenylacetaldehyde gave the phenylacetaldehyde troponylhydrazone (140). Cyclization of the hydrazone (140) was effected by heating in aqueous sulphuric acid to give the 3-phenylcyclohepta(b)-pyrrol-8-one (141) (Scheme 33).

Scheme 33

\begin{center}
\begin{tikzpicture}
  \node (a) at (0,0) {\includegraphics[width=0.5\textwidth]{scheme33.png}};
\end{tikzpicture}
\end{center}
Synthesis starting from cycloheptanedione monophenylhydrazone

5H-cyclohept(b)indol-6-one

In 1973 Yamane et al. \(^{47}\) synthesized 7,8,9,10-terahydro-5H-cyclohept(a)b)indol-6-one(143) from cycloheptanedione monophenylhydrazone(142) \(^{49,50}\). From this Yamane and Fujimori \(^{51}\) were able to prepare 5H-cyclohept(b)indol-6-one(7) in 1977 by using Collington and Jones' method for bromination/dehydrobromination (Scheme 39).

Scheme 39

From photolysis of 2,2'-diisocyanobiphenyl and acridine-N-oxide

The synthesis of 5H-cyclohept(b)indol-6-one(7) was reported by de Jong and Boyer \(^{52}\) in 1972. Photolysis of 2,2'-diisocyanobiphenyl(144) yielded a mixture of 10-isocyanocyclohept(b)indole (145) and 6-aminocyclohept(b)indole(146). Reaction of the amine (146) with alcoholic alkali afforded the indolotropone(7) (Scheme 40).

Scheme 40
Cycloheptindoles

The synthesis of cycloheptindoles can be divided into five groups:

(I) - Those which start from dehydrogenation of pyrrolotropones.

(II) - Those which start from conversion of the cycloheptanedione monophenylhydrazone to 7,8,9,10-tetrahydro-5H-cyclohept(b)indol-6-one and subsequent bromination/dehydrobromination procedure.

(III) - Those which start from the photolysis of 2,2-diisocyanobiphenyl and also acridine-N-oxide.

(IV) - Those which start from selective oxidation of 5,6,7,8,9,10-hexahydrocyclohept(b)indole at position 10 to 6,7,8,9-tetrahydrocyclohept(b)indol-10-(5H)-one, followed by bromination and dehydrobromination.

And finally (V) - the synthesis of 5-methylcyclohept(b)-indol-8-one from 1-methyl-2-formylindole.

Conversion of pyrrolotropon to the 5H-cyclohepta(b)indol-6-one

As mentioned previously (Scheme 32), 2,3,4,5-tetrahydro-1H-cyclohept(b)indol-6-one (137) is obtained by application of Fischer’s indole synthesis. Yamane et al. also dehydrogenated this pyrrolotropon (137) with either chloranil or DDQ to give 5H cyclohept(b)indol-6-one (7) (Scheme 34).

Scheme 34

\[ \text{Conversion of pyrrolotropon to 5H-cyclohepta(b)indol-6-one} \]
Irradiation of acridine-N-oxide(147) gave under various conditions, some of 5H-cyclohept(b)indol-6-one(7) and 5H-cyclohept(b)indol-10-one(8) along with other products. Trapping experiments for the primary products were reported by Yamada et al.\textsuperscript{55,56} In order to trap some of these products, a solution of acridine-N-oxide (0.2% in dry benzene) was irradiated. As soon as all the N-oxide was consumed, the irradiation was terminated and solution was then subjected rapidly to the following reaction in the dark:

(I) - stirred for several hours after addition of methanol containing 5\% triethylamine.

(II) - Flashed with HCl gas for a few minutes.

These results were compared with that obtained by the longer irradiation experiment (III). The results from all these reactions are listed below (Table 1).

Though the actual isolation of the intermediate (149) has not been achieved as yet, its structure can be deduced as the oxazepine (149), which reacts with solvent to give the additional product (152). Formation of the isomeric products (8,7,151) is believed to be as follows:

the oxaziniridine (148) derived from the photo-excited N-oxide (147) tautomerizes to the more stable 1,2-oxazepine (149). The oxazepine then undergoes further thermal rearrangement via the spiro compound (150) to give the products (8,7,151) (Scheme 41).

** - Photolyses were carried out in an immersion apparatus with Pyrex filter and 450 W high-pressure mercury arc lamp.
Scheme 41

\[
\begin{align*}
&\text{(147)} \xrightarrow{\text{hv}} \text{(148)} \\
&\text{(149)} \xrightarrow{\text{MeOH}} \text{(148)} \\
&\text{(150)} \xrightarrow{\text{MeOH}} \text{(151)} \\
&\text{(152)} \xrightarrow{\text{MeOH}} \text{(7)} \\
&\text{(7)} \xrightarrow{\text{MeOH}} \text{(8)}
\end{align*}
\]

<table>
<thead>
<tr>
<th>Comp.</th>
<th>(147)</th>
<th>(151)</th>
<th>(8)</th>
<th>(7)</th>
<th>(152)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(I)</td>
<td>5%</td>
<td>2%</td>
<td>10%</td>
<td>10%</td>
<td>60%</td>
</tr>
<tr>
<td>(II)</td>
<td>3%</td>
<td>2%</td>
<td>60%</td>
<td>10%</td>
<td>-</td>
</tr>
<tr>
<td>(III)</td>
<td>-</td>
<td>5%</td>
<td>30%</td>
<td>20%</td>
<td>-</td>
</tr>
</tbody>
</table>
From selective oxidation of

5,6,7,8,9,10-hexahydrocyclohept(b)indole

In 1976, Yamane and Fujimori \(^{51}\) reported the synthesis of 5H-cyclohept(b)indol-10-one from 5,6,7,8,9,10-hexahydrocyclohept(b)indole(153). Selective oxidation of the latter (153) with DDQ at room temperature in wet dioxane gave 6,7,8,9-tetrahydrocyclohept(b)indol-10(5H)-one(154). Subsequent bromination and dehydrobromination of the ketone(154) gave 5H-cyclohept(b)indol-10-one(8) (Scheme 42).

Scheme 42
Conversion of 1-methyl-2-formylindole to the indolotropone

5-Methyl-cyclohept(b)indole-8-one

In 1980 Dulflos et al. synthesized 1-methyl-2,3-diformylindole (158) and from this they were able to prepare 5H-methyl-cyclohept(b)indol-8-one (161). Treatment of 1-methyl-2-formylindole (155) with phosphorus oxychloride and dimethylformamide afforded 1-methyl-2-dichloromethyl-3-formylindole (156). Reaction of the dichloro compound with sodium methoxide yielded the acetal (157), which was subsequently hydrolysed to give 1-methyl-2,3-diformylindole (158). Treatment of the dialdehyde (158) with methyl acetonedicarboxylate gave the diester (159), which was hydrolysed to the diacid (160). Decarboxylation of the diacid (160) with copper powder afforded the 5-methylcyclohept(b)indol-8-one (161) (Scheme 43).
Scheme 43

(155) \[ \text{CHO} \quad \text{DMF/POCl}_3 \quad \text{CHCl}_3 \quad \text{CH}_3\text{ONa} \]

(156)

(157) \[ \text{CHO} \quad \text{H}^+ \quad \text{H}^+ \quad \text{O=C(CH}_2\text{CO}_2\text{CH}_3\text{)}_2 \]

(158)

(159) \[ \text{CHO} \quad \text{HCl} \quad \text{Cu powder} \quad \Delta \]

(160)

(161)
Cycloheptafuranones

As with the synthesis of cycloheptapyrrolones, the synthesis of cycloheptafuranones can be divided into two main groups, that is, either starting from a tropone or those which start from a furan.

Syntheses starting from a tropone

2-Methyl-8H-cyclohepta(b)furan-8-one

In 1965, Takase synthesized 7-acetonyltropolone and from this he was able to prepare 2-methyl-8H-cyclohepta(b)furan-8-one. Condensation of 3-bromotropolone with ethyl acetonacetate yielded 3-acetyl-8-hydroxy-2H-cyclohepta(b)furan-2-one, which on treatment with aqueous sodium hydroxide gave 7-acetonyltropolone. The acetonyltropolone was then cyclized with concentrated sulphuric acid to give the 2-methyl-8H-cyclohepta(b)-8-one (Scheme 44).

Scheme 44
The syntheses of 2-methoxy and 2-phenyl-8H-cyclohepta(b)-furan-8-one (165 and 170) starting from tropolone tosylate (166) were reported by Nakazawa, Sato and Soma in 1969. Reaction of tropolone tosylate (166) with ethyl acetoacetate gave 3-acetyl-8-hydroxy-2H-cyclohepta(b)furan-2-one (167), which was hydrolysed to give 3-acetonyltropolone (127). Reaction of the latter (127) with benzylamine gave the tropone (165) and some 1-benzyl-2-methyl-1,8-dihydropyrrol-8-one (168). Similarly, condensation of tropolone tosylate (166) with ethyl 3-benzoyl-ethanoate gave 3-benzoyl-8-hydroxy-2H-cyclohepta(b)furan-2-one (169), hydrolysis of which gave a mixture of 3-phenacyltropolone (128) and 2-phenyl-8H-cyclohepta(b)furan-8-one (170) (Scheme 45). 

Scheme 45
In 1974 Pryde, Zsindely and Schmid reported the thermal rearrangement of 2-propargyloxycycloheptatriene (172) in mesitylene in an evacuated bomb at 170°C for 100 minutes to give the 2-methoxy-8H-cyclohepta(b)furan-8-one (165). The compound (172), itself was prepared by treating of propargyl bromide with tropolone (171). The mechanism of formation of cyclized product (165) is believed to be as follows: a (3,3) sigmatropic rearrangement, followed by enolization and subsequent cyclization gave the dipolar compound (173), which then undergoes a hydrogen shift to give the tropone (165) (Scheme 46).

Scheme 46
3-Phenyl(or 3-methyl)-8H-cyclohepta(b)furan-8-one

The synthesis of 3-methyl-(or 3-phenyl)-8H-cyclohepta-(b)furan-8-one (178 and 179) was reported by Imafuku et al in 1980. Reaction of 6,6-dimethyl-fulvene (173) or 6-methyl-6-phenylfulvene (174) with dichloroacetylchloride and triethylamine in hexane afforded the bicyclo(3.2.0)heptafulvenone (175) which was hydrolysed to the 3-isopropenyltropolone (176) and 3-(1-phenylvinyl)tropolone (177) respectively. Cyclodehydrogenation of the tropolones (176 and 177) can be effected either by DDQ or by treatment with performic acid followed by aqueous sodium hydroxide, giving the furotropones (178 and 179) respectively (Scheme 47).

Scheme 47

\[
\begin{align*}
(173) & \quad R=CH_3 \\
(174) & \quad R=Ph
\end{align*}
\]

\[
\begin{align*}
(176) & \quad R=CH_3 \\
(177) & \quad R=Ph
\end{align*}
\]

\[
\begin{align*}
(178) & \quad R=CH_3 \\
(179) & \quad R=Ph
\end{align*}
\]
Syntheses starting from a furan

4H-Cyclohepta(b)furan-4-one

The synthesis of 4H-cyclohepta(b)furan-4-one(9) was reported by G. Jones and et al. in 1973. Cyclisation of 5-(2-furyl)valeryl chloride(180) was effected by tin tetrachloride in carbon disulfide to give the 5,6,7,8-tetrahydro-4H-cyclohepta-(b)furan-4-one(181). The ketone(181) was brominated by using phenltrimethylammonium tribromide(PTAB) to give 5,5-dibromoketone (182), which was then dehydrobrominated with lithium carbonate in boiling dimethyl formamide to give the 4H-cyclohepta(b)furan-4-one(9) (Scheme 48).

Scheme 48

5-(2-furyl)valeryl chloride(180) → 5,6,7,8-tetrahydro-4H-cyclohepta-(b)furan-4-one(181) → 5,5-dibromoketone (182) → 4H-cyclohepta(b)furan-4-one(9)
**6H-Cyclohepta(c)furan-6-one**

The first synthesis of 6H-cyclohepta(c)furan-6-one(10) was reported by Cook and Forbes \(^6\) in 1968. Condensation of the 3,4-dialdehyde(183) with acetone in aqueous ethanolic sodium hydroxide gave directly the furotrone(10). They also prepared the furotrone(10) by the following route. Condensation of the dialdehyde(183) with diethyl acetonedicarboxylate gave 5,7-diethoxycarbonyl-6H-cyclohepta(c)furan-6-one(184), which was subsequently hydrolysed to the diacid(185). The diacid(185) was then decarboxylated by heating for three hours in a seal tube at 175-180 °C with 0.5M HCl to give the required furotrone(10) (Scheme 49).

**Scheme 49**

\[
\begin{align*}
\text{HCO} & \quad \text{CHO} \\
\text{C} & \quad \text{O} \\
\text{EtOH} & + \text{NaOH(aq)} \\
\end{align*}
\]

\[
\begin{align*}
\text{Acetone} & \quad \text{EtOH} + \text{NaOH(aq)} \\
\text{175-180 °C} & \\
\end{align*}
\]

\[
\begin{align*}
\text{CO}_2\text{Et} & \quad \text{CO}_2\text{Et} \\
\text{20% H}_2\text{SO}_4, 1000 \degree \text{C} & \\
\end{align*}
\]
6H-Cyclohepta(b)furan-6-one

The synthesis of 6H-cyclohepta(b)furan-6-one (187) was similarly reported by Borai, Guilard and Fournari. Condensation of furan-2,3-dialdehyde (186) with acetone in the presence of base afforded 6H-cyclohepta(b)furan-6-one (187) (Scheme 50).

Scheme 50
2-Hydroxy-6H-benzo(b)cyclohepta(d)furan-6-one

In 1962 Seto and Sato reported the synthesis of 2-hydroxy-6H-benzo(b)cyclohepta(d)furan-6-one (191).

Reaction of tropolone (171) with p-benzoquinone gave a mixture of 5-(4'-hydroxyphenoxy)tropolone (188) and 3-(p-benzoquinonyl)-tropolone (189). The quinone (189) was separated and then reduced with hydrogen using palladium on charcoal as a catalyst to give the dihydrophenyltropolones (190), which was dehydrated with p-toluenesulphonic acid to the benzocycloheptafuranone (191) (Scheme 51).

Scheme 51
2-Methylbenzo(b)cyclohepta(d)furan-8-one (and -10-one)

The synthesis of 2-methylbenzo(b)cyclohepta(d)furan-8-one (197) and 2-methylbenzo(b)cyclohepta(d)furan-10-one (198) was reported by Bladon et al. in 1966.

Ditropyl ether (192) heated with p-cresol on a steam bath gave the 2-tropyl-p-cresol (193). Treatment of the latter (193) with triphenylmethyl perchlorate yielded the 6-hydroxy-m-tolyltropylium perchlorate (194). Subsequent hydrolysis of the perchlorate (194) with aqueous sodium hydrogen carbonate gave 2-methylbenzo(b)cyclohepta(d)furan (195), which on subsequent treatment with triphenylmethyl perchlorate gave the tropylium perchlorate (196). The salt (196) was then hydrolysed with aqueous sodium hydrogen carbonate and gave three products; the two isomeric benzofurotropones (197 and 198) and some of the furan (195) (Scheme 52).
Scheme 52

(192) \[ \text{p-Cresol} \rightarrow \]

(193) \[ (\text{Ph})_3C^+ \text{ClO}_4^- \rightarrow -\text{H}^- \]

(194) \[ \text{NaHCO}_3(aq) \rightarrow \]

(195) \[ \text{(196)} \rightarrow \]

(197) \[ \text{NaHCO}_3(aq) \rightarrow \]

(198)
Cycloheptathiophenones

4H-Cyclohepta(b)thiophen-4-one and its 2-methyl derivative

The synthesis of 2-methyl-4H-cyclohepta(b)thiophen-4-one (204) was reported by G. Jones and et al. Acylation of 2-methylthiophene with the glutaric anhydride gave the keto-acid (199), which was subsequently reduced by the Huang-Minlon procedure to the pentanoic acid (200). The acid chloride of the acid (200) was cyclized with tin tetrachloride to give the cyclic ketone (201). Bromination of the latter with PTAB gave the dibromo-derivative (202), which was then dehydrobrominated with lithium chloride or carbonate in boiling dimethylformamide (DMF) to give the thienotropone (204). The same procedure starting from the thiophene was used by G. Jones and M.J. Robinson in 1977 to prepare 4H-cyclohepta(b)thiophen (203) (Scheme 53).

Scheme 53

\[
\begin{align*}
\text{R} & = \text{H or CH}_3 \\
\text{R} & = \text{H} ; \ (203) \ R = \text{Me} \\
\end{align*}
\]
The synthesis of 1,3-dimethyl-6H-cyclohepta(c)-thiophen-6-one (206) was reported by Ginesina, Kivokurtseva and El 'Tsov in 1969. Condensation of 3,4-diformyl-2,5-dimethylthiophene (205) with acetone gave the cycloheptathiophenone (206) (Scheme 54).

Scheme 54

A similarly, condensation of 3,4-diformylthiophene (207) with acetone gave the 6H-cyclohepta(c)thiophen-6-one (208) (Scheme 55).

Scheme 55
In 1971 Guilard and Fournari reported the synthesis of 6H-cyclohepta(b)thiophen-6-one (212). The aldehyde function of the 2-formyl-iodothiophene (209) was protected as a diethyl acetal enabling the iodothiophene (210) to be formylated to the formylthiophene (211) by using n-butyllithium in dimethylformamide. Condensation of the formylthiophene (211) with acetone, subsequent acid hydrolysis and the ring closure gave the cyclohepta(b)thiophen-6-one (212) (Scheme 56).

Scheme 56
They also reported a second route to the 6H-cyclohepta(b)thiophen-6-one (212). Condensation of 2,3-diformylthiophene (213) with diethyl 1,3-acetone-dicarboxylate yielded diethyl 5,7-6H-cyclohepta(b)thiophen-6-one dicarboxylate (213a). Subsequent hydrolysis and decarboxylation gave the 6H-cyclohepta(b)thiophen-6-one (212) (Scheme 57).

Scheme 57

\[
\begin{align*}
\text{CHO} & \quad \text{OC(CH}_2\text{CO}_2\text{Et})_2 \\
\text{CHO} & \quad \text{piperidine} \\
\text{R} & \quad \text{R=H} \\
\text{R} & \quad \text{R=CO}_2\text{Et}
\end{align*}
\]
Cycloheptapyridinones

9H-Cyclohepta(b)pyridin-9-one and its three isomers

In 1973 G. Jones et al. reported the synthesis of 9H-cyclohepta(b)pyridin-9-one (11a). The N-oxide (215) of 6,7,8,9-tetrahydro-5H-cyclohepta(b)pyridine (214), when treated with acetic anhydride, gave the 9-acetoxycyclohepta(b)pyridine (216), which was hydrolysed to the alcohol (217). Reaction between the alcohol (217) and N-bromosuccinimide gave in low yield the ketone (218) and two other products. Bromination of the ketone (218) by PTAB gave in low yield, the dibromo-ketone (219), which was subsequently dehydrobrominated by lithium carbonate in boiling dimethylformamide to give the 9H-cyclohepta(b)pyridin-9-one (11a) (Scheme 58).

Scheme 58

\[
\begin{align*}
\text{NBS} & \quad \rightarrow \quad \text{Br} \\
\text{LiCl/DMF} & \quad \rightarrow \quad \text{H}_2\text{O}_2, \text{AcOH} \\
\text{Ac}_2\text{O} & \quad \rightarrow \quad \text{KOH, KOH} \\
\text{PTAB/THF} & \quad \rightarrow \quad \text{NBS}
\end{align*}
\]
Very recently M.G. Hicks and G. Jones have synthesized the other three isomers of 9H-cyclohepta-(b)pyridin-9-one (11a). Oxidation of the cycloheptapyridine (214) with chromium trioxide reagent gave in moderate yield, a mixture of 6,7,8,9-tetrahydro-5H-cyclohept(b)pyridine-5-one (220) and unchanged starting material. The route of Ayerst and Schofield was followed to prepare the 6,7,8,9-tetrahydro-5H-cyclohepta(c)pyridine (222). Oxidation of the cyclohepta(c)pyridine (222) was carried as for the cyclohepta(b)pyridine (214) using the method of Sugimoto, Kagita and Tanaka. In this case both isomeric ketones (223 and 226) were formed but still some unchanged starting material was recovered. Bromination of the ketones (220, 223 and 226) was best effected by treatment with N-bromosuccinimide using azobisisobutyronitrile as a radical generator to give the corresponding dibromo-ketones (221, 224 and 227).

Dehydrobromination was carried out in the usual manner with lithium carbonate in boiling dimethylformamide to give 5H-cyclohepta(b)pyridin-5-one (12a), 5H-cyclohepta(c)pyridin-5-one (225) and 9H-cyclohepta(c)pyridin-9-one (228) respectively (Scheme 59).
Scheme 59

(214) \[ \xrightarrow{\text{Cr O}_3} \] (220) \( R=H \)  
(221) \( R=Br \)

(12a)

(222) \[ \xrightarrow{\text{Cr O}_3} \] (223) \( R=H \)  
(224) \( R=Br \)

(225)

(226) \( R=H \)  
(227) \( R=Br \)

(228)
7H-Cyclohepta(b)pyridin-7-one

The synthesis of 7H-cyclohepta(b)pyridin-7-one (13a) was reported by Duflos et al \textsuperscript{77} in 1973.

2,3-Diformylpyridine (229) condensed with diethyl 1,3-acetonedicarboxylate to give diethyl 6,9-7H-cyclohepta(b)pyridin-7-one dicarboxylate (230). This was subsequently hydrolysed and decarboxylated to give the 7H-cyclohepta(b)pyridin-7-one (139) (Scheme 60).

Scheme 60

\[
\begin{align*}
\text{CHO} & \quad \text{OC(CH}_2\text{CO}_2\text{Et})_2 \\
\text{CHO} & \quad \text{Benzene, OH}^- \\
(229) & \quad \rightarrow \\
\text{CO}_2\text{Et} & \quad \text{CO}_2\text{Et} \\
\text{CO}_2\text{Et} & \quad \text{H}_3\text{O}^+ \\
(230) & \quad \rightarrow \\
\text{CO}_2\text{H} & \quad \text{CO}_2\text{H} \\
(13a) & \quad (\text{i) Ag}^+ \\
& \quad (\text{ii) H}_2/220 \text{ } ^{0}\text{C}
\end{align*}
\]
Chapter 2

Results and discussion
Synthesis of 2-methoxy-5H-benzocyclohepten-5-one (38)

Prior to this work 2-methoxy-5H-benzocyclohepten-5-one (38) had been prepared in two different routes with poor overall yields. In 1972 Srivastava and Dev 8 reported synthesis of methoxybenzocycloheptenones starting from the 2-methoxy-6,7,8,9-tetrahydro-5H-benzocyclohepten-5-one (11). Reduction of the tetrahydro-compound (11) by lithium aluminium hydride gave the alcohol (231) which was then dehydrated to give dihydro-compound (232). Bromination with N-bromosuccinimide (NBS) in carbon tetrachloride with subsequent elimination of hydrogen bromide yielded 3-methoxy-5H-benzocycloheptene (233) along with two other products. Oxidation of 3-methoxy-5H-benzocycloheptene (233) with selenium dioxide gave, 1.6% of 2-methoxy-5H-benzocyclohepten-5-one (38); 10% of 3-methoxy-5H-benzocyclohepten-5-one (234); 20% of 2-methoxy-7H-benzocyclohepten-7-one (235) and 0.2% of 6-methoxy-1-naphthaldehyde (Scheme 61).

It must be noted that the spectroscopic evidence quoted by Srivastava and Dev 8 did not clearly prove the structure; in particular the $^1H$ n.m.r. spectral details could not be used to distinguish between the 2-methoxy- and the 3-methoxy-benzotropenes.
Scheme 61

(11) $\xrightarrow{\text{LiAlH}_4}$ MeO $\xrightarrow{\text{MeO}}$ (231) $\xrightarrow{\text{p-TsOH, Benzene}}$

(232) $\xrightarrow{\text{NBS/CCl}_4}$ MeO $\xrightarrow{\text{MeO}}$ (233) $\xrightarrow{\text{Se}_2\text{O}_3}$

(38) + (234) + (235)
As stated above Crabbe et al. synthesized 2-methoxy-5H-benzocyclohepten-5-one (38) from 6-methoxy-1-tetralone (30). Treatment of the enol acetate (32) with sodium chlorodifluoroacetate yielded the 1-acetoxy-6-methoxy-1,2-difluoromethylene-1,2,3,4-tetrahydro-naphthalene (34), on boiling under reflux with methanolic sodium hydroxide elimination of two moles of hydrogen fluoride yields 2-methoxy-5H-benzocyclohepten-5-one (38) (Scheme 62).

Scheme 62
The starting materials employed during our synthesis of 2-methoxy-5H-benzocyclohepten-5-one (38) was diethyl ethyldienemalonate (236). Fones found that diethyl ethyldienemalonate (236) can be obtained directly from the condensation of one mole of acetaldehyde with one mole of diethyl malonate in the presence of acetic anhydride. Following his procedure, diethyl ethyldienemalonate (236) was prepared in 75% yield and was subsequently characterized by its physical and $^1$H n.m.r. spectral data (Scheme 63).

Scheme 63

\[
\begin{align*}
\text{CH}_3\text{CO}_2\text{H} + \text{H}_2\text{C(CO}_2\text{Et})_2 + (\text{CH}_3\text{CO})_2\text{O} & \rightarrow \\
\text{H}_2\text{C(CO}_2\text{Et})_2 & \rightarrow 2 \text{CH}_3\text{CO}_2\text{H}
\end{align*}
\]

(236)

By a modification of the reported method for the condensation of aromatic aldehyde with diethyl ethyldienemalonate (236), 3-methoxycinnamylidenemalonamic acid (237) was prepared. A solution of freshly prepared benzyltrimethylammonium hydroxide was stirred for 48 hours at room temperature with m-methoxybenzaldehyde and diethyl ethyldienemalonate (236). The reaction mixture was diluted with water, refluxed for two hours, cooled, acidified, and then the yellow product was crystallized to give the pure 3-methoxycinnamylidenemalonamic acid (237) (Scheme 64).
The infra-red spectrum showed two characteristic bands at 1700 Cm\(^{-1}\) due to the C=O bond and another band at 1600 Cm\(^{-1}\) which can be attributed to the C=C bond.

The \(^1\)H n.m.r. spectrum exhibited a sharp singlet at \(\delta 3.9\) p.p.m. which could be assigned to the three protons of methoxy group and a multiplet at \(\delta 8.45-6.8\) p.p.m. due to the seven aromatic protons and diene protons.

Scheme 64

![Chemical structure](image)

The route of Horton and Pitchforth \(^79\) was followed, with the exception of the hydrogenation which was carried out using palladium-charcoal catalyst instead of the prescribed Raney nickel, to give 3-(m-methoxyphenyl)propylmalonic acid (238) (Scheme 65).

The infra-red absorption frequency of the carbonyl groups was at 1710 Cm\(^{-1}\) and another band at 1610 Cm\(^{-1}\) can be attributed to a C=C bond stretching mode within the ring system.

The \(^1\)H n.m.r. spectrum showed resonances for ten protons in the alkane region and a multiplet at \(\delta 7.35-6.60\) p.p.m. which can be attributed to the four aromatic protons.
The malonic acid(238) was placed in a claisen distillation flask and decarboxylated by distillation in vacuo to give 5-(m-methoxyphenyl)valeric acid(239); the latter was obtained in good yield and was subsequently characterized by its $^1$H n.m.r. spectral data (Scheme 66).

The $^1$H n.m.r. spectrum showed eleven protons in the alkane region. A multiplet which occurred at $\delta$ 2.80-2.20 p.p.m. is due to four protons of two methylenes at positions 2- and 5- of the valeric acid(239) and another multiplet at $\delta$ 1.8-1.6 p.p.m. due to two methylene groups at positions 3- and 4- of the valeric acid(239).
There have been two reported syntheses of 2-methoxy-6,7,8,9-tetrahydro-5H-benzocyclohepten-5-one (11).

The first route due to Khan and Proctor⁶, involved the conversion of the valeric acid (239) to acid chloride by using phosphorus pentachloride, followed by cyclization of the acid chloride with anhydrous stannic chloride in dry benzene.

The second route, which we used, was by Horton and Pitchforth⁷⁹, and is much more applicable to large scale preparative work. The valeric acid (239) was added to the mixture of phosphorus pentoxide and 85% orthophosphoric acid (polyphosphoric acid) and heated at 100 °C with vigorous stirring for six hours. The reaction mixture was poured into ice-water and then extracted with ether. Evaporation of ether and distillation of crude product yielded pure 2-methoxy-6,7,8,9-tetrahydro-5H-benzocyclohepten-5-one (11) in good yield (Scheme 67).

The infra-red spectrum showed three characteristic peaks, one at 1680 Cm⁻¹ attributed to the C=O bond stretching mode within the ring system, one at 1580 Cm⁻¹ which can be assigned to the C=C bond stretching mode in the benzene ring, and one at 1247 Cm⁻¹ due to OCH₃ bond stretching.

The ¹H n.m.r. spectrum showed resonance for eight protons in the alkane region and three protons in the aromatic region and a singlet at δ 3.75 p.p.m. due to the three protons of methoxy group at position 2. A doublet at δ 7.72-7.54 p.p.m. due to H₄, exhibits a downfield shift, this deshielding arising probably from the anisotropy of the carbonyl group.
at position 5. A multiplet at δ 6.78-6.54 p.p.m. could be assigned to the two protons at positions 1 and 3. This observation confirms that the ketone is 2-methoxy-6,7,8,9-tetrahydro-5H-benzocyclohepten-5-one (11) and not 4-methoxy-6,7,8,9-tetrahydro-5H-benzocyclohepten-5-one.

Scheme 67

Bromination and dehydrobromination of 2-methoxy-6,7,8,9-tetrahydro-5H-benzocyclohepten-5-one (11)

During attempts to synthesis 11-methylazepino(1,2-a)-indol-10-one (242) and 1,2,3-tribromopyrrolo(1,2-a)azepin-9-one (245), Collington and G. Jones 7, 81 discovered that cyclic ketones of the general type (240 and 243) can be brominated in high yield to give 9,9-dibromo-7,8,9,10-tetrahydro-11-methyl-6H-azepino(1,2-a)indol-10-one (241) and 1,2,3,8,8-pentabromo-6,7,8,9-tetrahydro-5H-pyrrolo(1,2-a)azepin-9-one (244). They subsequently described how the azepinoindolone (242) and the pyrroloazepinone (245) can be prepared in high yield by the one step double dehydrobromination of the corresponding α,α-dibromoketones (241 and 242) using lithium chloride in boiling dimethylformamide (Scheme 68).
It will be shown that these sequences of double bromination and double dehydrobromination reactions; can be applied to the synthesis of benztropones and its derivatives.

Scheme 68

Marquet and et al \(^8\) have successfully used phenyltrimethylammonium tribromide (PTAB) for the selective \(\alpha\)-bromination of a ketone in the presence of a double bond and it was hoped that the use of the reagent on the bicyclic ketone(11) would avoid the possibility of bromination on the benzene ring.
A solution of 2-methoxy-6,7,8,9-tetrahydro-5H-benzocyclohepten-5-one (11) in tetrahydrofuran was treated with two molar equivalents of PTAB at room temperature. The solution became warm and insoluble phenyltrimethylammonium bromide slowly precipitated. After stirring for 24 hours the solution was filtered and evaporated giving 6,6-dibromo-2-methoxy-tetrahydro-5H-benzocyclohepten-5-one (246) (Scheme 69).

The absence of any peaks in the $\delta$ 5-6 p.p.m. of the $^1$H n.m.r. spectrum and the presence of two multiplets due to 6 protons in the alkyl region show that both bromine atoms are on the same carbon atom. The most downfield signal was a single proton doublet at $\delta$ 7.42-7.30 p.p.m., $J_{3,4} = 9$ Hz, allocated to the H4. The extra downfield shift in the H4 resonance is probably due to the proximity of the carbonyl group at position 5.

The mass spectrum peak at m/e 350,348 and 346(M$^+$) in the ratio 1:2:1, relating to the two isotopes of bromine in three possible combination, confirming that the compound (246) contains two bromine atoms.

The infra-red absorption spectrum has peaks at 1680, 1600 and 1100 cm$^{-1}$ which are characteristic of this class of compound.

Scheme 69
A solution of 6,6-dibromo-2-methoxy-6,7,8,9-tetrahydro-5H-benzocyclohepten-5-one (246) with 4 molar equivalents of anhydrous lithium chloride was boiled in dimethylformamide for 4 hours. Removal of the dimethylformamide under reduced pressure gave a crude residue which was then distilled from a bulb tube to give the pure 2-methoxy-5H-benzocyclohepten-5-one (38) (Scheme 70).

The carbonyl absorption in the infra-red was at 1640 Cm⁻¹.

The H n.m.r. spectrum showed a doublet (J₃,₄= 9Hz) at the lowest field δ 8.5-8.4 p.p.m. which is considered to be H4 with an ortho splitting by H3. The multiplet between δ 6.7 and 6.5 p.p.m. is assigned to H8 and another multiplet between δ 7.4 and 6.9 p.p.m. which integrates for 5 protons must then be due to the protons around the seven ring membered ring and to H1 and H3.

The mass spectrum shows the molecular ion to be at m/e 186 which is correct for 2-methoxybenzotropone (38).

The carbonyl resonance in the ¹³C n.m.r. spectrum occurs at δ 186.9 p.p.m. consistent with a conjugated carbonyl group, all other resonances occurring in the aromatic and alkene regions.

Scheme 70
When a solution of 2-methoxy-6,7,8,9-tetrahydro-5H-benzocyclohepten-5-one (11) in carbon tetrachloride was boiled with 4 molar equivalents of bromine for one hour, removal of the solvent gave a light brown oil which solidified on trituration with light petroleum and identified as a mixture of dibromo (246) and tribromo (246a) derivatives. Subsequent dehydrobromination of the mixture with anhydrous lithium chloride in boiling dimethylformamide for 3 hours followed by removal of the dimethylformamide under reduced pressure gave a brown residue which was found by thin layer chromatography to be a mixture of two compounds. An attempt was made to crystallise the mixture, but this failed and the mixture was eventually separated by p.l.c.

The compound from the lower band was shown from spectral evidence to be 2-methoxy-5H-benzocyclohepten-5-one (38).

The upper band was extracted to give a yellow solid which was identified as 2-methoxy-6-bromo-5H-benzocyclohepten-5-one (247) (Scheme 71).

Scheme 71

![Chemical Structures](image)
A similar occurrence was reported by Collington and G. Jones, dehydrobromination of 6,6-dibromo-6,7,8,9-tetrahydrobenzocyclohepten-5-one (17) with sodium chloride in boiling dimethylformamide gave a mixture of products the main one being 5H-benzocyclohepten-5-one (1) and 6-bromo-5H-benzocyclohepten-5-one (27). They have postulated that the 6-bromo-5H-benzocyclohepten-5-one (27) was produced by bromination of the 5H-benzocyclohepten-5-one (1) by bromine formed during the reaction. Treatment of the benzotropone (1) with either hydrogen bromide or bromoacetone in dimethylformamide had no effect but when bromine in dimethylformamide was used the 6-bromo-5H-benzocyclohepten-5-one (27) was formed (Scheme 72).

Scheme 72
The mass spectrum of 2-methoxy-6-bromo-5H-benzocyclohepten-5-one (247) shows two peaks at m/e 266 and 264 (M+) in a ratio of 1:1 confirming that the compound possesses one bromine atom.

The infra-red absorption spectrum has peaks at 1640, 1610, 1584 cm\(^{-1}\) which are characteristic of this class of compound.

The \(^1\)H n.m.r. spectrum showed a doublet at lowest field \(\delta 8.56-8.47\) p.p.m. considered to be H4 with ortho splitting by H3. The quartet at \(\delta 7.95-7.85\) p.p.m. was assigned to H7 adjacent to the bromine atom and has coupling constants of \(J_{8,7} = 9\) Hz and \(J_{7,9} = 0.7\) Hz. The multiplet between \(\delta 6.6\) and \(6.4\) p.p.m. (\(J_{8,9} = 11.7\) Hz) was assigned to H8 by direct comparison with the position of H8 in 2-methoxy-5H-benzocyclohepten-5-one (38). If the bromine substituent was in position 9, it would be most likely for proton 8 to be deshielded sufficiently to appear further downfield.

The \(^13\)C n.m.r. spectrum is similar to that of the 2-methoxy-5H-benzocyclohepten-5-one (38), with the exception that one of the alkene peaks, that at \(\delta 111.9\) p.p.m. is now a singlet in the off resonance spectrum.

* doublet of doublets
Synthesis of 3-methoxy-5H-benzocyclohepten-5-one(234)

The starting materials employed during the synthesis of 3-methoxy-5H-benzocyclohepten-5-one(234) were benzene and glutaric anhydride(248). Somerville and Allen reported benzene can be acylated directly by the condensation of glutaric anhydride (248) in the presence of aluminium chloride. Following their procedure, 4-benzoyl-n-butyric acid (249) was prepared in 45% yield and was subsequently characterized by its physical and $^1$H n.m.r. spectral data (Scheme 73).

Scheme 73

The 4-benzoyl-n-butyric acid (249) was reduced to the 5-phenylvaleric acid (250) by the Huang-Minlon modification of the Wolff-Kishner reaction, in which the keto-acid (250), hydrazine hydrate, and potassium hydroxide, were heated under reflux in 2,2'-dihydroxydiethyl ether (Scheme 74).

The 5-phenylvaleric acid (250) was then cyclized by an internal Friedel-Crafts acylation, by heating it with polyphosphoric acid(PPA) to give 6,7,8,9-tetrahydro-5H-benzocyclohepten-5-one(6) (Scheme 74).
The $^1$H n.m.r. spectrum shows resonances for eight protons in the alkane region and four protons in the aromatic region. A multiplet at $\delta$ 7.80-7.50 p.p.m. due to H4 exhibited a downfield shift, this deshielding arising probably due to the anisotropy of the carbonyl group at position five.

Scheme 74

Smith and Berry $^{89}$ have prepared 3-nitro-6,7,8,9-tetrahydro-5H-benzocyclohepten-5-one (15) from the 6,7,8,9-tetrahydro-5H-benzocyclohepten-5-one (6) by nitration with fuming nitric acid at low temperature (Scheme 75). This synthesis was repeated and the product (15) was identified by its $^1$H n.m.r. spectral data. The aromatic protons were split distinctly into the three separate protons. The signal due to H4 was shifted furthest downfield to $\delta$ 8.1 p.p.m. and was recognised
its weak meta-coupling ($J_{2,4} = 2$ Hz) to H2. H2 showed a doublet of doublets resulting from coupling with H1 and H4 ($J_{4,2} = 2$ Hz and $J_{1,2} = 8$ Hz), while H1 is coupled only to H2 ($J_{2,1} = 8$ Hz).

Scheme 75

If the temperature was allowed to rise during the nitration the product was 2-(3-carboxypropyl)-5-nitrobenzoic acid (15a) (Scheme 76), which was identified by its $^1$H n.m.r. spectrum data. The most downfield signal was a proton doublet at $\delta 8.4$ p.p.m. allocated to H6. The extra downfield shift in the H6 resonance is probably due to the proximity of carbonyl and nitro groups at positions one and five respectively.

Scheme 76
In 1975 Johnston, Povall and Entwistle\textsuperscript{90} developed a method for conversion of nitro aromatic compounds to their amino aromatic compounds. Treatment of 4-methoxy-2,5-dinitroanisole (251) with boiling cyclohexene and palladium-charcoal yielded 3,6-dimethoxy-5-nitroaniline (252). The reduction was effected rapidly, selectively and in high yield by transfer of hydrogen from cyclohexene to the aromatic nitro compound via the palladium-charcoal catalyst (Scheme 77).

Scheme 77

![Scheme 77](image)

By treatment of 3-nitro-6,7,8,9-tetrahydro-5H-benzo-cyclohepten-5-one (15) with cyclohexene and palladium-charcoal, 3-amino-6,7,8,9-tetrahydro-5H-benzocyclohepten-5-one (253) was prepared (Scheme 78).

Scheme 78

![Scheme 78](image)
The 3-amino-6,7,8,9-tetrahydro-5H-benzocyclohepten-5-one (253) was then used to prepare 3-hydroxy-6,7,8,9-tetrahydro-5H-benzocyclohepten-5-one (254). The diazonium salt was made in situ and this was heated to produce the phenol (254) (Scheme 79).

The methylation of 3-hydroxy-6,7,8,9-tetrahydro-5H-benzocyclohepten-5-one (254) was carried out in chloroform using dimethyl sulphate and sodium hydroxide to give 3-methoxy-6,7,8,9-tetrahydro-5H-benzocyclohepten-5-one (255) (Scheme 79).

Scheme 79

Bromination of 3-methoxy-6,7,8,9-tetrahydro-5H-benzocyclohepten-5-one (255) was best effected by treatment with phenyltrimethylammonium tribromide using tetrahydrofuran as a solvent. After addition of a few drops of acetone, the filtered solution was evaporated. An $^1$H n.m.r. spectrum of the crude product showed some 3-methoxy-6-bromo-6,7,8,9-tetrahydro-5H-benzocyclohepten-5-one (256a) to be present. Separation of the mixture
on a chromatotron (petroleum eluent) gave the two pure monobromo and dibromo derivatives (256a and 256)(Scheme 80).

The mass spectrum of the dibromoketone (256) contained peaks at 350, 348 and 346(M⁺) in the ratio of 1:2:1 confirming that the compound contained two bromine atoms.

Subsequent dehydrobromination of the dibromoketone (256) with anhydrous lithium chloride in boiling dimethylformamide for two hours, followed by removal of dimethylformamide under reduced pressure gave an oil which was purified on a chromatotron (eluent ethyl acetate/petroleum, 1:9) to give the 3-methoxybenztropone (234)(Scheme 80).

The mass spectrum shows the molecular ion to be at m/e 186 which is correct for 3-methoxybenztropone (234).

The infra-red absorption spectrum has peaks at 1600, 1645 and 1660 cm⁻¹.

The ¹H n.m.r. spectrum showed a doublet (J₂,₄=3 Hz) at the lowest field δ8.0 ppm due to H4 with meta splitting by H2. H2 showed a doublet of doublets resulting from coupling with H1 and H4 (J₁,₂=8.6 Hz, J₄,₂=3 Hz), while H1 is coupled only to H2 (J₁,₂=8.6 Hz). Another doublet at δ7.35-7.25 ppm is due to H9. It was distinguished from H1 and H2 by its major coupling constant (J₈,₉=11.3 Hz). A multiplet at δ7.1-7.0 ppm integrated for two protons and is due to H6 and H7. And finally H8 occurs as a doublet of doublets of doublets at δ6.7-6.5 ppm resulting from coupling with H7, H9 and H6 (J₈,₇=7 Hz, J₈,₆=2.2 Hz and J₈,₉=11.3 Hz).
Attempts to synthesize 1-methoxy-5H-benzocyclohepten-5-one

In order to prepare 5-(2-methoxyphenyl)valeric acid (259), the stage before cyclisation to cyclic ketone, the 2-methoxybenzaldehyde and diethyl ethylidenemalonate (236) were employed as starting materials.

By the modification of the reported method used by Horton and Walker \(^{91,92}\) 2-methoxycinnamylidenemalononic acid (257) was prepared. Condensation of 2-methoxybenzaldehyde with diethyl ethylidenemalonate (236) and benzyltrimethylammonium hydroxide gave 2-methoxycinnamylidenemalononic acid (257) (Scheme 81).

The infra-red spectrum showed two characteristic bands at 1725 and 1600 cm\(^{-1}\).

The exchangeable peak at \(\delta\) 9.28-8.90 p.p.m. in the \(^1\)H n.m.r. spectrum is consistent with compound being an acid.

The hydrogenation of 2-methoxycinnamylidenemalononic acid (257) was carried out using palladium charcoal catalyst to give 3-(2-methoxyphenyl)propylmalonic acid (258) (Scheme 81).

The \(^1\)H n.m.r. spectrum showed resonances for ten protons...
protons in the alkane region. A multiplet at δ 7.1-6.6 p.p.m. integrated for four protons and is due to the aromatic protons.

The 3-(2-methoxyphenyl)propylmalonic acid (258) was then decarboxylated in a claisen distillation flask by distillation under vacuo to give the 5-(2-methoxyphenyl)valeric acid \(^9\) (259) in good yield (Scheme 81).

The \(^1\)H n.m.r. spectrum showed eleven protons in the alkane region. A multiplet occurred at δ 2.7-2.2 p.p.m. is due to the four protons of two methylene groups at positions two and five of the valeric acid (238) and another multiplet at δ 7.3-6.2 p.p.m. was due to four aromatic protons.

Scheme 81

Since 1-methoxy-6,7,8,9-tetrahydro-5H-benzocyclohepten-5-one was desired as an important intermediate which can be easily brominated and then dehydrobrominated to give the corresponding 1-methoxy-5H-benzocyclohepten-5-one, the cyclisation of 5-(2-methoxyphenyl)valeric acid (259) was investigated. Attempted cyclisation of 5-(2-methoxyphenyl)valeric
acid (259) by a mixture of phosphorus pentoxide and 85% orthophosphoric acid gave a crude product. It was found that this crude product could not be purified by recrystallization but purification was eventually carried out by a careful chromatographic separation to give the pure product (260) (Scheme 82) which was identified as a dimer (260) by its $^1$H n.m.r. spectral data.

The $^1$H n.m.r. spectrum exhibited a doublet of doublets at $\delta$ 8.0-7.9 p.p.m. which could be assigned to the two protons a (see formula). These two protons are the only ones showing coupling to other ortho (b; $J_{a,b} = 8.5$ Hz) and meta (c; $J_{a,c} = 2.2$ Hz) protons. The extra downfield shift is due to the proximity of the carbonyl group. The meta-coupling occurred between the protons at positions c $\delta$ 7.7 p.p.m., and the protons at positions a. The ortho-coupling occurred between the protons at positions b $\delta$ 7.0-6.9 p.p.m. and protons at positions a. The methoxy protons showed as a singlet at $\delta$ 3.95 p.p.m. Two multiplets between $\delta$ 2.9-2.5 and 1.8-1.7 p.p.m. each integrating for eight protons were due to two (CH$_2$CO) and two (CH$_2$Ar) groups and to the other two (CH$_2$CH$_2$) groups.

This observation confirms that the ketone is a dimer (260) and not 1-methoxy-6,7,8,9-tetrahydro-5H-benzocyclohepten-5-one. This reaction has been reported by Gardner, Horton, Thompson and Twelves $^{92,93}$ to give a high-melting neutral product, insoluble in common solvents. Bien later reported $^{94}$ the formation of dimer (260), but no spectral data were given to support the alleged structure.
Scheme 82

\[
\begin{align*}
\text{CH}_3\text{O} & \quad (\text{CH}_2)_4\text{CO}_2\text{H} \\
& \quad \xrightarrow{\text{PPA}} \\
\end{align*}
\]

(259) \quad \rightarrow \quad (260)
Synthesis of 1-methoxy-4-methyl-5H-benzocyclohepten-5-one (268)

Since cyclisation of 5-(2-methoxyphenyl)valeric acid (259) with polyphosphoric acid gave the dimer (260) it was decided to block the para position of the phenyl group in 5-(2-methoxyphenyl)valeric acid (259). In order to prepare 5-(2-methoxy-5-methylphenyl)valeric acid (265) necessary for cyclisation to the cyclic ketone (266) p-hydroxytoluene was employed as a starting material. A mixture of p-hydroxytoluene and dimethyl sulphate in acetone was heated under reflux to give p-methoxyanisole 95 (261) (Scheme 83).

The $^1$H n.m.r. spectrum exhibited a singlet at $\delta$ 3.66 p.p.m. which could be assigned to the methoxyl group.

Formylation of p-methyl anisole (261) was carried out with zinc cyanide and dry hydrogen chloride to give 5-methyl-2-methoxybenzaldehyde 96 (262).

The $^1$H n.m.r. spectrum showed a singlet at $\delta$ 10.4 p.p.m. due to the proton of the formyl group and a doublet at $\delta$ 7.55 p.p.m. attributed to H6 ($J_{4,6}$ = 3 Hz). Meta- and ortho-coupling occurred between H4 $\delta$ 7.4-7.2 and H3 $\delta$ 6.8-6.7 p.p.m. ($J_{4,6}$ = 3 Hz and $J_{4,3}$ = 10 Hz, doublet of doublets).

Scheme 83

\[
\begin{align*}
\text{OH} & \quad \xrightarrow{(\text{CH}_3)_2\text{SO}_4, \text{acetone}} \quad \text{OCH}_3 \\
\text{CH}_3 & \quad \xrightarrow{(i) \text{Zn(CN)}_2, \text{HCl}} \quad \text{CHO} \\
\text{OCH}_3 & \quad \xrightarrow{(ii) \text{H}_2\text{O}} \quad \text{OH}
\end{align*}
\]
Condensation of 5-methyl-2-methoxy-benzaldehyde (262) with diethyl ethylidenemalonate (236) and benzyltrimethylammonium hydroxide gave 5-methyl-2-methoxycinnamylidenemalonic acid (263) (Scheme 84).

The infra-red spectrum showed two characteristic bands at 1710 and 1612 cm⁻¹.

The exchangeable peak centred at δ 9.3 p.p.m. in the ¹H n.m.r. spectrum is consistent with the compound being an acid. A multiplet at δ 8.1-6.7 p.p.m. integrating for six protons must be due to aromatic and diene protons.

Hydrogenation of 5-methyl-2-methoxycinnamylidenemalonic acid (263) was carried out using palladium-charcoal catalyst to give 3-(2-methoxy-5-methylphenyl)propylmalonic acid (264) (Scheme 84).

The ¹H n.m.r. spectrum showed resonances for thirteen protons in the alkane region. A multiplet at δ 7.2-6.4 p.p.m. integrating for three protons and must be due to the aromatic protons.

Decarboxylation of 3-(2-methoxy-5-methylphenyl)propylmalonic acid (264) in a Claisen distillation flask in vacuo gave 5-(2-methoxy-5-methylphenyl)valeric acid (265) (Scheme 84).

¹H n.m.r. spectrum showed fourteen protons in the alkane region. A multiplet occurred at δ 7.1-6.5 p.p.m. due to the three protons of aromatic group.

Cyclisation of 5-(2-methoxy-5-methylphenyl)valeric acid (265) was successful using a mixture of phosphorus pentoxide and 85% orthophosphoric acid giving 1-methoxy-4-methyl-6,7,8,9-tetrahydro-5H-benzocyclohepten-5-one (266) (Scheme 84).
The infra-red spectrum showed three characteristic peaks; at 1688 cm\(^{-1}\) attributed to C=O bond stretching mode within the ring system, at 1594 cm\(^{-1}\) which can be assigned to the C=C bond stretching mode in the benzene ring, and at 1190 cm\(^{-1}\) due to OCH\(_3\) bond stretch.

The \(^1\)H n.m.r. spectrum exhibited two doublets at 6.7-6.8 and 6.7-6.6 p.p.m. which could be assigned to H3 and H2 respectively (\(J_{2,3}=8.4\) Hz). Two singlets at 6.3.7 and 2.2 p.p.m. are due to methoxyl and methyl protons. Two multiples at 6 3.9-2.4 and 1.9-1.5 p.p.m. can be assigned to the four protons at positions six and nine and to four protons at positions seven and eight respectively.

**Scheme 84**

![Scheme 84](image)
The 1-methoxy-4-methyl-6,7,8,9-tetrahydro-5H-benzo-
cyclohepten-5-one (266) in tetrahydrofuran was treated with
phenyltrimethylammonium tribromide at room temperature.
Progress of this reaction was followed by using t.l.c. The
desired product (267) has the largest Rf value followed by mono-
brominated ketone, which in turn is followed by the starting
material. The resulting product (267) was difficult to
crystallise and purification required column chromatography,
giving the pure 6,6-dibromo-1-methoxy-4-methyl-6,7,8,9-tetrahydro-
5H-benzo-cyclohepten-5-one (267) (Scheme 85).

The mass spectrum peaks at m/e 364, 362 and 360 (M+) in a
ratio of 1:2:1, relating to the two isotopes in their three
possible combinations, confirming that the compound (267) contains
two bromine atoms.

The infra-red absorption spectrum has peaks at 1716, 1605 and 1275 Cm⁻¹ which are characteristic of this class
of compound.

The absence of any peaks in the 65-6 p.p.m. of the ¹H n.m.r.
spectrum and the presence of two multiplets due to six protons
in the alkane region showed that both bromine atoms are on
the same carbon atom.

Scheme 85

(266)  \[ \xrightarrow{\text{PTAB/THF}} \]  (267)
The 6,6-dibromo-1-methoxy-4-methyl-6,7,8,9-tetrahydro-
-5H-benzocyclohepten-5-one (267) was then treated with lithium
chloride in boiling dimethylformamide to give the
1-methoxy-4-methyl-5H-benzocyclohepten-5-one (268) which was
eventually purified by p.l.c. (Scheme 86).

The mass spectrum shows the molecular ion to be at m/e 200
which is correct for compound (267).

The frequency of the carbonyl absorption in the infra-red
was at 1650 Cm⁻¹.

The ¹H n.m.r. spectrum showed a quartet at the lowest field
δ 7.9-7.8 p.p.m. considered to be due to H9. It was
distinguished from protons H3 and H2 by its major coupling
constant (Jg,9 = 11.8 Hz). It is further downfield probably due
to being adjacent to aromatic ring and also being deshielded
by carbonyl group at position five. Two doublets at
δ 7.3-7.2 p.p.m. and 6.9-6.8 p.p.m. could be assigned to
H3 and H2 respectively. A complex multiplet between δ 6.8 and 6.5 p.p.m.
which integrates for three protons must be due to the protons
around the seven membered ring. Two singlets at δ 3.8 and 2.4
p.p.m. are due to methoxyl and methyl protons respectively.

The carbonyl resonance in the ¹³C n.m.r. spectrum occurs
at δ 192.8 p.p.m. consistent with a conjugated carbonyl,
all other resonances occurring in the aromatic and
alkene regions along with two peaks at δ 56.0 and 22.9
p.p.m. due to the methoxy and methyl carbons respectively.
Syntheses of 5H-benzocyclohepten-5-one (1) and of 6,8-dinitro-5H-benzocyclohepten-5-one (269)

The 6,6-dibromo-6,7,8,9-tetrahydro-5H-benzocyclohepten-5-one 83 (17) was prepared in almost quantitative yield by brominating a carbon tetrachloride solution of the 6,7,8,9-tetrahydro-5H-benzocyclohepten-5-one (6).

The position of bromine atoms was confirmed by the ¹H n.m.r. spectrum which showed the seven and nine methylene groups as broadened triplets between δ 3.00 and 2.60 p.p.m.

Heating the dibromoketone (17) with an excess of lithium chloride in boiling dimethylformamide gave 5H-benzocyclohepten-5-one 83 (1) in good yield (Scheme 87).

The infra-red absorption spectrum has peaks at 1640, 1609 and 1589 Cm⁻¹ which are characteristic of this class of compound.

The ¹H n.m.r. spectrum of 5H-benzocyclohepten-5-one (1) has been analysed by Bertelli, Gering and Herbelin.

The multiplet at δ 8.5-8.3 p.p.m. is assumed to be H4 shifted downfield due to the anisotropic deshielding effect.
of the carbonyl group in position five. The other three aromatic protons occur as a multiplet at $\delta$ 7.7-7.5 p.p.m.
A quartet at $\delta$ 7.3-7.1 p.p.m. is attributed to H9 which has a major coupling constant of $J_{8,9}=11.3$ Hz and a minor coupling constant of $J_{7,9}=1.2$ Hz. H6 and H7 give a complex pattern between $\delta$ 7.0 and 6.8 p.p.m. from which $J_{7,8}=8.3$ Hz, $J_{6,8}=1.2$ Hz and $J_{6,7}=11.5$ Hz. Another multiplet at highest field $\delta$ 6.7-6.5 p.p.m. must then be due to H8.

The carbonyl resonance in the $^{13}$C n.m.r. spectrum occurs at 187.4 p.p.m. consistent with a conjugated carbonyl, all other resonances occurring in the aromatic and alkene regions.

Buchanan and Lockhart have prepared 6,8-dinitro-5H-benzocyclohepten-5-one (269) from 5H-benzocyclohepten-5-one (1) by nitration with concentrated nitric acid and sulphuric acid at room temperature. This reaction was repeated and the product purified by column chromatography (Scheme 87).

The infra-red absorption spectrum showed strong absorption at 1525 and 1332 Cm$^{-1}$ due to asymmetrical and symmetrical stretching of the nitro group.

The $^1$H n.m.r. spectrum showed two doublets ($J_{7,9}=1.2$ Hz) centred at $\delta$ 8.9 p.p.m. and 8.6 p.p.m. considered to be due to H7 and H9. These protons were shifted downfield from the remainder of the aromatic protons due to the inductive effect of the nitro groups at positions six and eight.
Scheme 87

(6) \[\xrightarrow{2Br_2/CCl_4} \] (17) \[\xrightarrow{LiCl/DMF} \]

(1) \[\xrightarrow{HNO_3} \] (269) \[\xrightarrow{H_2SO_4} \]
Syntheses of 3-nitro-5H-benzocyclohepten-5-one (20) and 3-amino-5H-benzocyclohepten-5-one (270)

Treatment of 3-nitro-6,7,8,9-tetrahydro-5H-benzocyclohepten-5-one (15) with bromine gave 3-nitro-6,6-dibromo-6,7,8,9-tetrahydro-5H-benzocyclohepten-5-one \(^{83}(18)\) as a colourless solid (Scheme 88).

The infra-red absorption spectrum showed a carbonyl stretching frequency at 1710 Cm\(^{-1}\), and strong absorptions at 1610 and 1342 Cm\(^{-1}\) due to the asymmetrical and symmetrical stretching of the nitro group.

The \(^1\)H n.m.r. spectrum again showed a broadened multiplet between 63.2 and 2.7 p.p.m. attributed to the methylene groups at positions 7 and 9.

The nitrodibromoketone (18) was dehydrobrominated by lithium chloride in refluxing dimethylformamide to give 3-nitro-5H-benzocyclohepten-5-one \(^{83}(20)\) in good yield (Scheme 88).

The infra-red absorption spectrum has peaks at 1641, 1602 and 1584 Cm\(^{-1}\) which are characteristic of benzotropones.

The doublet (J\(_{1,2}\) = 2.4 Hz) at 6 9.3-9.2 p.p.m. is considered to be H4 with meta splitting by H2. The quartet at 6 8.5-8.3 p.p.m. is due to H2 and has a major coupling constant of J\(_{1,2}\) = 8.7 Hz. H1 occurs as a doublet at 6 7.8-7.7 p.p.m. The multiplet between 6 7.5 and 6.9 p.p.m. which integrates for four protons must then be due to the protons around the seven membered ring.

The carbonyl resonance in the \(^{13}\)C n.m.r. spectrum occurs at 186.1 p.p.m. consistent with a conjugated carbonyl,
all other resonances occurring in the aromatic and alkene regions.

The conversion of 3-nitro-5H-benzocyclohepten-5-one (20) to the 3-amino-5H-benzocyclohepten-5-one (270) was then successfully carried out by the treatment with boiling cyclohexene and a palladium-charcoal catalyst (Scheme 88).

The infra-red absorption spectrum has peaks at 3430, 3350 and 1380 cm\(^{-1}\) due to NH\(_2\) stretch and deformation, and a carbonyl peak at 1660 cm\(^{-1}\).

The \(^1\)H n.m.r. spectrum showed a doublet (\(J_{2,4} = 2.3\) Hz) at \(\delta 7.8-7.7\) p.p.m. which is due to H4 with meta splitting by H2. The signal due to H1 occurs as a doublet (\(J_{1,2} = 8.5\) Hz) at \(\delta 7.5-7.4\) p.p.m. and that due to H9 as a quartet at \(\delta 7.3-7.2\) p.p.m. having a major coupling constant of \(J_{9,8} = 11.4\). The multiplet between \(\delta 7.1\) and \(6.9\) p.p.m. which integrates for two protons must then be due to H2 and H7. Another quartet between \(\delta 6.8\) and \(6.7\) p.p.m. was assigned to H6 and a complex octet occurred at \(\delta 6.6-6.4\) p.p.m. due to H8.

The carbonyl resonance in the \(^13\)C n.m.r. spectrum occurs at \(\delta 186.0\) p.p.m. consistent with a conjugated carbonyl, all other resonances occurring in the aromatic and alkene regions.
Scheme 88

(15) \[ \text{O}_2\text{N} \text{C} \] \[ \text{H} \text{C} \] \[ \text{O} \text{N} \] \[ \text{C} \] \[ \text{Br} \] \[ \text{C} \] \[ \text{H} \text{C} \] \[ \text{O}_2\text{N} \] \[ \text{C} \] \[ \text{H} \text{C} \] \[ \text{Br} \] \[ \text{C} \] \[ \text{H} \text{C} \] \[ \text{LiCl/DMF}\]

(18) \[ \text{O}_2\text{N} \text{C} \] \[ \text{H} \text{C} \] \[ \text{O}_2\text{N} \] \[ \text{C} \] \[ \text{H} \text{C} \] \[ \text{C} \] \[ \text{H} \text{C} \] \[ \text{H}_2\text{N} \] \[ \text{C} \] \[ \text{C} \] \[ \text{H} \text{C} \] \[ \text{H}_2\text{N} \] \[ \text{Pd/C}\]

(20) \[ \text{O}_2\text{N} \text{C} \] \[ \text{H} \text{C} \] \[ \text{O}_2\text{N} \] \[ \text{C} \] \[ \text{H} \text{C} \] \[ \text{C} \] \[ \text{H} \text{C} \] \[ \text{H}_2\text{N} \] \[ \text{C} \] \[ \text{C} \] \[ \text{H} \text{C} \] \[ \text{H}_2\text{N} \] \[ \text{C} \] \[ \text{C} \] \[ \text{H} \text{C} \] \[ \text{Pd/C}\]

(270)
Syntheses of 3-acetamido-5H-benzocyclohepten-5-one(21) and 3-amino-2,4-dibromo-5H-benzocyclohepten-5-one(272)

The 3-acetamido-6,7,8,9-tetrahydro-5H-benzocyclohepten-5-one \(^{89}\) (16) was obtained by reaction of 3-amino-6,7,8,9-tetrahydro-5H-benzocyclohepten-5-one(253) with acetyl chloride in pyridine (Scheme 89).

To avoid the possibility of nuclear bromination the acetamidoketone(16) in tetrahydrofuran was treated with phenyltrimethylammonium tribromide at room temperature to give 3-acetamido-6,6-dibromo-6,7,8,9-tetrahydro-5H-benzocyclohepten-5-one(19) (Scheme 89).

The \(^1\)H n.m.r. spectrum again showed broadened triplets between \(\delta 3.00\) and \(\delta 2.50\) p.p.m. attributed to the methylene groups at positions 7 and 9. The NH proton, which was shown to exchange on shaking with \(D_2O\), appeared as a rather broad singlet centred at \(\delta 8.50\) p.p.m.

The dibromoketone(19) was then easily dehydrobrominated with lithium chloride in boiling dimethylformamide to give 3-acetamido-5H-benzocyclohepten-5-one(21). Due to its low solubility in chloroform the \(^1\)H n.m.r. spectrum was carried out in trifluoroacetic acid. However protonation caused many signals to overlap and a definite assignment of the individual aromatic protons was not possible. Proof of the desired structure was obtained from analysis and the infra-red spectrum which shows peaks at 3416 Cm\(^{-1}\) due to NH stretch, and at 1690 and 1640 Cm\(^{-1}\) comparable with those obtained in the other tropones (Scheme 89).
The carbonyl resonance in the $^{13}$C n.m.r. spectrum occurs at $\delta$ 185.9 p.p.m. consistent with a conjugated carbonyl, all other resonances occurring in the aromatic and alkene region apart from two peaks at $\delta$ 168.5 and $\delta$ 24.0 p.p.m. due to the carbonyl and methyl carbons of the acetamido group at position three.

Scheme 89

The 3-acetamidobenzotropone (21) was also synthesized by reaction of 3-amino-5H-benzocyclohepten-5-one (270) with acetyl chloride in pyridine (Scheme 89).
Bromination of 3-amino-6,7,8,9-tetrahydro-5H-benzocyclohepten-5-one (253) with four equivalents of bromine in carbon tetrachloride gave 3-amino-2,4,6,6-tetrabromo-6,7,8,9-tetrahydro-5H-benzocyclohepten-5-one (271).

The \(^1\)H n.m.r. spectrum again showed broadened triplets between \(\delta 2.82\) and \(2.35\) p.p.m. attributed to the methylene groups at positions 7 and 9. The NH\(_2\) protons appeared as a rather broadened singlet centred at \(\delta 4.72\) p.p.m.

The dibromoketone (271) was subsequently dehydrobrominated with lithium chloride in boiling dimethylformamide to give 3-amino-2,4-dibromo-5H-benzocyclohepten-5-one (272), which was purified by column chromatography (Scheme 90).

The mass spectrum peaks at m/e 331, 329 and 327(M\(^+\)) in the ratio of 1:2:1, relating to the two isotopes in their three possible combination, confirmed that the compound (272) contains two bromine atoms.

The \(^1\)H n.m.r. spectrum showed a singlet at lowest field \(\delta 7.56\) p.p.m. due to H1 moved downfield by deshielding by bromine atoms at positions two and four. A doublet of doublets at \(\delta 7.00-6.82\) p.p.m. is due to H9 which has a major coupling constant of \(J_{8,9}=11.2\) Hz. The multiplet between \(\delta 6.76\) and 6.2 p.p.m. which integrates for three protons must then be due to the protons around the seven-membered ring.
Syntheses of 2-acetamido-6,7,8,9-tetrahydro-5H-benzocyclohepten-5-one (276) and of methyl 6,7,8,9-tetrahydro-5H-benzocyclohepten-2-carboxylate (280)

Since 2-acetamido-6,7,8,9-tetrahydro-5H-benzocyclohepten-5-one (276) was desired as an intermediate in route to 2-acetamido-5H-benzocyclohepten-5-one, the intermediate (276) was synthesized by the following route; 3-nitrobenzaldehyde and diethyl ethylidenemalonate (236) were employed as starting materials.

Condensation of 3-nitrobenzaldehyde with diethyl ethylidenemalonate (236) and benzyltrimethylammonium hydroxide yielded the 3-nitrocinnamylidenemalonate acid (273) in good yield (Scheme 91).

The infra-red absorption spectrum showed strong absorption at 1520 and 1332 Cm⁻¹ due to asymmetrical and symmetrical stretching of the nitro group.
The $^1$H n.m.r. spectrum of the pure material was comparable with those of the other cinnamylidenemalonic acids previously described. The acid protons were shown to exchange on shaking with D$_2$O, appeared as a singlet centred at $\delta$ 9.25 p.p.m.

The hydrogenation of 3-nitrocinnamylidenemalonic acid (273) was carried out using a palladium-charcoal catalyst to give 3-[(m-aminophenyl)propyl]malonic acid (274) (Scheme 91).

The malonic acid (274) was then decarboxylated by heating in vacuo in a claisen distillation flask. Heating the resulting crude product of distillation with acetic anhydride on a steam bath for one hour gave 3-[(m-acetamidophenyl)valeric acid (275) (Scheme 91).

Cyclisation of 3-[(m-acetamidophenyl)valeric acid (275) by a mixture of phosphorus pentoxide and 85% phosphoric acid gave 2-acetamido-6,7,8,9-tetrahydro-5H-benzocyclohepten-5-one (276) (Scheme 91).

The $^1$H n.m.r. spectrum shows a resonance for eleven protons in the alkane region and three protons in the aromatic region, and a broad singlet at $\delta$ 9.2 p.p.m. due to the NH proton.

The synthesis was not carried through to the benztropone due to circumstances beyond the author's control.
Scheme 91

\[
\begin{align*}
\text{Scheme 91} & \\
\text{(236)} & \xrightarrow{(\text{CH}_3\text{HC}=\text{C(CO}_2\text{Et)}_2} & \text{(273)} \\
\text{(274)} & \xrightarrow{\text{h}_{2}, 10\% \text{Pd/C}} & \text{(ii) acetic anhydride} \\
\text{(275)} & \xrightarrow{\text{PPA}} & \text{(276)}
\end{align*}
\]
Another incomplete synthesis was that of methyl 5H-benzocyclohepten-5-one-2-carboxylate and methyl 5H-benzocyclohepten-5-one-3-carboxylate. For this methyl 6,7,8,9-tetrahydro-5H-benzocyclohepten-2-carboxylate (280) was desired as an intermediate. This compound (280) could undergo bromination at the positions five or nine by reaction with one molar equivalent of N-bromosuccinimide. Subsequent hydrolysis of the resulting mono-bromo compound to the alcohol and subsequent oxidation would give the required methyl 6,7,8,9-tetrahydro-5H-benzocyclohepten-5-one-2(or -3)-carboxylate.

An alternative synthetic route would be by direct oxidation of compound (280) in which the oxidation would be expected to occur at the positions five or nine to give directly methyl 6,7,8,9-tetrahydro-5H-benzocyclohepten-5-one-2(or -3)-carboxylate.

In these cases the substituent at positions two or three would be an electron-withdrawing group, otherwise difficult to obtain.

The 6,7,8,9-tetrahydro-5H-benzocyclohepten-5-one (6) was reduced to the 6,7,8,9-tetrahydro-5H-benzocycloheptene (277) by the Huang-Minlon modification in which the cyclic ketone (6), hydrazine hydrate and potassium hydroxide were heated under reflux in 2,2'-dihydroxydiethyl ether (Scheme 92).
The $^1$H n.m.r. spectrum showed resonances for ten protons in the alkane region and a singlet at $\delta 6.9$ p.p.m. due to the phenyl protons.

Friedel-Crafts acylation was carried out by reaction of 6,7,8,9-tetrahydro-5H-benzocycloheptene (277) with acetyl chloride in a stirred suspension of anhydrous aluminium chloride to give 2-acetyl-6,7,8,9-tetrahydro-5H-benzocycloheptene (278) (Scheme 92).

The infra-red frequency of the carbonyl group in the 2-acetyl-compound (278) is 1680 Cm$^{-1}$.

The 2-acetyl-6,7,8,9-tetrahydro-5H-benzocycloheptene (278) was then converted into 6,7,8,9-tetrahydro-5H-benzocycloheptene-2-carboxylic acid (279) by reaction with potassium iodide-iodine reagent and sodium hydroxide. Subsequent methylation of the acid (279) was carried out with diazomethane to give methyl 6,7,8,9-tetrahydro-5H-benzocycloheptene-2-carbonate (Scheme 92).

The infra-red absorption spectrum has peaks at 1683, 1606 and 1240 Cm$^{-1}$.

The $^1$H n.m.r. spectrum showed resonances for ten protons in the alkane region and a singlet at $\delta 3.7$ p.p.m. due to three protons of the methyl group. The aromatic protons were found in two regions, H1 and H3 shifted furthest to $\delta 7.8-7.6$ p.p.m. A doublet ($J_{3,4} = 8.5$ Hz) at $\delta 7.2-7.0$ p.p.m. must then be due to H4.
Scheme 92

\[
\begin{align*}
\text{CH}_3\text{CO} \xrightarrow{\text{I}_2/\text{IK}, \text{NaOH}} & \text{HO}_2\text{C} \\
\text{CH}_2\text{N}_2 \xrightarrow{\text{NH}_2\text{NH}_2, \text{KOH}} & \rightarrow \\
\text{CH}_3\text{CO} \xrightarrow{\text{CH}_3\text{COC}1, \text{AlCl}_3} & \rightarrow
\end{align*}
\]
A number of tropones with annulated heterocyclic rings were also prepared for an examination of their photochemical properties.

Synthesis of 1-methyl-3-phenylcyclohepta(b)pyrrol-8-one (281)

As mentioned above, K. Yamane et al. reported the synthesis of 3-phenylcyclohepta(b)pyrrol-8-one \( ^{102} \) (141). Addition of phenylacetaldehyde to 2-hydrazinotroponone (133) gave phenylacetaldehyde troponyl hydrazone (140), treatment of which with aqueous sulphuric acid gave the pyrrolotroponone (141) (Scheme 33).

A sample of the pyrrolotroponone (141) was supplied by professor K. Yamane.

The carbonyl resonance in the \( ^{13} \)C n.m.r. spectrum occurs at \( \delta \) 176.4 p.p.m. consistent with a conjugated carbonyl, all other resonances occurring in the aromatic and alkene regions.

Methylation of 3-phenylcyclohepta(b)pyrrol-8-one (141) was carried out by reaction of pyrrolotroponone (141) with methyl iodide and sodium hydride in boiling 1,2-dimethoxyethane (DME) to give 1-methyl-3-phenylcyclohepta(b)pyrrol-8-one (281) which was purified by p.l.c. plates (Scheme 93).

The infra-red absorption spectrum has peaks at 1638, 1550 and 1520 Cm\(^{-1}\).

The \( ^{1} \)H n.m.r. spectrum exhibited a doublet of doublets at \( \delta \) 7.6-7.5 p.p.m. due to H4 with a major coupling constant of \( J_{4,5} = 10.8 \) Hz. H5 occurs as a distinct octet at \( \delta \) 6.7-6.5 p.p.m. resulted from coupling with H4, H6 and H7 (\( J_{4,5} = 10.8 \) Hz, \( J_{5,6} = 6.9 \) Hz and \( J_{5,7} = 2.3 \) Hz). Two multiplets
at δ 7.5-7.4 p.p.m. and δ7.2-7.0 p.p.m. which integrate for six and two protons respectively, must then be due to the phenyl protons and H2, and to H6 and H7 respectively.

The carbonyl resonance in the $^{13}$C n.m.r. spectrum occurs at δ178.4 p.p.m. consistent with a conjugated carbonyl, all other resonances occurring in the aromatic and alkene regions apart from a peak at δ 38.8 due to the methyl carbon.

Scheme 93
Synthesis of 5-ethylcyclohept(b)indol-10(5H)-one (285),
5-methylcyclohept(b)indol-10(5H)-one (289) and
cyclohept(b)indol-10(5H)-one (8)

As stated above (Scheme 42) in 1976 Yamane and Fujimori \(^{51}\) and later in 1977 Oikawa and Yonemitsu \(^{100}\) reported the selective oxidation of the 5,6,7,8,9,10-hexahydro-
cyclohept(b)indole (153) and 5-methyl-6,7,8,9,10-hexahydro-
cyclohept(b)indole (286) with DDQ in aqueous tetrahydrofuran \(^{100}\)
(or dioxane \(^{51}\) ) at room temperature to give 6,7,8,9-tetrahydro-
cyclohept(b)indol-10(5H)-one (154) and 5-methyl-6,7,8,9-tetra-
hydrocyclohept(b)indol-10(5H)-one (287) (Scheme 94).

Using Collington and Jones' bromination/dehydrobromination procedure, Yamane and Fujimori \(^{51}\) also
synthesized cyclohept(b)indol-10(5H)-one (8) and
5-methylcyclohept(b)indol-10(5H)-one (289) (Scheme 94).

For the synthesis of 5-ethylcyclohept(b)indol-10(5H)-one
(285) we used a similar route.

Ethylation of 5,6,7,8,9,10-hexahydrocyclohept(b)indole
(153) was carried out by reaction of the cyclohept(b)indole
(153) with ethyl p-toluenesulphonate and sodium hydride in
boiling xylene to give 5-ethyl-6,7,8,9,10-hexahydrocyclohept(b)-
indole (282).

Treatment of the 5-ethyl-6,7,8,9,10-hexahydrocyclohept(b)-
indole (282) with two equivalents of DDQ in aqueous
tetrahydrofuran at room temperature under a nitrogen
atmosphere readily gave 5-ethyl-6,7,8,9-tetrahydrocyclohept(b)-
indol-10(5H)-one (283) (Scheme 94).

The infra-red absorption frequency of the carbonyl
group in the compound (283) is at 1645-1600 cm$^{-1}$. The $^1$H n.m.r. spectrum shows thirteen protons in the alkane region and the multiplet at $\delta$ 8.4-8.2 p.p.m. is assumed to be H1 which was shifted downfield from the remainder of the aromatic protons at $\delta$ 7.1-7.0 due to the anisotropic deshielding effect of the carnonyl group in position ten.

Bromination of 5-ethyl-6,7,8,9-tetrahydrocyclohept(b)-indol-10(5H)-one (283) was best effected by treatment with phenyltrimethylammonium tribromide in tetrahydrofuran to give 6,6'-dibromo-6,7,8,9-tetrahydro-5-ethylcyclohept(b)indol-10(5H)-one (284) (Scheme 94).

The mass spectrum of the dibromoketone (284) contained peaks at 432, 430, and 428 (M$^+$) in the ratio 1:2:1 confirming that the compound contained two bromine atoms.

The $^1$H n.m.r. spectrum again showed a broadened triplet between $\delta$ 3.2 and 2.8 p.p.m. attributed to the methylene groups at positions 6 and 8.

Subsequent dehydrobromination of the dibromoketone (284) with anhydrous lithium chloride in boiling dimethylformamide gave 5-ethylcyclohept(b)indol-10(5H)-one (285) (Scheme 94).

The mass spectrum shows the molecular ion to be at m/e 268 which is correct for the compound (285).

The infra-red absorption spectrum has peaks at 1635, 1565 and 1480 cm$^{-1}$.

The $^1$H n.m.r. spectrum showed a multiplet with major coupling constant of ($J_{1,2}=7.3$ Hz) at lowest field at $\delta$ 9.1-8.9 p.p.m. is considered to be H1. A multiplet between $\delta$ 7.5 and 6.6 p.p.m. which integrates
for seven protons must then be due to the protons around aromatic and the seven membered rings.

The carbonyl resonance in $^{13}$C n.m.r. spectrum occurs at $\delta 182.7$ p.p.m. consistent with a conjugated carbonyl, all other resonances occurring in the aromatic and alkene regions apart from two peaks at $\delta 38.0$ and $\delta 14.6$ p.p.m. due to methylene and methyl carbons.

Similarly 5-methylcyclohept(b)indol-10(5H)-one(289) and cyclohept(b)indol-10(5H)-one(8) were also prepared by oxidation, bromination and dehydrobromination sequences from 5-methyl-6,7,8,9,10-hexahydrocyclohept(b)indole(286) and 5,6,7,8,9,10-hexahydrocyclohept(b)indole(153) (Scheme 94).

Scheme 94

\[
\begin{align*}
\text{(282) } R &= \text{Et} \\
\text{(286) } R &= \text{CH}_3 \\
\text{(153) } R &= \text{H} \\
\text{(283) } R &= \text{Et} \\
\text{(287) } R &= \text{CH}_3 \\
\text{(154) } R &= \text{H} \\
\end{align*}
\]

\[
\begin{align*}
\text{(284) } R &= \text{Et} \\
\text{(288) } R &= \text{CH}_3 \\
\text{(290) } R &= \text{H} \\
\text{(285) } R &= \text{Et} \\
\text{(289) } R &= \text{CH}_3 \\
\text{(8) } R &= \text{H} \\
\end{align*}
\]
Synthesis of 4H-cyclohepta(b)furan-4-one(9)

As mentioned previously G. Jones et al. reported a synthesis of 4H-cyclohepta(b)furan-4-one(9). They used Collington and G. Jones' general synthesis of tropones, via dehydrobromination of a 5,5-dibromo-ketone(182) using lithium salts in boiling dimethylformamide (Scheme 48).

In order to prepare 4H-cyclohepta(b)furan-4-one(9) 2-furaldehyde and acetaldehyde were employed as starting materials.

Condensation of 2-furaldehyde and acetaldehyde in the presence of sodium hydroxide gave 2-furylacrylaldehyde(291) (Scheme 95).

Condensation of 2-furylacrylaldehyde(291) with ethyl acetate in the presence of sodium wire yielded ethyl 5-(2-furyl)-pentadienoate(292) (Scheme 95).

The hydrogenation of 5-(2-furyl)pentadienonate(292) was carried out using Raney nickel in ethanol to give ethyl 5-(2-furyl)valerate(293) (Scheme 95).

The $^1$H n.m.r. spectrum showed resonances for three protons of furyl group and thirteen protons in alkane region.

The ethyl 5-(2-furyl)valerate (293) was hydrolysed to 5-(2-furyl)valeric acid(294) and then converted to the 5-(2-furyl)valeryl chloride(180) by reaction with thionyl chloride in diethyl ether.
Cyclisation of 5-(2-furyl)valeryl chloride (180) was carried out by reaction with tin tetrachloride in carbon disulfide to give 5,6,7,8-tetrahydro-4H-cyclohepta(b)furan-4-one 105 (181) (Scheme 95).

Bromination of the ketone (181) was best effected by treatment with phenyltrimethylammonium tribromide to give 5,5-dibromo-5,6,7,8-tetrahydro-4H-cyclohepta(b)furan-4-one (182) 62(Scheme 95).

The 1H n.m.r. again showed a broadened triplet between 63.2 and 2.8 p.p.m. attributed to the methylene groups at positions 6 and 8.

Dehydrobromination of the dibromo-ketone (182) was carried out with lithium carbonate in boiling dimethylformamide to give 4H-cyclohepta(b)furan-4-one(8) 62 (Scheme 95).

The 1H n.m.r. spectrum showed two doublets at δ 7.4 and 7.2 p.p.m. due to the protons at positions 2 and 3. Two doublet of doublets at δ7.4 and 7.1 p.p.m. due to the protons at positions 8 and 5, and finally two multiplets centred atδ7.25 and 6.85 p.p.m. due to the protons at positions 6 and 7 respectively.
Scheme 95

\[
\begin{align*}
\text{Furan} & \xrightarrow{\text{CH}_3\text{CHO}} \text{Furan} & \text{Ethyl acetate} \\
& \xrightarrow{\text{Na wire}} \\
\text{Furan} & \xrightarrow{\text{Raney nickel}} \text{Furan} & \xrightarrow{\text{H}_3\text{O}^+} \\
& \xrightarrow{\text{H}_2} \\
\text{Furan} & \xrightarrow{\text{SOCl}_2} \text{Furan} & \xrightarrow{\text{SnCl}_4} \\
& \xrightarrow{\text{PTAB/THF}} \\
\text{Furan} & \xrightarrow{\text{Li}_2\text{CO}_3/\text{DMF}} \\
\end{align*}
\]
Chapter 3

Introduction

A review of the previous photochemistry of tropones and annulated tropones.
Photochemistry

The review of the photochemistry or a number of tropones, substituted benztropones, and tropones with fused hetero rings follows.

Colchicine

The first reported photochemistry reaction of a troponoid compound was published in 1865 when Hubler reported that solutions of colchicine (295) turned brown on standing in sunlight.

Later Forbes in 1955 reported the photochemical isomerization of colchicine (295). Colchicine is one of the more complex tropolones, and was converted in aqueous solution by sunlight into three photoisomers, the $\beta$- and $\gamma$-lumicolchicines (296), (297) and the $\alpha$-isomer. These results demonstrate that the tropolone ring has been involved in the transformation (Scheme 96).

It is necessary to consider first the photochemistry of much simpler troponoid compounds in order to learn what sort of transformations are allowed.
Scheme 96

\[
\begin{align*}
\text{Sunlight} & \quad 8 \text{ to } 10 \text{ weeks} \\
\end{align*}
\]

\[
\begin{align*}
\text{(295)} \\
\end{align*}
\]

\[
\begin{align*}
\beta\text{-Lumicolchicine} & \quad \gamma\text{-Lumicolchicine} \\
\end{align*}
\]

\[
\begin{align*}
\text{(296)} & \quad \text{(297)} \\
\end{align*}
\]
**α-Tropolone methyl ether**

In 1960, Forbes and Ripley\(^\text{108}\) reported the photolysis of α-tropolone methyl ether (298) in aqueous solution to give the methyl ester of 4-oxo-2-cyclopentene-1-acetic acid (299) (Scheme 97).

**Scheme 97**

\[
\begin{split}
\text{hv} & \quad \overset{\text{H}_2\text{O}}{\longrightarrow} \\
(298) & \quad (299)
\end{split}
\]

Dauben et al\(^\text{109}\) subsequently reported that the irradiation of α-tropolone methyl ether (298) in methanol gave rise initially to a bicyclic system (300) of the type predicted by Chapman and Pasto\(^\text{110}\) which underwent rearrangement to another bicyclic system (301). Addition of water followed by further irradiation leads to formation of the methyl ester compound (299) as previously reported by Forbes and Ripley\(^\text{108}\) (Scheme 98).

**Scheme 98**

\[
\begin{split}
\text{hv} & \quad \overset{\text{MeOH}}{\longrightarrow} \\
(298) & \quad (300) \\
\text{hv} & \quad \overset{\text{H}_2\text{O}}{\longrightarrow} \\
(301) & \quad (299)
\end{split}
\]
The mechanism for this sequence of reactions is defined clearly by the photochemical rearrangements of 4-methyltropolone methyl ether (302) and 6-methyltropolone methyl ether (303). They gave ketoester products (304) and (305) under similar conditions. The mechanism is shown in Scheme (99).

Scheme 99

Further investigations of these photolyses by Chapman and Lassila in 1968 have shown that the 1-methoxy-3,6-bicyclo(3,2,0)heptadiene-2-one (300) could undergo photochemical rearrangement to the 7-methoxy-3,6-bicyclo(3,2,0)heptadiene-2-one (301) via a ketene intermediate (306). The presence of such an intermediate (306) was indicated by the appearance of a band in the infra-red spectrum of the reaction mixture at 2118 cm\(^{-1}\), which appeared after two minutes’ irradiation and reached a maximum after 1 to 3 hours. This band was observable only when the photolysis was carried out at temperatures below -70 °C (Scheme 100).

Scheme 100
Y-Tropolone methyl ether

Y-Tropolone methyl ether (307) was reported by Chapman and Pasto\textsuperscript{110} to give one product, 5-methoxy-3,6-bicyclo(3,2,0)heptadiene-2-one (309), plus a quantity of polymeric material. The mechanism proposed could in principle lead to either of the two bicyclic ketones (309) and (311), but it was felt that the intermediate (308) would be stabilised by having the positive charge on the carbon atom carrying the methoxyl group, whereas the intermediate (310) would not, and this difference accounted for the formation of only one bicyclic ketone (309) in this case (Scheme 101).

\textbf{Scheme 101}
It is worthwhile to mention that neither β-tropolone methyl ether nor tropone itself undergo the photoisomerisation described above.

Tropone

In spite of the use of a variety of solvents for the photolysis of tropone (312) itself, to date no simple bicyclic photoproducts have been isolated. On the other hand, a large number of photodimers have been identified.

In 1966 Mukai et al.112 reported the first example of (6+6) π-type cycloaddition of tropone (312). In 2N sulfuric acid or water, tropone dimerizes in low yield (7.5%) to the trans diketone (313). This dimer is converted back to tropone (312) thermally in 60% yield (Scheme 102).

Photodimerization of tropone (312) in acetonitrile was reported by Kende113 in 1966, but the (6+6) dimer is not obtained. Three products, the (6+4) (314), (6+2) (315), and (4+2) (316) cycloadducts, are formed instead (Scheme 102). Upon heating, dimer (314) reverts to tropone, while neither dimer (315) nor dimer (316) undergo thermal conversion to tropone (Scheme 102).
Scheme 102

\[ \text{hv CH}_2\text{CN} \rightarrow (312) \]

\[ \Delta \text{H}_2\text{O or H}_2\text{SO}_4 \rightarrow (313) \]

\[ + (314) \]

\[ + (315) \]

\[ (316) \]
2,3,6-Trimethoxy-5H-benzocyclohepten-5-one and 2,3,4,6-tetramethoxy-5H-benzocyclohepten-5-one

Forbes and Griffiths in 1966 found that irradiation of an ethanolic solution of the 2,3,6-trimethoxy-5H-benzocyclohepten-5-one (317) under nitrogen gave a complex mixture of products, from which was isolated the photoisomer (318)(Scheme 103).

Later work by Forbes et al showed that irradiation of 2,3,4,6-tetramethoxy-5H-benzocyclohepten-5-one (319) in an aprotic solvent (benzene, cyclohexane or methylene chloride) under nitrogen gave the tricyclic ketone (320) as a major product (Scheme 103).

Scheme 103

(317) R=H  
(319) R=OMe  
(318) R=R'=H  
(320) R=R'=OMe

\[ \text{(i) } R=H, \text{ EtOH} \]  
\[ \text{(ii) } R=\text{OMe}, C_6H_6 \]
5H-Benzocyclohepten-5-one

In 1969 Collington and G. Jones reported the first photoisomerization of an unsubstituted annulated tropone. Irradiation of methanolic solution of 5H-benzocyclohepten-5-one (1) with a mercury-vapour lamp gave the 2a,7a-dihydrocyclobuta(inden-7-one (321) and a dimer of as yet undetermined structure (Scheme 104).

Scheme 104

6-Hydroxy-5H-benzocyclohepten-5-one

In 1970 Ebine et al reported a new type of photochemical valence isomerization of 6-hydroxy-5H-benzocyclohepten-5-one (322). Irradiation of a dilute solutions of compound (322) in methanol with pyrex filtered light resulted in the formation of an unusual isomer of structure (323). This reaction represents a novel type of photorearrangement of 6-hydroxy-benzocyclohepten-5-one (322) and may be explained either by the initial formation of (324) followed by rearrangement to (323), or by a mechanism in which (325) is postulated as an intermediate (Scheme 105).
7-Hydroxy-5H-benzocyclohepten-5-one

In 1971 Yoshioka and Hoshino\textsuperscript{117} reported the irradiation of 7-hydroxy-5H-benzocyclohepten-5-one (326). Irradiation of the benztropone (326) in methanol gave the ester (327) with a small amount of the polycyclic ketone (328) (Scheme 106).
A mechanism for the formation of the ester(327) was postulated, addition of methanol to the tricyclic ketone(329) followed by a rearrangement gave the ester(327) (Scheme 107).

Scheme 107

\[ \text{Cyclohepta(b)thiophen-4-ones} \]

In 1977 G. Jones and Robinson reported the photochemistry of some cyclohepta(b)thiophen-4-ones (203), (204), (330) and (334).

Irradiation of methanolic solutions of the cyclohepta(b)thiophen-4-ones (203), (204) and (330) gave \((\pi_4 + \pi_2)\) dimers (331-333), formed by the reaction of the 5,6-bond of the thienotropone with the 5,7-diene system of another. The dimers were found to be of the head-to-head type having a trans junction (Scheme 108).

Scheme 108

\[ \text{(203)} \quad R = R^1 = R^2 = H \]
\[ \text{(330)} \quad R = R^1 = H, R^2 = Me \]
\[ \text{(204)} \quad R = Me, R^1 = R^2 = H \]
\[ \text{(331)} \]
\[ \text{(332)} \]
\[ \text{(333)} \]
Irradiation of 2,6-dimethylcyclohepta(b)thiophen-4-one (334) leads to an intramolecular electrocyclic disrotatory reaction, giving the tricyclic ketone (335), which provided indirect evidence that the 5,6-bond is involved in dimer formation, since a 6-methyl group is seen to suppress dimerisation (Scheme 109).

Scheme 109

Pyridotropones

Recently M. G. Hicks and G. Jones have studied the photochemistry of some pyridotropones. On irradiation the pyridotropones (11a, 12a, 225 and 228) were shown to be largely unreactive. Three of the four isomers gave only polymeric material, the 5H-cyclohepta(b)pyridin-5-one (12a) gave a dimer of as yet undetermined structure. Thus it appears that the nitrogen atom causes too much deactivation for the ring closure reaction to occur.
6-Methyl-7H-benzocyclohepten-7-one

Mukai and et al\textsuperscript{118} studied the photochemistry of 6-methyl-7H-benzocyclohepten-7-one (336).

Irradiation of the benztropone (336) gives the (\(\pi_2+\pi_2\)) dimer (337) and the dehydrogenated product (338). The dimerisation is not solvent sensitive, since a variety of solvents give the same products in identical yield (Scheme 110).

Scheme 110

\[
\text{336} \xrightarrow{h\nu} \text{337} + \text{338}
\]
Chapter 4

Results and discussion
Apart from a communication by Collington and G. Jones on the unsubstituted 5H-benzocyclohepten-5-one (1) the photosensitivity of substituted 5H-benzocyclohepten-5-ones and of tropones with fused hetero rings appears to have passed unreported. For closer study of photo-reactivity of a number of substituted benztropones and related hetero compounds has been investigated. The photochemical results are as follows:

1-Methoxy-4-methyl-5H-benzocyclohepten-5-one (268)

A solution of 1-methoxy-4-methyl-5H-benzocyclohepten-5-one (268) in absolute methanol was irradiated with a Hanovia medium pressure mercury lamp while the flask was flushed with nitrogen. Samples were taken and evaporated at intervals for t.l.c. and $^1$H n.m.r. examination. Irradiation was stopped after 26 hours when the concentration of new component remained constant. Removal of the solvent under reduced pressure gave a brown gum which was triturated with dried diethyl ether and then filtered. The combined filtrates was evaporated to give a pale yellow solid which was chromatographed on preparative plates using toluene /ethyl acetate (80:20) as eluent; some 3-methoxy-6-methyl-2a,7a-dihydrocyclobut(a)inden-7-one (339) was found in addition to polymeric material left on the base line (Scheme 111).

The major photoproduct (339) had a molecular weight of 200 and was hence an isomer of compound (268).

The tricylic compound (339) showed characteristically high frequency carbonyl absorption at 1700 cm$^{-1}$. 
The two doublets $\delta$ 7.1-7.0 and 6.9-6.8 p.p.m. can be attributed to the protons at positions five and four respectively. Spin decoupling of any of the four separated protons at positions 2,1,2a,7a causes simplification of the other three protons, for example irradiation at $\delta$ 3.78-3.74 p.p.m. (H7a) causes the distorted octet (ddd) at $\delta$ 6.65-6.62 p.p.m. to collapse to doublet of doublets which could be attributed to the proton at position two by analogy with similar structures, and also collapses the doublet of doublets at $\delta$ 6.35-6.31 p.p.m. (H1) to a doublet and changes the signal due to the proton at position 2a ($\delta$ 4.3-3.2 p.p.m.). Spin decoupling of the signal due to the proton at position 2 causes the distorted octet (ddd, H7a) to collapse to a distinguishable doublet of doublets as well as simplifying the signals for the other two protons. Thus the two distorted octets at $\delta$ 6.65-6.62 p.p.m. and $\delta$ 3.78-3.74 p.p.m. are both doublets of doublets of doublets. Significantly irradiation of the proton at position 2a causes no changes on proton at position 1; this indicated that the coupling constant of proton 1 and 2a is undetectable. Thus result the following coupling constants $J_{2,1}=2.44$ Hz, $J_{2,2a}=0.85$ Hz, $J_{2,7a}$ = very small, $J_{7a,1}=0.85$ Hz and $J_{7a,2a}=2.80$ Hz.

The fully decoupled $^{13}$C spectrum shows that there are thirteen carbon atoms present in the molecule. Comparison with the off resonance decoupled spectrum gives five quaternary carbon atoms. The two farthest downfield signals are both
due to quaternary carbon atoms, which occur at 
$\delta 203.7$ p.p.m. consistent with carbonyl carbon resonance, 
and at $\delta 154.5$ p.p.m. due to quaternary aromatic carbon 3 
bonded to the methoxyl group.

Scheme 111

![Scheme 111](image)

2-Methoxy-5H-benzocyclohepten-5-one(11) and its 6-bromo derivative

On irradiation the 2-methoxybenztropone(11) and 
2-methoxy-6-bromo-5H-benzocyclohepten-5-one(247) were shown 
to be largely unreactive. Thus it appears that when the methoxyl 
group is meta to C9 there is insufficient activation for the 
ring closure to occur. On repetition of irradiation for 
several times, on one occasion only was a trace amount of 
4-methoxy-2a,7a-dihydrocyclobut(a)inden-7-one(340) detected 
(Scheme 112).

The infra-red spectrum of the photoisomer(340) 
showed a carbonyl stretching frequency at $1702 \text{ Cm}^{-1}$ which 
could be compared with that of 1-indanone $120$ at $1710 \text{ Cm}^{-1}$.

The $^1\text{H n.m.r.}$ spectrum is also consistent with compound 
being the tricyclic ketone(340).
Irradiation of the 3-methoxybenztropone (234) was carried out for 48 hours in a solution of methanol under a nitrogen atmosphere. Over this period the solution turned cloudy; the precipitate however proved to be polymeric material. The solid material recovered from the ether extract was a yellow waxy compound and subsequently was purified by bulb distillation to give the photoproduct (341) (Scheme 113).

The compound (341) had a molecular weight of 186 and was hence an isomer of compound (234).

The tricyclic compound (341) showed characteristically high frequency carbonyl absorption at 1700 cm⁻¹ which is also consistent with the compound (341).

The ¹H n.m.r. spectrum of the pure material was comparable with those of the other tricyclic compounds previously described.
3-Acetamido-5H-benzocyclohepten-5-one (21) and 5H-benzocyclohepten-5-one (1)

A methanolic solution of the 3-acetamidobenzotropone (21) was irradiated using a Hanovia medium pressure mercury lamp. Irradiation was stopped when the photochemical product concentration remained constant. The pure 5-acetamido-2a,7a-dihydrocyclobuta(1)inden-7-one (342) was separated on preparative plates from polymeric material, which was mostly left on the base line (Scheme 114).

The compound (342) showed a molecular weight of 213 and was hence an isomer of compound (21).

The infra-red absorption frequency of the carbonyl group in the tricyclic compound was at 1710 Cm$^{-1}$.

From the $^1$H n.m.r. spectrum it was possible to assign individually all the protons around the tricyclic compound (342). The doublet of doublets ($J_{3,4} = 8.3$ Hz and $J_{6,4} = 2$ Hz) at $\delta$ 8.0–7.9 p.p.m. is considered to be the proton at position four. The two doublets at $\delta$ 7.7 and $\delta$ 7.4–7.3 p.p.m. are assigned to the protons at positions six and three respectively. The broad doublet of doublets at $\delta$ 6.29–6.26 p.p.m. was assigned to the proton at position one with coupling constants of $J_{1,2} = 2.5$ Hz and $J_{1,7a} = 0.98$ Hz. The doublet at $\delta$ 6.59–6.56 p.p.m. was considered to be the proton at position two with a major coupling constant of $J_{1,2} = 2.5$ Hz. Another broad doublet of doublets at highest field $\delta$ 3.82–3.79 p.p.m. was assigned to the proton at position 7a.
with coupling constants of $J_{7a,2a}=2.9$ Hz and $J_{7a,1}=0.98$ Hz. The broad doublet at $\delta 4.29-4.26$ p.p.m. must then be due to proton at position 2a.

The fully decoupled $^{13}$C spectrum shows that there are thirteen carbon atoms present in the molecule. Comparison with the off-resonance decoupled spectrum gives five quaternary carbon atoms. The three signals furthest downfield are due to quaternary carbon atoms, in which the carbonyl resonances occur at $\delta 201.9$ and 169.0 p.p.m. consistent with carbon at position seven and the carbonyl group of the acetamide respectively, and at $\delta 146.5$ p.p.m. due to the quaternary aromatic carbon of position five, bonded to the acetamido group.

Scheme 114

Irradiation of 5H-benzocyclohepten-5-one (1) also gave the 2a,7a-dihydrocyclobut(b)inden-7-one (321) as reported by Collington and G. Jones (Scheme 104).
Other substituted 5H-benzocyclohepten-5-ones and the tropones with fused hetero rings

When a methanolic solution of 3-nitro-5H-benzocyclohepten-5-one (20) or 6,8-dinitro-5H-benzocyclohepten-5-one (269) was irradiated under similar conditions, the product after work up showed some starting material and polymeric material however in the cases of 3-amino- or 3-amino-2,4-dibromo-5H-benzocyclohepten-5-one (270) and (272), 3-phenylcyclohepta(b)pyrrol-8-one (141) and its methyl derivative (281), cyclohept(b)indol-10(5H)-one (8) and its methyl and ethyl derivatives (289) and (285) and finally 4H-cyclohepta(b)furan-4-one (9) only polymeric material were formed.
Conclusion

Examination of the results which we have obtained from irradiation of annulated tropones has demonstrated a differential photoreactivity within a class of annulated tropones. The methoxybenztropones (268, 11, 247 and 234) appear to show an alternating effect, dependent on the position of the methoxyl group. When the methoxyl group is in a position where the group's electron-donating ability can influence the alkene chain, that is, ortho or para to C9 the photoreaction is enhanced. When the methoxyl group is meta to C9 the photoreaction is suppressed and proceeds slowly in poor yield. Similar differential reactivity has been known for a long time in the photochemistry of tropolone methyl ethers. On irradiation α- and γ-tropolone methyl ethers (298, 307) give bicyclic photoproducts (300, 309) whereas β-tropolone methyl ether (343) shows no such reaction. Chapman has attributed this differential reactivity to the possible stabilization of a dipolar intermediate (344, 345) by methoxyl group (Scheme 115). In the cases of α- and γ-tropolone methyl ethers (298 and 307) collapse of the intermediate gives the observed photoproducts.
If one can postulate that similar zwitterionic intermediates exist for the methoxytropones (268), (11), (247) and (234); the photoproducts would be in good agreement with those of tropolone methyl ethers (Scheme 116).
In the case of the aminobenzotropone (270) which apparently does not fit with the above suggestion, one may suppose that the intermediate would by further consecutive reactions proceed towards polymer.

In the case of the nitrobenzotropone (20) again it is very obviously rationalized through the intermediate (347) much less stabilised than those of the methoxybenzotropones (345) and (346) (Scheme 116).

If electron-donating ability of the aminobenzotropone (270) is reduced by converting the amino group to an acetamido group, the photoprodct also seems to modify from polymer to tricyclic ketone (342). This may indicate that very electron-donating groups such as the amino group and very electron-withdrawing groups such as the nitro group can both suppress the course of reaction towards the desired photoprodcts whereas the moderate electron-donating groups such as methoxy1 or acetamido would enhance the reaction towards the desired tricyclic ketone.

In the case of the aminodibromobenzotropone (272) it might first converted to the aminobenzotropone (270) and then polymerized since Soumillion and Wolf have shown that the chlorobenzene can undergo photoreduction to benzene in methanol. It is worthwhile to mention that no trace of the aminobenzotropone (270) could be detected when the aminodibromobenzotropone (272) was irradiated.
Reduction of the nitrobenzene derivatives to the corresponding aminobenzene derivatives are also known but during the irradiation of the nitrobenztropone(20) no trace of the aminobenztropone(270) could be detected.

Scheme 116

On irradiation the pyrrolotropones (141 and 281), indolotropones(8,285 and 289) and the furotropone(9) yielded only polymeric materials. Since the pyrrolotropones(141) and (281) and the furotropone(9)are like the thienotropones(203), (204) and (330), electron rich they might have been expected to be photoreactive. Similar resonance structures to those
shown for the methoxybenztropones (Scheme 116) can be drawn for the furotropane (9) (Scheme 117) or pyrrolootropones (141 and 281) or indoloctropones (8, 285 and 289), but pyrroles and furans are generally accepted as having a more localized electron distribution than thiophens and as having more diene character, and then may lead to a greater tendency to polymerisation, which compete successfully with the electrolyclization.

Scheme 117

![Diagram of compounds](image-url)
Chapter 5

Experimental
Preliminary notes

Melting points were determined on a Kofler hot-stage apparatus and are uncorrected.

Infrared absorption spectra were recorded on a Perkin-Elmer 420 spectrophotometer. Solids were recorded either as solutions or as potassium bromide discs or as nujol mulls.

Nuclear magnetic spectra were routinely measured on a Hitachi Perkin-Elmer R.24 and / or R.24 B instrument at 60 MHz.

Carbon 13 n.m.r. spectra and proton n.m.r. spectra at 100 MHz were recorded on a Jeol FX100 Fourier Transform instrument. Chemical shift values are quoted in delta (δ) values in p.p.m. with respect to tetramethyl silane as internal standard.

Mass spectra were recorded on a Hitachi Perkin-Elmer RMU-6 instrument and A.E.I. MS12 instrument. Exact mass measurements were carried out by PCMU (Harwell).

Micro-analyses were carried out on a Perkin-Elmer 240 carbon/hydrogen/nitrogen analyser.

Ultraviolet and visible absorption spectra were recorded on a Perkin-Elmer 402 spectrophotometer.

Column chromatography was carried out using either silica gel (60-120 mesh) or Woelm alumina (neutral grade). The activity values quoted refer to the Brockmann scale.

Thin layer chromatography was carried out on 20 X 5 Cm glass plates coated with Merck Kieselgel HF 254. Components were visualized under U.V. light. Preparative layer chromatography (P.L.C.) was performed on 40 X 20 Cm glass plates coated with a 1.5 mm layer of Kieselgel HF 254. The separate
components were visualized under U.V. light, scraped off the plates and extracted three times with boiling methanol. The methanol solution was evaporated, the residue taken up in dichloromethane, filtered and evaporated.

Abbreviations used:

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>s</td>
<td>singlet</td>
</tr>
<tr>
<td>d</td>
<td>doublet</td>
</tr>
<tr>
<td>dd</td>
<td>doublet of doublets</td>
</tr>
<tr>
<td>t</td>
<td>triplet</td>
</tr>
<tr>
<td>q</td>
<td>quartet</td>
</tr>
<tr>
<td>m</td>
<td>multiplet</td>
</tr>
</tbody>
</table>
3-Methoxycinnamylidenemalonic acid (237)

A solution of sodium hydroxide (17 g) in methanol (170 ml) was added to a flask containing benzyltrimethylammonium hydroxide (77.6 g). The solution was left to stand overnight. It was then filtered by suction, and sodium chloride formed as by-product was washed with a small portion of methanol. m-Methoxybenzaldehyde (11.8 g) and diethyl ethyldienemalonate (36.6 g) were added to the above base. The flask was swirled, and stirred for 48 hrs at room temperature. It was then diluted with 500 ml of water, refluxed for 2 hrs, cooled and acidified with hydrochloric acid. After standing at 5°C for 24 hrs, yellow crystals were obtained. These were filtered, washed with cold water and dried on a steam bath. Purification of crude crystals by crystallization from benzene-ethyl acetate (25:75) gave the compound (237) as canary yellow crystals (23.9 g, 99%).

m.p. 201-202°C Lit79 202°C

1H N.M.R. (CDCl₃) δ

11.5 s 2H (CO₂H)₂
8.45-6.88 m 7H Other protons
3.9 s 3H OCH₃

I.R.νₘₐₓ (Nujol) 1700(CO), 1600 and 1230 cm⁻¹

3-(m-Methoxyphenyl)propylmalonic acid (238)

A solution of 3-methoxycinnamylidenemalonic acid (237) (23.9 g) in ethanol (1200 ml) and palladium on charcoal (1.2 g), was placed in a two litre Buchner flask equipped with a rubber bung and teflon coated magnetic stirrer. The mixture was hydrogenated at atmospheric pressure.
and room temperature, and hydrogenation continued until hydrogen absorption had ceased and the yellow colour of the reaction mixture had disappeared. The mixture was filtered, the residue washed with ethanol, and the solvent evaporated off to give the compound (238) (24 g, 98%) as a pale yellow oily liquid.

\[ \text{H N.M.R. (CDCl}_3\text{) } \delta \]

-10.2 s 2H (CO\textsubscript{2}H)\textsubscript{2}
-7.55-6.6 m 4H Aromatic protons
3.72 s 3H OCH\textsubscript{3}
5.70-3.32 t 1H CH
2.70-2.50 t 2H PhCH\textsubscript{2}
2.20-1.60 m 4H (CH\textsubscript{2})\textsubscript{2}

I.R. \( \nu_{\text{max}} \) (Neat) 1710(CO), 1610, 1260 cm\(^{-1}\)

\( 5\)-(m-Methoxyphenyl)valeric acid (239)

\( 3\)-(m-Methoxyphenyl)propylmalonic acid (238) (23.9 g) was placed in a Claisen distillation flask and decarboxylated in vacuo. The expected compound (239) was obtained as colourless liquid (15.8 g, 80%).

\( \text{b.p.} 142^\circ C/0.17 \text{ mm Hg} \text{ Lit}^79 200^\circ C/1 \text{ mm Hg} \)

\[ \text{H N.M.R. (CDCl}_3\text{) } \delta \]

9.50 s 1H CO\textsubscript{2}H
7.30-6.70 m 3H Aromatic protons
3.72 s 3H OCH\textsubscript{3}
2.80-2.20 m 4H PHCH\textsubscript{2} and CH\textsubscript{2}CO\textsubscript{2}H
1.80-1.60 m 4H (CH\textsubscript{2})\textsubscript{2}
1R. $v_{\text{max}}$(CHCl$_3$) 1700(CO) and 1280 cm$^{-1}$

2-Methoxy-6,7,8,9-tetrahydro-5H-benzocyclohepten-5-one (11)

5-(m-Methoxyphenyl)valeric acid (239) (15.8 g) was added in portions (5 x 3g) at 15 minute intervals to a mixture of phosphorus pentoxide (61.7 g) and 85% orthophosphoric acid (39.5 ml), which had been heated for 4 hrs to dissolve the phosphorus pentoxide. The mixture was heated at 100 °C for 6 hrs with vigorous stirring. Within 25 minutes an amber-brown homogeneous solution was obtained. The colour changed to cherry-red after 40 minutes. The reaction mixture was poured into ice-water and allowed to stand overnight. After extraction with ether and removal of the acidic material with 5% sodium hydroxide, the organic layer was dried over magnesium sulphate and the solvent removed by evaporation under reduced pressure to give a brownish oily liquid which was distilled under vacuum to give the compound (11) (13.3 g, 94%).

m.p. 57-58 °C Lit$^7$ 58-59 °C

$^1$H N.M.R. (CDCl$_3$) $\delta$

\[
\begin{align*}
7.72-7.54 & \text{ d } 1\text{H} \text{ H on C4} & J_{3,4} = 9\text{Hz} \\
6.78-6.54 & \text{ m } 2\text{H} \text{ H on C1 and C3} \\
3.75 & \text{ s } 3\text{H} \text{ OCH$_3$} \\
3.01-2.20 & \text{ m } 4\text{H} \text{ H on C6 and C9} \\
2.01-1.40 & \text{ m } 4\text{H} \text{ H on C7 and C8} \\
\end{align*}
\]

I.R. $v_{\text{max}}$(Nujol) 1680(CO), 1580 and 1247 cm$^{-1}$

6,6-Dibromo-6,7,8,9-tetrahydro-5H-benzocyclohepten-5-one (246)

Phenyltrimethylammonium tribromide (3.75 g) was added in ten portions (0.3 g), at 10 minutes intervals, to a solution of 2-methoxy-6,7,8,9-tetrahydro-5H-benzocyclohepten-5-one (11) (1 g).
in anhydrous tetrahydrofuran (100ml) at room temperature and the mixture was stirred for 24 hrs. The excess of phenyltrimethylammonium tribromide was destroyed by addition of a few drops of acetone. The mixture was filtered and phenyltrimethylammonium bromide collected was washed with a little tetrahydrofuran. The combined filtrates were evaporated in vacuo. A light brown oil was obtained and solidified on trituration with petroleum ether. Crystallisation from methanol gave pure compound (246) (1.17 g, 62%).

m.p. 82.5-83 °C

Analysis C$_{12}$H$_{12}$Br$_2$O$_2$

<table>
<thead>
<tr>
<th>Found</th>
<th>Required</th>
</tr>
</thead>
<tbody>
<tr>
<td>C 41.73%</td>
<td>C 41.37%</td>
</tr>
<tr>
<td>H 3.44%</td>
<td>H 3.44%</td>
</tr>
</tbody>
</table>

$^1$H N.M.R. (CDCl$_3$) δ

| 7.42-7.30 | 6.82-6.52 | 3.80 | 2.90-2.60 | 2.20-1.60 |
| d      | m      | s    | t      | m      |

1H on C4  J$_{3,4}$=9 Hz
2H on C1 and C3
3H OCH$_3$
2H on C7
4H on C9 and C8

I.R. ν$_{max}$ (CHCl$_3$) 1680(CO), 1600 and 1100 cm$^{-1}$
2-Methoxy-6,6,9-tribromo- and
6,6-dibromo-6,7,8,9-tetrahydro-5H-benzocyclohepten-5-one
(246a and 246)

Bromine (6.4 g) in carbon tetrachloride (15 ml) was
added dropwise to a stirred solution of the ketone (11) (3.8 g)
in carbon tetrachloride (50 ml). After addition, the solution
was boiled for 1 hr, cooled and the solvent removed under
reduced pressure. The light brown oil which solidified on
trituration with light petroleum was identified as the di-
and tribromoketone (7.4 g), mixed m.p. 75-78°C. Pure
tribromoketone (246a) was crystallised from methanol.

m.p. 75-76.5°C

Analysis

<table>
<thead>
<tr>
<th></th>
<th>C₀₁₂H₁₁Br₃O₂</th>
</tr>
</thead>
<tbody>
<tr>
<td>Found</td>
<td>C 34.03% H 2.58%</td>
</tr>
<tr>
<td>Required</td>
<td>C 33.72 H 2.58</td>
</tr>
</tbody>
</table>

¹H N.M.R. (CDCl₃) δ

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>7.43-7.31</td>
<td>d 1H H on C4 J₃,₄=9 Hz</td>
</tr>
<tr>
<td>6.82-6.52</td>
<td>m 2H 2H on C1 and C3</td>
</tr>
<tr>
<td>5.30-5.10</td>
<td>m 1H CHBr</td>
</tr>
<tr>
<td>3.80</td>
<td>s 3H OCH₃</td>
</tr>
<tr>
<td>2.90-2.59</td>
<td>t 2H 2H on C7</td>
</tr>
<tr>
<td>2.20-1.58</td>
<td>m 2H 2H on C8</td>
</tr>
</tbody>
</table>

2-Methoxy-5H-benzocyclohepten-5-one (38) and
2-methoxy-6-bromo-5H-benzocyclohepten-5-one (247)

A mixture of the di- and tribromoketone (246 and 246a
(7.3 g), anhydrous lithium chloride (3.65 g) and DMF (450 ml)
2-Methoxy-6,6,9-tribromo- and 6,6-dibromo-6,7,8,9-tetrahydro-5H-benzocyclohepten-5-one (246a and 246)

Bromine (6.4g) in carbon tetrachloride (15 ml) was added dropwise to a stirred solution of the ketone(11)(3.8 g) in carbon tetrachloride (50 ml). After addition, the solution was boiled for 1 hr, cooled and the solvent removed under reduced pressure. The light brown oil which solidified on trituration with light petroleum was identified as the di- and tribromoketone (7.4 g), mixed m.p. 75-78 °C. Pure tribromoketone(246a) was crystallized from methanol.

m.p. 75-76.5 °C
Analysis C_{12}H_{11}Br_{3}O_2
  Found  C 34.03% H 2.58%
  Required C 33.72 H 2.58

^1H N.M.R. (CDCl_3) δ

7.43-7.31 d 1H H on C4 J_{3,4}=9 Hz
6.82-6.52 m 2H 2H on C1 and C3
5.30-5.10 m 1H CHBr
3.80 s 3H OCH_3
2.90-2.59 t 2H 2H on C7
2.20-1.58 m 2H 2H on C8

2-Methoxy-5H-benzocyclohepten-5-one(38) and 2-methoxy-6-bromo-5H-benzocyclohepten-5-one(247)

A mixture of the di- and tribromoketone(246 and 246a (7.3 g), anhydrous lithium chloride(3.65 g) and DMF(450 ml)
was boiled and stirred under nitrogen atmosphere for 3 hrs. The mixture was cooled and the DMF removed under reduced pressure. Water was added, the aqueous solution extracted with diethyl ether. The combined ethereal extracts were dried over magnesium sulphate and then distilled to give a brown oil. The oil was distilled in a bulb tube to give a yellow oil which solidified after a few minutes. The mixture was separated by p.l.c. To obtain better resolution the plates were immersed three times into the solvent (ethyl acetate- toluene, 10:90) with drying after each immersion. The following bands were obtained.

Band (I) ($R_f$=0.22) was obtained as yellow prisms. It was identified as 2-methoxy-5H-benzocyclohepten-5-one (38)(2.62 g).

This compound was also prepared by similar procedure from pure 2-methoxy-6,6-dibromo-6,7,8,9-tetrahydro-benzocyclohepten-5-one (246)(0.7 g) which gave compound (38)(0.26 g, 70%).

<table>
<thead>
<tr>
<th>m.p.</th>
<th>71-72 °C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Analysis</td>
<td>$C_{12}H_{10}O_2$</td>
</tr>
<tr>
<td>Found</td>
<td>C 77.59%</td>
</tr>
<tr>
<td>Required</td>
<td>C 77.42</td>
</tr>
</tbody>
</table>

$^1$H N.M.R. (100 MHz, CDC$_3$) $^6$

- 8.52-8.43 d 1H H on C4 $J_{3,4}=$ 9.0 Hz
- 7.40-6.90 m 5H Other protons
- 6.70-6.50 m 1H H on C8
- 3.90 s 3H OCH$_3$
I.R. \( \nu_{\text{max}} \) (CHCl\(_3\)) 1640(CO), 1615, 1580, 1320
1280, 1120 cm\(^{-1}\)

U.V. \( \lambda_{\text{max}} \) \( (\log_{10} e)(\text{EtOH}) \)
232 (4.29), 277 (4.44),
325 (3.58), 350 (3.40) n.m.

\(^{13}\)C N.M.R. (CDCl\(_3\)) \( \delta \) (multiplicity)
186.9(s), 162.1(s), 138.9 (d)
137.7(s), 136.5(d), 134.5 (d)
133.1(d), 132.6(s), 126.7 (d)
117.9(d), 115.6(d), 55.3 (q) p.p.m.

Band (II) \( (R_f=0.38) \) was obtained as yellow needles,
which were crystallised from methanol to give
2-methoxy-6-bromo-5H-benzocyclohepten-5-one(247) (1.15 g)
m.p. 156-157 °C

Analysis

\[ \text{C}\_{12}\text{H}_{9}\text{Br}_2 \text{O}_2 \]

\[
\begin{align*}
\text{Found} & : C \ 54.25\% \quad H \ 3.40\% \\
\text{Required} & : C \ 54.33\% \quad H \ 3.51
\end{align*}
\]

\(^1\)H N.M.R. (100MHz,CDCl\(_3\)) \( \delta \)
8.56-8.47 d 1H H on C4
7.95-7.85 dd 1H H on C7
7.34-7.25 dd 1H H on C9
7.32-7.20 dd 1H H on C3
7.06-7.03 d 1H H on C1
6.60-6.40 dd 1H H on C8
\[ J_{1,5}=2.4 \text{ Hz}, \ J_{3,4}=9.0 \text{ Hz}, \ J_{7,6}=9.0 \text{ Hz}, \ J_{7,9}=9.73 \text{ Hz} \]
\[ J_{8,9}=11.7 \text{ Hz} \]
3.94 s 3H OCH\(_3\)
Photolysis of 2-methoxy-5H-benzocyclohepten-5-one (38)

A solution of compound (11) (0.74 g) in methanol (800 ml) was irradiated by a Hanovia medium pressure lamp, through a pyrex filter and under a nitrogen atmosphere for 36 hrs. Removal of solvent gave a brown gum, which was separated by p.l.c. (ethyl acetate-toluene, 10:90) into 3 bands:

Band (I) - starting material (38) (0.18 g).
Band (II) - polmeric material (0.42 g).
Band (III) (Rf = 0.55) was triturated with ether giving a small quantity of pale yellow material, which was identified to be the photochemical isomer, 4-methoxy-2a, 7a-dihydrocyclobut(a)inden-7-one (340) (0.06 g, 8%)

Analysis: $C_{12}H_{10}O_2$

Found: C 77.35% H 5.44%
Required: C 77.42% H 5.38%

$^1H$ N.M.R. (CDCl$_3$) $\delta$

<table>
<thead>
<tr>
<th>$\delta$</th>
<th>Multiplicity</th>
<th>Assignments</th>
<th>$J$ (Hz)</th>
</tr>
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<tbody>
<tr>
<td>7.72-7.56</td>
<td>d 1H</td>
<td>H on C6</td>
<td>$J_{5,6} = 9$ Hz</td>
</tr>
<tr>
<td>6.96-6.76</td>
<td>m 2H</td>
<td>2H on C5  and C3</td>
<td></td>
</tr>
<tr>
<td>6.56-6.52</td>
<td>m 1H</td>
<td>H on C2</td>
<td>$J_{1,2} = 3$ Hz</td>
</tr>
<tr>
<td>6.36-6.28</td>
<td>dd 1H</td>
<td>H on C1</td>
<td>$J_{1,7a} = 1.2$ Hz</td>
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<tr>
<td>4.28-4.22</td>
<td>d 1H</td>
<td>H on C2a</td>
<td>$J_{2a,7a} = 3$ Hz</td>
</tr>
<tr>
<td>3.91-3.74</td>
<td>m 4H</td>
<td>OCH$_3$ and H on C7a</td>
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</tr>
</tbody>
</table>
Photolysis of 2-methoxy-6-bromo-5H-benzocyclohepten-5-one (247)

Carried out as described above for compound (38) on compound (247) (0.8 g) irradiating for 80 hrs. Removal of solvent gave some starting material (247) (0.1 g) and a brown polymeric material from which nothing could be isolated.

4-Benzoyl-n-butyric acid (249)

4-Benzoyl-n-butyric acid (249) prepared in 45% yield from glutaric anhydride (248) (100 g), benzene (453 g) and aluminium chloride (258 g) as described by Somerville and Allen.

m.p. 126 °C  Lit 126-127 °C

$^1$H N.M.R. (CDCl$_3$) δ

<table>
<thead>
<tr>
<th>Chemical Shift (δ)</th>
<th>Multiplicity</th>
<th>Number of Protons</th>
</tr>
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<tbody>
<tr>
<td>10.0</td>
<td>s</td>
<td>1H CO$_2$H</td>
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<tr>
<td>8.2-7.7</td>
<td>m</td>
<td>3H on C2, C4 and C6</td>
</tr>
<tr>
<td>7.5-7.1</td>
<td>m</td>
<td>2H on C3 and C5</td>
</tr>
<tr>
<td>3.1-2.9</td>
<td>t</td>
<td>2H CH$_2$CO$_2$H</td>
</tr>
<tr>
<td>2.6-1.8</td>
<td>m</td>
<td>4H Other protons</td>
</tr>
</tbody>
</table>

I.R. $v_{\text{max}}$ (CHCl$_3$) 1705 and 1685 cm$^{-1}$

5-Phenylvaleric acid (250)

A mixture of hydrazine hydrate (143.6 g) in water (56 ml) and potassium hydroxide (148.2 g) was added to solution of 4-benzoyl-n-butyric acid (249) (123 g) in 2,2'-dihydroxydiethyl ether (1664 ml) and left refluxing for 1 hr. The condenser was removed and the excess hydrazine and water distilled off until the temperature of the
solution had reached 184-200 °C, and refluxing was continued for about 3 hrs. The mixture was cooled, poured into a mixture excess HCl and ice and then extracted with ether and dried (MgSO₄). Removal of ether and distillation of the residue under reduced pressure gave compound (250) (72.4 g, 63.5 %)

b.p. 145-150 °C/0.35 mm Hg Lit⁸⁶ 186 °C/0.65 mm Hg

¹H N.M.R. (CCl₄) δ

9.15 s 1H CO₂H
7.2 s 5H Aromatic protons
2.8-2.2 m 4H ArCH₂ and CH₂CO₂H
1.9-1.5 m 4H CH₂CH₂

I.R. νmax (CHCl₃) 1705(CO), 1280 cm⁻¹

6,7,8,9-Tetrahydro-5H-benzocyclohepten-5-one (6)

Compound (6) prepared in 77% from 5-phenylvaleric acid (250) (30 g), phosphorus pentoxide (181 g) and orthophosphoric acid (116 ml) as described for compound (11)

b.p. 77-79 °C/0.1 mm Hg Lit⁸⁶ 77-79 °C/0.1 mm Hg

¹H N.M.R. (CCl₄) δ

7.8-7.5 m 1H H on C4
7.4-6.9 m 3H 3H on C1, C2 and C3
3.0-2.4 m 4H 4H on C6 and C9
2.0-1.6 m 4H 4H on C7 and C8

I.R. νmax (Neat) 1675(CO), 1600 and 1260 cm⁻¹

3-Nitro-6,7,8,9-tetrahydro-5H-benzocyclohepten-5-one (15)

Compound (15) prepared in 85% yield as a white solid from compound (6) (6 g) and fuming nitric acid (17.5 ml) (note 1).

m.p. 92-93 °C Lit⁸⁹ 92-92.8 °C
Note one

If the temperature was suddenly raised a yellow gas evolved and after pouring the mixture into ice-water a pale brown solid precipitated and filtered. The crude product was crystallised from water to give 2-(3-carboxypropyl)-5-nitrobenzoic acid (15a) (5.9 g, 62%).

m.p. 122-123 °C

Analysis C₁₁H₁₁NO₆

<table>
<thead>
<tr>
<th>Found</th>
<th>C 52.25%</th>
<th>H 4.31%</th>
<th>N 5.89%</th>
</tr>
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<tbody>
<tr>
<td>Required</td>
<td>C 52.17</td>
<td>H 4.35</td>
<td>N 5.53</td>
</tr>
</tbody>
</table>

¹H N.M.R. (CDCl₃)  δ

- 10 s 2H 2(CO₂H)
- 8.40 d 1H H on C6  J₆,₄=2 Hz
- 8.20-8.05 dd 1H H on C4  J₃,₄=8 Hz
- 7.35-7.20 d 1H H on C3
- 3.10-2.55 m 4H ArCH₂ and CH₂CO₂H
- 2.15-1.78 m 2H CH₂
3-Amino-6,7,8,9-tetrahydro-5H-benzocyclohepten-5-one (253)

The method of Johnston, Povall and Entwistle was employed. Cyclohexene (41 g) and palladium 10% on charcoal (2 g) were added to the compound (15) (12.5 g) dissolved in ethanol (350 ml). The reaction mixture was heated vigorously under reflux. After 18 hrs, examination of t.l.c. plate showed one component, indicating that the reaction had reached completion. The catalyst was filtered off and washed with hot ethanol. The solvent was evaporated off and the residue was crystallised from ethanol to give the pure compound (253) (8.5 g, 80%) as brownish yellow crystals.

m.p. 103-104 °C

H N.M.R. (CDCl₃) δ

- 6.98-6.94 d 1H H on C4 J₂,₄=3 Hz
- 6.84-6.70 d 1H H on C1 J₁,₂=8 Hz
- 6.70-6.54 dd 1H H on C2
- 3.80-3.50 s 2H NH₂
- 2.90-2.54 m 4H 4H on C6 and C9
- 1.90-1.60 m 4H 4H on C7 and C8

3-Hydroxy-6,7,8,9-tetrahydro-5H-benzocyclohepten-5-one (254)

Prepared in 76% yield from compound (253) as described by Smith and Berry.

m.p. 98-99 °C

Lit 98-99 °C

3-Methoxy-6,7,8,9-tetrahydro-5H-benzocyclohepten-5-one (255)

Prepared in 90% yield from compound (254) as described by Khan, Proctor and Rees.

b.p. 105-107 °C/0.1 mm Hg

Lit 120-124 °C/0.4 mm Hg
6,6-Dibromo-3-methoxy- and 6-bromo-3-methoxy-
-5H-6,7,8,9-tetrahydrobenzocyclohepten-5-one (256 and 256a)

A stirred solution of the methoxyketone(255)(1.3 g) in tetrahydrofuran(50 ml) was treated with PTAB(7 g) over a period of several hrs, and the mixture stirred overnight. After addition of a few drops of acetone, the filtered solution was evaporated. An $^1$H N.M.R. spectrum of the crude product showed some monobrominated derivatives to be present. Separation of the mixture on a chromatotron (petroleum eluent) gave the two products.

6-Bromo-3-methoxy-5H-6,7,8,9-tetrahydrobenzocyclohepten-5-one(256a).

b.p.(bulb tube) 130 $^0$C /0.05 mmHg

Analysis $C_{12}H_{13}BrO_2$

Found  C 53.2%  H 5.0%

Required  C 53.55  H 4.85

$^1$H N.M.R. (CDCl$_3$)

7.3-6.8  m  3H  Aromatic protons
5.0-4.7  dd  1H  CHBr
3.8  s  3H  OCH$_3$
3.0-2.7  m  2H  ArCH$_2$
2.6-1.7  m  4H  CH$_2$CH$_2$

6,6-Dibromo-3-methoxy-5H-6,7,8,9-
tetrahydrobenzocyclohepten-5-one(256) (1.5 g 63%).

b.p.(bulb tube) 140 $^0$C /0.05 mmHg
Analysis

\[
\begin{array}{ccc}
\text{C}_{12}\text{H}_{12}\text{Br}_{2}\text{O}_{2} & \\
\text{Found} & \text{C} & 41.4\% \\
& \text{H} & 3.45\%
\end{array}
\]

\[
\begin{array}{ccc}
\text{Required} & \text{C} & 41.4 \\
& \text{H} & 3.45
\end{array}
\]

\[^1\text{H N.M.R.} \quad (\text{CDCl}_3) \delta\]

7.2-6.9 \quad m \quad 3H \quad \text{Aromatic protons}

3.8 \quad s \quad 3H \quad \text{OCH}_3

3.0-2.5 \quad m \quad 4H \quad 4H \text{ on C7 and C9}

2.2-1.7 \quad m \quad 2H \quad 2H \text{ on C8}

3-Methoxy-5H-benzocyclohepten-5-one (234)

Dehydrobromination using lithium carbonate (1 g) and dibromoketone (256) (1 g) in DMF (50 ml) gave after work-up an oil, separated on a chromatotron (eluent, ethyl acetate-petroleum, 1:9) to give the 3-methoxybenzopone (0.49 g, 91%).

b.p. (bulb tube) \quad 105-110^\circ \text{C}/0.05 \text{ mmHg}

\[^1\text{H N.M.R.} \quad (\text{C}_6\text{H}_6-\text{D}_6) \delta\]

8.0 \quad d \quad 1H \quad \text{H on C4}

7.6 \quad d \quad 1H \quad \text{H on C1} \quad J_{1,2}=8.6 \text{ Hz}

7.35-7.25 \quad d \quad 1H \quad \text{H on C9} \quad J_{8,9}=11.3 \text{ Hz}

7.3-7.2 \quad dd \quad 1H \quad \text{H on C2} \quad J_{2,4}=3 \text{ Hz}

7.1-7.0 \quad m \quad 2H \quad 2H \text{ on C6 and C7} \quad J_{6,7}=12.1 \text{ Hz}

6.7-6.5 \quad ddd \quad 1H \quad \text{H on C8} \quad J_{7,8}=7 \text{ Hz} \quad J_{6,8}=2.2 \text{ Hz}

\[\text{I.R. } \nu_{\text{max}} \quad (\text{Neat}) \quad 1645 \text{ and } 1600 \text{ cm}^{-1}\]

\[\text{U.V. } \lambda_{\text{max}} \quad (\log_{10} \epsilon) \quad (\text{EtOH})\]

375 (3.80), 333 (3.94), 320 (3.98),

250 (4.47), 233 (4.46) n.m.
Photolysis of 3-methoxy-5H-benzocyclohepten-5-one (234)

Carried out as described above for compound (38) on compound (243) (0.52 g) irradiating for 48 hrs. Removal of the solvent under reduced pressure gave a brown solid. The solid was extracted with diethyl ether and undissolved material filtered off. Evaporation of ether gave a residue, which was purified by bulb distillation (0.05 mm Hg, 128-130 °C) giving the pure 5-methoxy-2a,7a-dihydrocyclobut(a)inden-7-one (341) (0.13 g, 25%).

\[ \text{\(^1H\) N.M.R. (CDCl}_3\) } \delta \\
7.60-7.20 \text{ m } 3H \text{ Aromatic protons} \\
6.75-6.70 \text{ d } 1H \text{ H on C2 } J_{1,2} = 3 \text{ Hz} \\
6.52-6.45 \text{ m } 1H \text{ H on C1} \\
4.47-4.20 \text{ d } 1H \text{ H on C2a } J_{2a,7a} = 3 \text{ Hz} \\
4.10-3.95 \text{ m } 4H \text{ OCH}_3 \text{ and H on C7a} \\
\text{I.R. } v_{\text{max}} \text{ (CHCl}_3) = 1700 \text{ cm}^{-1} \\

\text{Analysis } C_{12}H_{10}O_2 \\
\text{Found } C \ 77.35\% \ H \ 5.60\% \\
\text{Required } C \ 77.40\% \ H \ 5.40\%

2-Methoxycinnamylidenemalonic acid (257)

This compound prepared in 82% yield, as described for the compound (237), from 2-methoxybenzaldehyde (6.8 g) and diethyl ethylidenemalonate (257) (18.7 ml). The product (257) crystallised from benzene-ethyl acetate.
m.p. 201-202 °C  Lit92 201-202 °C

Analysis C_{13}H_{12}O_{5}

Found C 62.64%  H 4.68%

Required C 62.90%  H 4.83%

^1H N.M.R. (DMSO-D_6) δ
9.28-8.9  s  2H  2 CO_2H
8.10-6.76  m  7H Other protons
3.85  s  3H OCH_3

I.R. ν_max (Nujol) 1725(CO), 1635, 1605 and 1385 cm^{-1}

3-(2-Methoxyphenyl)propylmalonic acid (258)

This compound prepared in 98% yield, as described for the compound (238), from hydrogenation of compound (257).

m.p. 115 °C  Lit92 115-116 °C

^1H N.M.R. (CDCl_3) δ
10.25  s  2H  2 CO_2H
7.12-6.68  m  4H Aromatic protons
3.72  s  3H OCH_3
3.55-3.25  m  1H CH
2.80-2.40  m  2H ArCH_2
2.10-1.55  m  4H (CH_2)_2

I.R. ν_max (Nujol) 1745-1700(CO), 1600, 1250 cm^{-1}

5-(2-Methoxyphenyl)valeric acid (259)

This compound prepared in 83% from the compound (258) by distillation in vacuo.

b.p. 136-140 °C/0.25 mm Hg
m.p. 82-83 °C  Lit92 78-81 °C
\[ ^1H\text{N.M.R. (CDCl}_3\text{) } \delta \]

10.30   s   1H   CO\textsubscript{2}H
7.3-6.2 m   4H   Aromatic protons
3.7     s   3H   OCH\textsubscript{3}
2.7-2.2 m   4H   ArCH\textsubscript{2} and CH\textsubscript{2}CO\textsubscript{2}H
1.8-1.5 m   4H   CH\textsubscript{2}CH\textsubscript{2}

I.R. \( \nu_{\max} \) (CHCl\textsubscript{3}) 1707(CO) and 1280 cm\textsuperscript{-1}

Attempted cyclization of

5-(2-methoxyphenyl)valeric acid (259)

Cyclization was carried out, as described for compound (11), from 5-(2-methoxyphenyl)valeric acid (259) (5.1 g), phosphorus pentoxide (22.6 g) and orthophosphoric acid (14.5 ml). On addition of mixture into an ice-water the colour changed to purple. The flocculent mixture was extracted with benzene and dried over magnesium sulphate and the solvent was evaporated off. The residue was chromatographed on alumina (IV), eluting with toluene-petroeum ether (30:70) to give white crystals. The \(^1H\text{N.M.R.} \) suggested that the compound formed was a dimer (260) (2.55 g, 56%) which was crystallized from benzene.

\begin{align*}
\text{m.p.} & \quad 203-205 \degree C \\
\text{Analysis} & \quad C_{24}H_{28}O_4 \\
\text{Found} & \quad C \ 75.48\% \quad H \ 7.31\% \\
\text{Required} & \quad C \ 75.48 \quad H \ 7.36 \\
\end{align*}

Lit\textsuperscript{94} 205 \degree C
**N.M.R. (100 MHz, CDCl₃) δ**

8.06-7.95  dd  2H  2H on Ca and Cb  Jₐ,b = 8.5 Hz
7.77-7.95  d  2H  2H on Cc and Cc  Jₐ,c = 2.2 Hz
7.07-7.75  d  2H  2H on Cb and Cb
3.95  s  6H  2( OCH₃ )
2.92-2.55  m  8H  2( CH₂CO ) and 2( ArCH₂)
1.81-1.72  m  8H  2( CH₂CH₂)

I.R. v_max (CHCl₃)  1668 and 1602 cm⁻¹

***

4-Methylanisole (261)

Prepared in 92% yield from p-hydroxytoluene (162 g), dimethyl sulphate (189 g) and sodium hydroxide (60 g) in acetone (400 ml).

b.p.  40 °C/0.25 mm Hg  Lit  174 °C/760 mm Hg

**¹H N.M.R. (CDCl₃) δ**

7.08-6.92  d  2H  2H on C3 and C5  J₂,₃ = 8.6
6.76-6.61  d  2H  2H on C2 and C6
3.66  s  3H  OCH₃
2.24  s  3H  CH₃

5-Methyl-2-methoxybenzaldehyde (262)

Zinc cyanide (52 g) was added to a solution of 4-methylanisole (261) (30 g) in benzene (75 ml). The mixture was cooled, stirring was commenced and dry HCl was passed into the reaction mixture for 1 hr. After this treatment, the reaction was cooled, and stirring continued. Anhydrous aluminium chloride (45 g) was added slowly, HCl was again passed into the reaction
vessel while the mixture was heated at 40-45 °C for 3-4 hrs. The reaction mixture was added to an excess of HCl (10%), this resulted in the precipitation of the imide hydrochloride. The mixture was refluxed for 1 hr, this caused rapid decomposition with the formation of an oily product, the aldehyde. The aldehyde (262) was extracted with chloroform, dried over sodium sulphate and finally purified by distillation under reduced pressure (30 g, 80%).

\[
\text{b.p. } 250-252 \degree C \quad \text{Lit}^{96} 250-252 \degree C
\]

\[ ^1H \text{ N.M.R. (CDCl}_3 \] \delta

- 10.4 s 1H CHO
- 7.55 d 1H H on C6 \( J_{4,6}=3 \text{ Hz} \)
- 7.40-7.18 dd 1H H on C4 \( J_{3,4}=10 \text{ Hz} \)
- 6.82-6.75 d 1H H on C3
- 3.86 s 3H OCH\text{3}
- 2.30 s 3H CH\text{3}

**5-Methyl-2-methoxycinnamylidenemalonic acid (263)**

This compound prepared in 76% yield, as described for the compound (237), from 5-methyl-2-methoxybezaldehyde (262), diethyl ethylidenemalonate (236) and base in methanol. The product (263) crystallised from benzene-ethyl acetate.

**Analysis**  
\[ C_{14}H_{14}O_5 \cdot H_2O \]

- Found  C 60.35%  H 6.13%
- Required  C 60.05  H 5.76
m.p. 140 °C

$^1$H N.M.R. (Acetone-$D_6$) $\delta$

- 9.5-9.1 s 2H $\text{C}$(CO$_2$H)$_2$
- 8.10-6.75 m 6H Aromatic protons
- 3.88 s 3H OCH$_3$
- 2.28 s 3H CH$_3$

I.R. $\nu$ max (Nujol) 1710 (CO), 1612 and 1230 cm$^{-1}$

3-(2-Methoxy-5-methylphenyl)propylmalonic acid (264)

This compound prepared in 99% yield, as described for the compound (238), from hydrogenation of compound (263).

$^1$H N.M.R. (CDCl$_3$) $\delta$

- 10.3 s 2H 2 X CO$_2$H
- 7.2-6.4 m 3H Aromatic protons
- 3.75 s 3H OCH$_3$
- 3.74-3.30 m 2H CH
- 2.75-2.40 m 2H ArCH$_2$
- 2.28 s 3H CH$_3$
- 1.55-2.20 m 4H CH$_2$CH$_2$

5-(2-Methoxy-5-methylphenyl)valeric acid (265)

This compound prepared in 91% yield from the compound (264) by distillation in vacuo.

b.p. 160 °C/0.05 mm Hg
m.p. 47-48 °C

Analysis C$_{13}$H$_{18}$O$_3$

Found C 70.34% H 8.14%
Required C 70.27% H 8.10%
\[ ^1H \text{ N.M.R. } (\text{CDCl}_3) \delta \]

<table>
<thead>
<tr>
<th>Chemical Shift (\text{ppm})</th>
<th>Multiplicity</th>
<th>Proton Count (H)</th>
<th>Assignment</th>
</tr>
</thead>
<tbody>
<tr>
<td>9.01</td>
<td>s</td>
<td>1H</td>
<td>CO\textsubscript{2}H</td>
</tr>
<tr>
<td>7.1-6.6</td>
<td>m</td>
<td>3H</td>
<td>Aromatic protons</td>
</tr>
<tr>
<td>3.72</td>
<td>s</td>
<td>3H</td>
<td>OCH\textsubscript{3}</td>
</tr>
<tr>
<td>2.7-2.3</td>
<td>m</td>
<td>7H</td>
<td>ArCH\textsubscript{2}, CH\textsubscript{2}CO\textsubscript{2}H and CH\textsubscript{3}</td>
</tr>
<tr>
<td>1.8-1.5</td>
<td>m</td>
<td>4H</td>
<td>CH\textsubscript{2}CH\textsubscript{2}</td>
</tr>
</tbody>
</table>

\[ \text{I.R. } \nu_{\text{max}} \ (\text{CHCl}_3) \]

3300-3500 (OH), 1710 (CO), 1600, 1410 and 930 cm\(^{-1}\)

\[ ^1H \text{ N.M.R. } (\text{CDCl}_3) \delta \]

<table>
<thead>
<tr>
<th>Chemical Shift (\text{ppm})</th>
<th>Multiplicity</th>
<th>Proton Count (H)</th>
<th>Assignment</th>
</tr>
</thead>
<tbody>
<tr>
<td>7.00-6.84</td>
<td>d</td>
<td>1H</td>
<td>H on C3 (J_{2,3}=8.4 \text{ Hz})</td>
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<tr>
<td>6.74-6.60</td>
<td>d</td>
<td>1H</td>
<td>H on C2</td>
</tr>
<tr>
<td>3.70</td>
<td>s</td>
<td>3H</td>
<td>OCH\textsubscript{3}</td>
</tr>
<tr>
<td>3.90-2.40</td>
<td>m</td>
<td>4H</td>
<td>ArCH\textsubscript{2} and CH\textsubscript{2}CO</td>
</tr>
<tr>
<td>2.18</td>
<td>s</td>
<td>3H</td>
<td>CH\textsubscript{3}</td>
</tr>
<tr>
<td>1.90-1.50</td>
<td>m</td>
<td>4H</td>
<td>CH\textsubscript{2}CH\textsubscript{2}</td>
</tr>
</tbody>
</table>

\[ \text{I.R. } \nu_{\text{max}} \ (\text{Neat}) \]

1688 (CO), 1594, 1580, 1480, 1430, 1190 cm\(^{-1}\)

\[ \text{1-Methoxy-4-methyl-6,7,8,9-tetrahydro-5H-benzocyclohepten-5-one (266)} \]

Cyclization was carried out, as described for compound (11), from 5-(2-methoxy-5-methylphenyl)valeric acid (265) (4.2 g) phosphorus pentoxide (20.5 g) and orthophosphoric acid (13 ml).

The reaction mixture was poured into ice-water and then extracted with benzene and dried over magnesium sulphate. Removal of the solvent in vacuo gave a residue, which was chromatographed on alumina (IV), eluting with benzene-petroleum ether (20:80) to give the compound (266) (2.0 g, 52%) as a pale yellow liquid.

Analysis

\[ \text{Found: } C_{\text{13}}\text{H}_{16}\text{O}_{2} \]

\[ \text{Required: } C_{\text{13}}\text{H}_{16}\text{O}_{2} \]

Analysis

\[ \text{C} 76.23\% \quad \text{H} 7.62\% \]

\[ \text{Required: } C 76.47 \quad \text{H} 7.89 \]

1-Methoxy-4-methyl-6,7,8,9-tetrahydro-5H-benzocyclohepten-5-one(266)
6,6-Dibromo-1-methoxy-4-methyl-
-6,7,8,9-tetrahydro-5H-benzocyclohepten-5-one (267)

Bromination was carried out, as described for the compound (246), from compound (266) (6.39 g) and phenyltrimethylammonium tribromide (6.4 g) in anhydrous tetrahydrofuran (170 ml). The reaction mixture was then filtered and the insoluble quaternary salt washed with a small portion of dried THF, and the combined filtrates evaporated off under reduced pressure to give a brown oil. The gummy material was chromatographed on alumina (IV), eluting with benzene-petroleum ether (40:60), and then crystallised chloroform-petroleum ether (20:80) to give the pure compound (267) (3.1 g, 98%) as colourless prisms.

m.p. 73-74 °C

Analysis

\[\text{C}_{13}\text{H}_{14}\text{Br}_{2}\text{O}_{2}\]

Found C 43.09%  H 3.78%

Required C 43.12%  H 3.90%

\(^1\text{H N.M.R. (CDCl}_3\) \(\delta\)

- 7.02-6.89 d 1H H on C3  \(J_{2,3}=8.4 \text{ Hz}\)
- 6.79-6.74 d 1H H on C2
- 3.70 s 3H OCH\(_3\)
- 3.50-3.20 m 2H CH\(_2\)Br\(_2\)
- 2.70-2.40 m 2H ArCH\(_2\)
- 2.20 s 3H CH\(_3\)
- 2.02-1.60 m 2H 2H on C8

I.R. \(\nu_{\text{max}}\) (Nujol) 1716 (CO), 1605, 1480, 1385, 1585, 1275 and 975 cm\(^{-1}\).
1-Methoxy-4-methyl-5H-benzocyclohepten-5-one (268)

The mixture of dibromoketone (267) (3.0 g), anhydrous lithium chloride (1.3 g) and anhydrous dimethylformamide (THF) (300 ml) was refluxed and stirred under a nitrogen atmosphere.

The extent of the reaction was followed by U.V. spectroscopy every 30 minutes. After 4 hrs there was no significance differences between the spectra, which indicated that the reaction had reached completion. The mixture was cooled and the DMF removed under reduced pressure. Water was added and the aqueous solution extracted with chloroform. The combined extracts were dried with magnesium sulphate and distilled under reduced pressure to yield a brownish-black gum, which was eventually purified by p.l.c. plates, \( R_f = 0.3 \), ethyl acetate-toluene, 10:90 to give the pure product (268) (1.4 g, 83%) as a pale yellow oil.

Analysis

\[ \text{C}_{13}\text{H}_{12}\text{O}_2 \]

<table>
<thead>
<tr>
<th>Found</th>
<th>C 77.64%</th>
<th>H 6.22%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Required</td>
<td>C 77.97</td>
<td>H 6.04</td>
</tr>
</tbody>
</table>

\[ ^1H \text{ N.M.R. (100 MHz, CDCl}_3 \] \)

| \( \delta \) | Multiplicity | \( J \) | |---|---|---|---|---|
| 7.92-7.87 | dd | \( 1H \) H on C9 | \( J_{8,9} = 11.8 \) Hz, \( J_{7,9} = 1.9 \) Hz |
| 7.35-7.26 | d | \( 1H \) H on C3 | \( J_{2,3} = 8.4 \) Hz |
| 6.95-6.87 | d | \( 1H \) H on C2 |
| 6.81-6.50 | m | \( 3H \) 3H on C6, C7 and C8 |
| 3.86 | s | \( 3H \) OCH\(_3\) |
| 2.41 | s | \( 3H \) CH\(_3\) |

I.R. \( \nu_{\text{max}} \) (CHCl\(_3\))

| 3020, 2970, 2940, 2840, 1650 (CO), 1620 |
| 1590, 1468, 1420, 1415, 1310, 1295, 1270 |
| 1250 and 1115 cm\(^{-1}\) |
U.V. $\lambda_{\text{max}}$ (log$_{10}$ ε) (EtOH)

200(4.25), 235(4.24), 285(3.81) and 338(3.38)

$^{13}$C N.M.R. (CDCl$_3$) δ (multiplicity)

192.8 (s), 154.5 (s), 139.7 (s), 133.3 (d), 133.1 (d), 131.9 (d), 129.0 (d), 128.5 (s), 125.3 (d), 124.5 (s), 110.8 (d), 56.0 (q), 22.9 (q) p.p.m.

Photolysis of 1-methoxy-4-methyl-5H-benzocyclohepten-5-one (268)

Carried out as described above for compound (38) on the compound (268) (0.65 g) irradiating for 26 hrs. Removal of the solvent under reduced pressure gave a brown gum, which was triturated with ether and filtered. The combined filtrates were evaporated under reduced pressure to give a yellow solid, which was chromatographed on p.l.c. plates (R$_f$=0.44, toluene-ethyl acetate, 80:20). The $^1$H N.M.R. spectrum indicated the product to be the photochemical isomer, 3-methoxy-6-methyl-2a,7a-dihydrocyclobuta(a)inden-7-one (339) (0.26 g, 40%).

m.p. 88-89 °C

Analysis C$_{13}$H$_{12}$O$_2$

Found C 77.79% H 6.21%

Required C 77.97% H 6.04
$^1$H N.M.R. (100 MHz, CDCl$_3$) $\delta$

| 7.11-7.02 | d | 1H H on C5 |
| 6.94-6.85 | d | 1H H on C4 |
| 6.65-6.62 | o | 1H H on C2 |
| 6.35-6.31 | dd | 1H H on C1 |
| 4.31-3.92 | m | 1H H on C2a |
| 3.86 | s | 3H OCH$_3$ |
| 3.78-3.74 | o | 1H H on C7a |
| 2.53 | s | 3H CH$_3$ |

$J_{1,2} = 2.44$ Hz, $J_{1,7a} = 0.85$ Hz, $J_{2,2a} = 0.85$ Hz

$J_{2,7a} = 0.37$ Hz, $J_{2a,7a} = 2.80$ Hz, $J_{4,5} = 8.5$ Hz

I.R. $\nu_{\text{max}}$ (CHCl$_3$) $\delta$

3000, 2940, 2830, 1700 (CO),
1585, 1500, 1280 and 1265 cm$^{-1}$

U.V. $\lambda_{\text{max}}$ ($\log_{10} \epsilon$) (EtOH)

201(4.22), 224(4.30) and 262(3.74) n.m.

$^{13}$C N.M.R. (CDCl$_3$) $\delta$ (multiplicity)

203.7 (s), 154.5 (s), 144.5 (d),
142.1 (s), 136.2 (d), 135.3 (s),
131.0 (s), 130.8 (d), 114.8 (d),
55.8 (q), 55.4 (d), 44.1 (d),
17.4 (q) p.p.m.

****

6,6-Dibromo-6,7,8,9-tetrahydro-5H-benzocyclohepten-5-one(17)

Bromine (4 g) in carbon tetrachloride was added dropwise to stirred solution of the bicyclic ketone (6)(2 g) in carbon tetrachloride (20 ml). The solution was boiled for a further one hr, cooled and the solvent removed under reduced pressure. The pure dibromoketone (17) (3.8 g, 91%) was crystallised from petroleum ether as colourless solid.
m.p. 42-44°C  Lit83 42-43°C

1H N.M.R. (CCl4) δ

7.8-7.1 m  4H Aromatic protons
3.0-2.6 m  4H ArCH2 and CBr2CH2
2.3-1.7 m  2H 2H on C8

I.R. v max (CHCl3) 1705(CO) cm⁻¹

5H-Benzocyclohepten-5-one(1)

A mixture of the dibromoketone (17)(3.2 g), anhydrous lithium chloride (1.7 g) and dimethylformamide (DMF) (100 ml) was refluxed and stirred under a nitrogen atmosphere, for 4 hrs. The mixture was cooled, and the DMF removed under reduced pressure. Water was added and the aqueous solution extracted with ether. The combined ethereal extracts were dried over magnesium sulphate and distilled under reduced pressure to give the 5H-benzocyclohepten-5-one (1) (1.4 g, 92%).

b.p. 106°C/0.04 mm Hg  Lit83 110°C/0.2 mm Hg

1H N.M.R. (CDCl3) δ

8.5-8.3 m  1H H on C4
7.7-7.4 m  3H 3H on C1, C2 and C3
7.3-7.1 dd  1H H on C9  J8,9=11.3 Hz, J7,9=1.2 Hz
7.0-6.8 m  2H 2H on C6 and C7
6.7-6.5 m  1H H on C8

I.R. v max (Neat) 1640, 1609 and 1589 cm⁻¹

U.V. λ max (log10ε) (EtOH)

229 (4.33), 260 (s), 307 (s)
320 (3.81), 343 (s) n.m.
Phenolsis of SH-benzocyclohepten-5-one(1)

Carried out as described above for the compound (38) on the SH-benzocyclohepten-5-one(1) (0.78 g). Irradiation was stopped when the concentration of new components remained constant. Evaporation of the solvent left a brown gum, which was separated by p.l.c. (ethyl acetate-toluene, 5:95) into three bands:

(I) -SH-Benzocyclohepten-5-one (1) (0.1 g, Rf = 0.56)
(II) -Polymeric material

Band (III) was triturated with diethyl ether giving a small quantity of solid which had a m.p. of 206-207 °C (Lit\textsuperscript{83}, dimer, m.p. 206-210 °C). The ether soluble material was distilled in a bulb tube to give the photochemical isomer, 2a,7a-dihydrocyclobut(a)inden-7-one(321) (89 mg, 11.4%)

b.p. 80 °C/0.02 mm Hg  Lit\textsuperscript{83} 80 °C/0.02 mm Hg

\textsuperscript{1}H N.M.R. (CDC\textsubscript{13}) \( \delta \)

<table>
<thead>
<tr>
<th>( \delta )</th>
<th>Multiplicity</th>
<th>Assignment</th>
</tr>
</thead>
<tbody>
<tr>
<td>7.7-7.0</td>
<td>m</td>
<td>4H Aromatic protons</td>
</tr>
<tr>
<td>6.5-6.4</td>
<td>d</td>
<td>1H H on C2 ( J_{1,2} = 3 ) Hz</td>
</tr>
<tr>
<td>6.3-6.1</td>
<td>m</td>
<td>1H H on C1</td>
</tr>
<tr>
<td>4.3-4.2</td>
<td>d</td>
<td>1H H on C2a ( J_{2a,7a} = 3 ) Hz</td>
</tr>
<tr>
<td>3.7-3.6</td>
<td>m</td>
<td>1H H on C7a</td>
</tr>
</tbody>
</table>

I.R. \( \nu_{max} \) (CHCl\textsubscript{3}) 1704 cm\textsuperscript{-1}

U.V. \( \lambda_{max} \) \( (\log_{10} \epsilon) \) (EtOH) 215(4.17), 248(3.98) and 295(3.37) n.m.
6,8-Dinitro-5H-benzocyclohepten-5-one (269)

The tropone (1) (0.65 g) was added to concentrated sulphuric acid (20 ml) and nitric acid (5 ml), the solution was kept at room temperature for 24 hrs. The mixture was poured on ice, filtered and then washed with water. The pure dinitro compound (269) (0.5 g, 50%), was chromatographed on alumina (IV), eluting with ethyl acetate, which was then crystallised from acetic acid.

m.p. 163-165 °C

\(^1\)H N.M.R. (DMSO-D\(_6\)) \(\delta\)
- 9.00-8.95 \(d\) 1H H on C7 \(J_{7,9} = 1.2\) Hz
- 8.64-8.58 \(d\) 1H H on C9
- 8.50-8.30 \(m\) 1H H on C4
- 8.10-7.50 \(m\) 3H 3H on C1, C2 and C3

I.R. \(\nu_{max}\) (Nujol) 1525 and 1332 cm\(^{-1}\)

Photolysis of 6,8-dinitro-5H-benzocyclohepten-5-one (269)

Carried out as described above for the compound (38) on the compound (269) (0.5 g) irradiating for 72 hrs. Removal of the solvent gave some starting material (269) (0.04 g) and a brown polymeric material from which nothing could be isolated.

6,6-Dibromo-3-nitro-6,7,8,9-tetrahydro-5H-benzocyclohepten-5-one (18)

A solution of bromine (1.6 g) in carbon tetrachloride (20 ml) was added dropwise to stirred solution of the nitroketone (15) (2 g) in carbon tetrachloride (200 ml). Stirring was continued for a further 15 hrs, and then the solvent removed under reduced pressure, and the residue was crystallised from ethanol to give the dibromonitroketone (18) (3.3 g, 91%).
3-Nitro-5H-benzocyclohepten-5-one (20)

Prepared as described for 5H-benzocyclohepten-5-one (1), from the dibromoketone (18) (3.6 g), lithium chloride (1.7 g) and dry DMF (200 ml). The nitrobenzocycloheptenone (20) (1.5 g, 75%) was crystallised from methanol as pale yellow needles.

**N.M.R. (100 MHz, CDCl₃) δ**

- 9.26-9.23 d 1H H on C4 J₂,₄ = 2.4 Hz
- 8.49-8.38 dd 1H H on C2 J₁,₂ = 8.7 Hz
- 7.86-7.77 d 1H H on C1
- 7.43-6.86 m 4H H on C6-9

**I.R. v max (CDCl₃) 1641, 1602 and 1584 cm⁻¹**

**U.V. λ max (log₁₀ e) (EtOH)**

- 219(4.31), 253(4.30), 346(4.20) n.m.

**13C N.M.R. (CDCl₃) δ (multiplicity)**

- 186.1(s), 148.0(s), 139.8(s), 139.3(s), 137.0(d), 136.6(d), 135.4(d), 134.9(d), 129.8(d), 126.4(d), 125.7(d) p.p.m.
Photolysis of 3-nitro-5H-benzocyclohepten-5-one (20)

Carried out as described above for the compound (38) on 3-nitro-5H-benzocyclohepten-5-one (20) (0.60 g). Monitoring of the photolysis by t.l.c. and $^1$H N.M.R. examination showed decreasing amounts starting material with formation of only polymeric material. Finally after 96 hrs irradiation some starting material (20) (0.09 g) and a brown polymeric material remained.

3-Amino-5H-benzocyclohepten-5-one (270)

A mixture of cyclohexene (8.2 g), palladium 10% on charcoal and 3-nitro-5H-benzocyclohepten-5-one (20) (2 g) in ethanol (350 ml) was heated vigorously under reflux. After 15 hrs, examination by t.l.c. plate indicated that the reaction had reached completion. The catalyst was filtered and washed with hot ethanol. The solvent was evaporated under reduced pressure to yield the crude product, which was crystallised from ethanol to give the aminobenzocycloheptenone (270) (1.4 g, 79%) as reddish brown prisms.

m.p. 150-152 °C

Analysis $C_{11}H_9NO$

<table>
<thead>
<tr>
<th>Found</th>
<th>Required</th>
</tr>
</thead>
<tbody>
<tr>
<td>C 76.98%</td>
<td>C 77.19</td>
</tr>
<tr>
<td>H 5.17%</td>
<td>H 5.26</td>
</tr>
<tr>
<td>N 8.29%</td>
<td>N 8.19</td>
</tr>
</tbody>
</table>
Photolysis of 3-amino-5H-benzocyclohepten-5-one (270)

The 3-amino-5H-benzocyclohepten-5-one (270) (0.7 g) in methanol (800 ml) was irradiated for 17 hrs. Removal of the solvent gave a light brown polymeric material from which nothing could be isolated.
3-Acetamido-6,7,8,9-tetrahydro-5H-benzocyclohepten-5-one (16)

This compound prepared in 80% yield from the aminoketone (253) (2.1 g) in pyridine (30 ml) and acetyl chloride (1.9 g). The pale yellow solid was filtered and washed with water, and crystallised from ethanol to give the pure acetamidoketone (16).

<table>
<thead>
<tr>
<th>m.p.</th>
<th>103-104 °C</th>
<th>Lit89 103-104 °C</th>
</tr>
</thead>
<tbody>
<tr>
<td>1H N.M.R. (CDCl₃) δ</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9.35</td>
<td>s</td>
<td>1H</td>
</tr>
<tr>
<td>7.85-7.60</td>
<td>m</td>
<td>2H</td>
</tr>
<tr>
<td>7.05-6.90</td>
<td>d</td>
<td>1H</td>
</tr>
<tr>
<td>2.95-2.50</td>
<td>m</td>
<td>4H</td>
</tr>
<tr>
<td>2.20</td>
<td>s</td>
<td>3H</td>
</tr>
<tr>
<td>1.90-1.55</td>
<td>m</td>
<td>4H</td>
</tr>
<tr>
<td>I.R. νₘₐₓ (CHCl₃)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3416, 3320 and 1675 cm⁻¹</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

3-Acetamido-6,6-dibromo-6,7,8,9-tetrahydro-5H-benzocyclohepten-5-one (19)

This compound prepared in 82% yield from the acetamidoketone (16) (2.2 g) in tetrahydrofuran (150 ml), and phenyltrimethylammonium tribromide (7.5 g) as described for the compound (246). It was crystallised from ethanol.

<table>
<thead>
<tr>
<th>m.p.</th>
<th>136-138 °C</th>
<th>Lit85 136-138 °C</th>
</tr>
</thead>
<tbody>
<tr>
<td>1H N.M.R. (CDCl₃) δ</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8.5</td>
<td>s</td>
<td>1H</td>
</tr>
<tr>
<td>8.3-7.1</td>
<td>m</td>
<td>3H</td>
</tr>
<tr>
<td>3.0-2.5</td>
<td>m</td>
<td>4H</td>
</tr>
<tr>
<td>2.18</td>
<td>s</td>
<td>3H</td>
</tr>
<tr>
<td>2.4-1.8</td>
<td>m</td>
<td>2H</td>
</tr>
</tbody>
</table>
3-Acetamido-5H-benzocyclohepten-5-one(21)

Method one

The acetamidodibromoketone(19)(1.9 g) was dehydrobrominated with lithium chloride (0.84 g) in boiling dimethylformamide (300 ml) in the usual way giving the acetamidobenzocycloheptenone(21) as yellow needles (1 g 95%). It was crystallised from methanol.

Method two

Acetyl chloride (0.9 g) was added dropwise to an ice-cooled solution of the 3-amino-5H-benzocyclohepten-5-one(270)(1 g) in pyridine (20 ml). The reaction mixture was left stirring for 2 hrs, then the mixture poured into a mixture of ice and HCl. The yellow crystals were filtered and washed with water and crystallised from methanol to give the compound(21) (1 g, 82%).

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
<th>Literature</th>
</tr>
</thead>
<tbody>
<tr>
<td>Analysis</td>
<td>C_{15}H_{11}NO_{2}</td>
<td></td>
</tr>
<tr>
<td>Found</td>
<td>C 73.38%</td>
<td>H 5.08%</td>
</tr>
<tr>
<td>Required</td>
<td>C 73.24%</td>
<td>H 5.16%</td>
</tr>
<tr>
<td>N 6.28%</td>
<td></td>
<td>N 6.57%</td>
</tr>
<tr>
<td>m.p.</td>
<td>214-215 °C</td>
<td>Lit^83 214-215 °C</td>
</tr>
<tr>
<td>I.R. \nu_{\text{max}} (CHCl_3)</td>
<td>3416, 3310, 1690, 1640 and 1612 cm^{-1}</td>
<td></td>
</tr>
<tr>
<td>U.V. \lambda_{\text{max}} (log_{10} e)(EtOH)</td>
<td>207 (4.04), 242 (4.42), 330 (3.99) and 375 (3.72) n.m.</td>
<td></td>
</tr>
</tbody>
</table>
$^{13}$C N.M.R. (DMSO-\textsubscript{D$_6$}) $\delta$ (multiplicity)

185.9 (s), 168.5 (s), 141.4 (s),
138.8 (s+d) two overlapping resonances,
136.0 (d), 135.5 (d), 133.8 (d),
130.7 (s), 124.7 (d), 122.9 (d),
118.2 (d), 24.0 (q) p.p.m.

**Photolysis of 3-acetamido-5H-benzocyclohepten-5-one(21)**

Carried out as described above for the compound (38) on the acetamidobenzocycloheptenone(21) (0.43 g) irradiating for 30 hrs when the concentration of new component remained constant. Removal of the solvent under reduced pressure gave a brown gum, which was triturated with ether and filtered. The combined filtrate was evaporated under reduced pressure to give a pale yellow solid, which was chromatographed on p.l.c. plates (R$_f$=0.18, toluene-ethyl acetate,90:10).

The $^1$H N.M.R. spectrum indicated the product to be the photochemical isomer,

3-acetamido-2a,7a-dihydrocyclob(a)inden-7-one(342) (0.15 g, 35%).

m.p. 173-174 $^0$C

Analysis C$_{15}$H$_{11}$NO$_2$

Found C 73.12% H 5.17% N 6.76%

Required C 73.24 H 5.16 N 6.57
\( ^1\text{H N.M.R. (100 MHz, CDCl}_3 \) \( \delta \)

\begin{align*}
9.0 & \quad s & 1\text{H} & \text{NH} \\
8.01-7.91 & \quad dd & 1\text{H} & \text{H on C4} & J_{3,4} = 8.3 \text{ Hz} \\
7.79-7.77 & \quad d & 1\text{H} & \text{H on C6} & J_{4,6} = 2 \text{ Hz} \\
7.40-7.32 & \quad d & 1\text{H} & \text{H on C3} \\
6.59-6.56 & \quad d & 1\text{H} & \text{H on C2} & J_{1,2} = 2.5 \text{ Hz} \\
6.29-6.26 & \quad dd & 1\text{H} & \text{H on C1} & J_{1,7\alpha} = 0.98 \text{ Hz} \\
4.29-4.26 & \quad d & 1\text{H} & \text{H on C2a} & J_{2a,7\alpha} = 2.9 \text{ Hz} \\
3.82-3.79 & \quad dd & 1\text{H} & \text{H on C7a} \\
2.08 & \quad s & 3\text{H} & \text{CH}_3
\end{align*}

\( ^1\text{H N.M.R. (100 MHz, CDCl}_3 \) \( \delta \)

1. R. \( \nu_{\text{max}} \) (CHCl \( _3 \))

\( 3430, 1710-1685 \text{(CO), 1615, 1370, 1325 and 1295 cm}^{-1} \)

U.V. \( \lambda_{\text{max}} \) (log \( _{10} \) \( \epsilon \)) (EtOH)

\( 224 (4.40), 247 (4.14), \) and \( 306 (4.05) \) n.m.

\( ^{13}\text{C N.M.R. (Acetone-D}_6 \) \( \delta \) (multiplicity)

\begin{align*}
201.9 & \quad (s), 169.0 \quad (s), 148.6 \quad (s), \\
146.5 & \quad (d), 140.2 \quad (s), 138.5 \quad (s), \\
136.5 & \quad (d), 127.0 \quad (d), 126.4 \quad (d), \\
115.0 & \quad (d), 56.7 \quad (d), 48.1 \quad (d), \\
24.1 & \quad (q) \quad \text{p.p.m.}
\end{align*}

******

3-Amino-2,4,6,6-tetrabromo-
-6,7,8,9-tetrahydro-5H-benzocyclohepten-5-one (271)

Bromine (6.4 g) in carbon tetrachloride (20 ml) was added dropwise into stirred solution of the aminoketone (253) (1.8 g) in carbon tetrachloride (100 ml). After addition, stirring was continued for a further 12 hrs. Evaporation of the solvent under reduced pressure and removal of the acidic
material (HBr) with 5% sodium hydrogen carbonate allowed extraction with dichloromethane. The combined extracts were dried with sodium sulphate and distilled off to the crude aminotetrabromoketone (271) (3.5 g, 71%) as a brown oily material.

\[ ^1H \text{N.M.R. (CDCl}_3 \text{)} \delta \]

<table>
<thead>
<tr>
<th>δ</th>
<th>1H</th>
<th>2H</th>
</tr>
</thead>
<tbody>
<tr>
<td>7.10</td>
<td>s</td>
<td>H on C1</td>
</tr>
<tr>
<td>4.72</td>
<td>s</td>
<td>NH$_2$</td>
</tr>
<tr>
<td>2.82-2.35</td>
<td>m</td>
<td>4H on C7 and C9</td>
</tr>
<tr>
<td>2.10-1.72</td>
<td>m</td>
<td>2H on C4</td>
</tr>
</tbody>
</table>

I.R. $\nu_{\text{max}}$ (CHC$_3$)$_3$ 1728 (CO), 1575 cm$^{-1}$

3-Amino-2,4-dibromo-5H-bezocyclohepten-5-one (272)

The aminotetrabromoketone (271) (3.5 g) was subsequently dehydrobrominated with lithium chloride (1.2 g) in boiling dimethylformamide (150 ml) in the usual way giving the 3-amino-2,4-dibromo-5H-benzocyclohepten-5-one (272) (0.94 g, 40%), which was chromatographed on alumina (IV), eluting with petroleum ether-ethyl acetate (90:10). It was crystallised from methanol.

m.p. 78-79°C

Analysis $C_{11}H_{7}Br_{2}NO$

<table>
<thead>
<tr>
<th>Found</th>
<th>Required</th>
</tr>
</thead>
<tbody>
<tr>
<td>C 39.47%</td>
<td>C 40.12%</td>
</tr>
<tr>
<td>H 2.23%</td>
<td>H 2.12%</td>
</tr>
<tr>
<td>N 4.21%</td>
<td>N 4.25%</td>
</tr>
</tbody>
</table>
Photolysis of 3-amino-2,4-dibromo-5H-benzocyclohepten-5-one (272)

The aminodibromobenzocycloheptenone (272) (0.5 g) in methanol (800 ml) was irradiated for 20 hrs in the usual way as described for the compound (38). Removal of the solvent gave a light brown polymeric material from which nothing could be isolated.

********

m-Nitrocinnamylidenemalonic acid (273)

This compound prepared in 79% yield, as described for the compound (237), from m-nitrobenzaldehyde (22.7 g), diethyl ethyldienemalonate (236) (39 ml) and base in methanol. The product (273) crystallised from benzene-ethyl acetate.

m.p. 156 °C

\[ ^1H \text{N.M.R. (Acetone-D}_6\text{)} \delta \]

<table>
<thead>
<tr>
<th>δ (ppm)</th>
<th>Multiplicity</th>
<th>J (Hz)</th>
<th>Assignments</th>
</tr>
</thead>
<tbody>
<tr>
<td>9.52</td>
<td>s</td>
<td></td>
<td>2H C(CO\textsubscript{2}H\textsubscript{2})</td>
</tr>
<tr>
<td>8.45</td>
<td>m</td>
<td></td>
<td>1H H on C2</td>
</tr>
<tr>
<td>8.23-8.12</td>
<td>m</td>
<td></td>
<td>1H H on C4</td>
</tr>
<tr>
<td>7.98-7.62</td>
<td>m</td>
<td></td>
<td>5H Other protons</td>
</tr>
</tbody>
</table>

I.R. \( \nu_{\text{max}} \) (Nujol) 1725,1605,1520 and 1345 cm\(^{-1}\)
3-(m-Aminophenyl)propylmalonic acid (274)

This compound (274) prepared in 92% yield, as described for the compound (238), from hydrogenation of m-nitrocinnamylidenemalonic acid (273) (13 g). It was crystallised from methanol.

m.p. 146-147 °C

Analysis

<table>
<thead>
<tr>
<th></th>
<th>Found</th>
<th>Required</th>
</tr>
</thead>
<tbody>
<tr>
<td>C12H15NO4</td>
<td>C 60.73%</td>
<td>H 6.44%</td>
</tr>
<tr>
<td></td>
<td>C 60.75</td>
<td>H 6.37</td>
</tr>
</tbody>
</table>

1H N.M.R. (DMSO- D6) δ

<p>| | | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>8.70</td>
<td>s</td>
<td>4H</td>
<td>2 x CO₂H and NH₂</td>
</tr>
<tr>
<td>7.0-6.2</td>
<td>m</td>
<td>4H</td>
<td>Aromatic protons</td>
</tr>
<tr>
<td>3.7-3.4</td>
<td>m</td>
<td>1H</td>
<td>CH</td>
</tr>
<tr>
<td>3.1-2.6</td>
<td>m</td>
<td>2H</td>
<td>ArCH₂</td>
</tr>
<tr>
<td>2.4-1.8</td>
<td>m</td>
<td>4H</td>
<td>CH₂CH₂</td>
</tr>
</tbody>
</table>

I.R. νₘₐₓ (Nujol) 1680-1550 (CO) cm⁻¹

5-(m-Acetamidophenyl)valeric acid (275)

3-(m-Aminophenyl)propylmalonic acid (274) (10.7 g) was placed in a Claisen distillation flask and decarboxylated by heating in vacuo. To the resulting crude product (5-(m-aminophenyl)valeric acid) was added water (25 ml) and acetic anhydride (25 ml), and the mixture was warmed on a steam bath for 1 hr. The solution was cooled and filtered. The expected product was washed with water and crystallised from aqueous ethanol to give the valeric acid (275) (6.4 g, 68%).

m.p. 138-139 °C

Lit 99 138-139 °C
\[
\begin{align*}
\text{\textsuperscript{1}H N.M.R. (DMSO-D\textsubscript{6})} & \quad \delta \\
10.5 & \quad s & \text{1H CO}_{2}\text{H} \\
9.50 & \quad s & \text{1H NH} \\
7.7-6.8 & \quad m & \text{4H Aromatic protons} \\
2.8-2.2 & \quad m & \text{4H ArCH\textsubscript{2} and CH\textsubscript{2}CO} \\
2.1 & \quad s & \text{3H CH}_{3} \\
1.8-1.5 & \quad m & \text{4H CH\textsubscript{2}CH\textsubscript{2}} \\
\text{I.R. } v_{\text{max}} (\text{CHCl\textsubscript{3}}) & \quad 1705 \text{ and } 1280 \text{ cm}^{-1}
\end{align*}
\]

2-Acetamido-6,7,8,9-tetrahydro-5H-benzocyclohepten-5-one(276)

Cyclisation was carried out, as described for the compound (H), from the 5-(m-acetamidophenyl)valeric acid (275) (4.7 g), phosphorus pentoxide (30 g) and orthophosphoric acid (20 ml). The pure product (276) (2.4 g, 56\%) was crystallised from aqueous ethanol.

\[
\begin{align*}
imp. & \quad 115-116 ^{\circ}\text{C} & \text{Lit}^{99} 116-117 ^{\circ}\text{C}
\end{align*}
\]

\[
\begin{align*}
\text{\textsuperscript{1}H N.M.R. (CDCl\textsubscript{3})} & \quad \delta \\
9.22 & \quad s & \text{1H NH} \\
7.80-6.90 & \quad m & \text{3H Aromatic protons} \\
2.94-2.44 & \quad m & \text{4H ArCH\textsubscript{2} and CH\textsubscript{2}CO} \\
2.16 & \quad s & \text{3H CH}_{3} \\
1.90-1.52 & \quad m & \text{4H CH\textsubscript{2}CH\textsubscript{2}} \\
\text{I.R. } v_{\text{max}} (\text{CHCl\textsubscript{3}}) & \quad 3414,3320 \text{ and } 1676 \text{ cm}^{-1}
\end{align*}
\]

\[\text{***} \quad \text{***} \quad \text{***} \quad \text{***}\]

---

\[
\begin{align*}
\text{\textsuperscript{1}H N.M.R. (DMSO-D\textsubscript{6})} & \quad \delta \\
10.5 & \quad s & \text{1H CO}_{2}\text{H} \\
9.50 & \quad s & \text{1H NH} \\
7.7-6.8 & \quad m & \text{4H Aromatic protons} \\
2.8-2.2 & \quad m & \text{4H ArCH\textsubscript{2} and CH\textsubscript{2}CO} \\
2.1 & \quad s & \text{3H CH}_{3} \\
1.8-1.5 & \quad m & \text{4H CH\textsubscript{2}CH\textsubscript{2}} \\
\text{I.R. } v_{\text{max}} (\text{CHCl\textsubscript{3}}) & \quad 1705 \text{ and } 1280 \text{ cm}^{-1}
\end{align*}
\]

2-Acetamido-6,7,8,9-tetrahydro-5H-benzocyclohepten-5-one(276)

Cyclisation was carried out, as described for the compound (H), from the 5-(m-acetamidophenyl)valeric acid (275) (4.7 g), phosphorus pentoxide (30 g) and orthophosphoric acid (20 ml). The pure product (276) (2.4 g, 56\%) was crystallised from aqueous ethanol.

\[
\begin{align*}
imp. & \quad 115-116 ^{\circ}\text{C} & \text{Lit}^{99} 116-117 ^{\circ}\text{C}
\end{align*}
\]

\[
\begin{align*}
\text{\textsuperscript{1}H N.M.R. (CDCl\textsubscript{3})} & \quad \delta \\
9.22 & \quad s & \text{1H NH} \\
7.80-6.90 & \quad m & \text{3H Aromatic protons} \\
2.94-2.44 & \quad m & \text{4H ArCH\textsubscript{2} and CH\textsubscript{2}CO} \\
2.16 & \quad s & \text{3H CH}_{3} \\
1.90-1.52 & \quad m & \text{4H CH\textsubscript{2}CH\textsubscript{2}} \\
\text{I.R. } v_{\text{max}} (\text{CHCl\textsubscript{3}}) & \quad 3414,3320 \text{ and } 1676 \text{ cm}^{-1}
\end{align*}
\]

\[\text{***} \quad \text{***} \quad \text{***} \quad \text{***}\]
6,7,8,9-Tetrahydro-5H-benzocycloheptene (277)

Reduction of the cyclic ketone (6) was carried out as described for the compound (250), from 6,7,8,9-tetrahydro-5H-benzocyclohepten-5-one (6) (6.4 g) and a mixture of hydrazine hydrate (10 g) and potassium hydroxide (9 g) in 2,2'-dihydroxydiethyl ether (150 ml). The crude product was distilled under reduced pressure to give the compound (277) (5.5 g, 92%).

b.p. 95-98°C/760 mm Hg Lit 121 99-100°C/760 mm Hg

1H N.M.R. (CDCl3) δ

| 6.9    | s     | 4H   | Aromatic protons |
| 2.85-2.60 | m   | 4H   | (ArCH2) |
| 1.80-1.45 | m   | 6H   | (CH2)3 |

I.R. v max (Neat) 3060, 3010, 2930, 1600 and 1490 cm⁻¹

2-Acetyl-6,7,8,9-tetrahydro-5H-benzocycloheptene (278)

Acetyl chloride (9.9 g) was added dropwise during 15 minutes to stirred suspension of anhydrous aluminium chloride (16.8 g) in carbon tetrachloride (150 ml) with cooling in an ice-bath (0-5°C). The compound (277) (13 g) in carbon tetrachloride (40 ml) was added dropwise over a period of 3 hrs into the above suspension with keeping temperature below 5°C. After addition stirring was continued for a further 1 hr, and then reaction mixture was poured into ice and HCl (1:1). The organic layer was washed with water and then dried with sodium sulphate. Evaporation of the solvent and distillation of the residue gave the pure compound (278) (16.2 g, 96%).

b.p. 139-143°C/2 mm Hg Lit 122 180°C/22 mm Hg
\[ ^1H \text{N.M.R. (CDCl}_3) \delta \]

- 7.72-7.50 m 2H 2H on C1 and C3
- 7.14-7.00 d 1H H on C4 \( J_{3,4} = 8.5 \text{ Hz} \)
- 2.95-2.65 m 4H 2 (ArCH\(_2\))
- 2.50 s 3H CH\(_3\)
- 1.99-1.35 m 6H 3 (CH\(_2\) )

I.R. \( \nu_{\text{max}} \) (Neat) 2930, 2860, 1608 (CO), 1570, 1280, 1260 and 1200 cm\(^{-1}\)

2-Carboxylic acid-6,7,8,9-tetrahydro-5H-benzocycloheptene(279)

Sodium hydroxide solution (120 ml, 10%) and then potassium iodide-iodine reagent\(^{123}\) was added dropwise to stirred solution of the compound (278) (15 g) in dioxane (600 ml) until a definite dark colour of iodine persists. Reaction mixture was left 5 minutes and then warmed in water bath at 60°C. The iodoform was filtered off and the excess of iodine removed by solution of sodium bisulfite. The solution was acidified and a pale yellow precipitate filtered and then crystallised from methanol to give the pure compound (279).

m.p. 177-178°C

Analysis

<table>
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<tr>
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<th>Found</th>
<th>Required</th>
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</thead>
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<tr>
<td>C</td>
<td>75.95%</td>
<td>75.78</td>
</tr>
<tr>
<td>H</td>
<td>7.47%</td>
<td>7.36</td>
</tr>
</tbody>
</table>

\[ ^1H \text{N.M.R. (DMSO-D}_6) \delta \]

- 8.90 s 1H CO\(_2\)H
- 7.75-7.55 m 2H 2H on C1 and C3
- 7.16-7.02 d 1H H on C4 \( J_{3,4} = 8.5 \text{ Hz} \)
- 2.96-2.65 m 4H 2 (ArCH\(_2\))\(_2\)
- 1.99-1.35 m 6H 3 (CH\(_2\)\(_3\))
I.R. $\nu_{\text{max}}$ (Nujol) 1675 (CO), 1606 and 1290 cm$^{-1}$

**Methyl 6,7,8,9-tetrahydro-5H-benzocyclohepten-2-carboxylate (280)**

The ethereal solution of diazomethane (0.63 g) was added dropwise to the solution of compound (279) (2.9 g) until gas evolution ceased (left over night). Evaporation of the solvent and distillation of residue in the bulb tube under reduced pressure gave the pure compound (280) (3 g, 97%).

b.p. 110-115 $^{0}$C / 0.15 mm Hg

Analysis

<table>
<thead>
<tr>
<th></th>
<th>Found</th>
<th>Required</th>
</tr>
</thead>
<tbody>
<tr>
<td>C</td>
<td>76.25%</td>
<td>76.47%</td>
</tr>
<tr>
<td>H</td>
<td>7.94%</td>
<td>7.84%</td>
</tr>
</tbody>
</table>

$^1$H N.M.R. (CDCl$_3$) $\delta$

<table>
<thead>
<tr>
<th>$\delta$</th>
<th>Multiplicity</th>
<th>Assignment</th>
</tr>
</thead>
<tbody>
<tr>
<td>7.84-7.64</td>
<td>m</td>
<td>2H H on C1 and C3</td>
</tr>
<tr>
<td>7.22-7.00</td>
<td>d</td>
<td>1H H on C4 $J_{3,4}=8.5$ Hz</td>
</tr>
<tr>
<td>3.70</td>
<td>s</td>
<td>3H CH$_3$</td>
</tr>
<tr>
<td>2.92-2.55</td>
<td>m</td>
<td>4H 2 (ArCH$_2$)</td>
</tr>
<tr>
<td>1.99-1.35</td>
<td>m</td>
<td>6H 3 (CH$_2$)$_2$</td>
</tr>
</tbody>
</table>

I.R. $\nu_{\text{max}}$ (Nujol) 1683 (CO), 1606 and 1240 cm$^{-1}$

**3-Phenylcyclohepta(b)pyrrol-8-one (141)**

m.p. 188-189 $^{0}$C

Lit$^{48}$ 188-189 $^{0}$C

$^{13}$C N.M.R. (CDCl$_3$) $\delta$ (multiplicity)

<table>
<thead>
<tr>
<th>$\delta$</th>
<th>Multiplicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>176.4(s)</td>
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</tr>
<tr>
<td>138.4(s)</td>
<td></td>
</tr>
<tr>
<td>136.6(d)</td>
<td></td>
</tr>
<tr>
<td>133.8(d)</td>
<td></td>
</tr>
<tr>
<td>133.4(s)</td>
<td></td>
</tr>
<tr>
<td>132.0(d)</td>
<td></td>
</tr>
<tr>
<td>129.5(d)</td>
<td></td>
</tr>
<tr>
<td>129.3(d)</td>
<td></td>
</tr>
<tr>
<td>126.9(d)</td>
<td></td>
</tr>
<tr>
<td>126.8(s)</td>
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<tr>
<td>126.2(s)</td>
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</tr>
<tr>
<td>125.2(d)</td>
<td></td>
</tr>
<tr>
<td>123.5(d)</td>
<td>p.p.m.</td>
</tr>
</tbody>
</table>

* - Two overlapping resonances.
Methyl 6,7,8,9-tetrahydro-5H-benzocyclohepten-2-carboxylate (280)

The ethereal solution of diazomethane (0.63 g) was added dropwise to the solution of compound (279)(2.9 g) until gas evolution ceased (left over night). Evaporation of the solvent and distillation of residue in the bulb tube under reduced pressure gave the pure compound(280)(3 g, 97%).

b.p. 110-115°C /0.15 mm Hg

Analysis

<table>
<thead>
<tr>
<th>C</th>
<th>H</th>
</tr>
</thead>
<tbody>
<tr>
<td>13H</td>
<td>16O2</td>
</tr>
</tbody>
</table>

Found  C 76.25%  H 7.94%

Required C 76.47  H 7.84

\( ^1H \) N.M.R. (CDCl\(_3\)) \( \delta \)

<p>| | | | | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
</table>
| 7.84-7.64 m | 2H | H on C1 and C3
| 7.22-7.00 d | 1H | H on C4 \( J_{3,4} = 8.5 \text{ Hz} \)
| 3.70 s | 3H | CH\(_3\)
| 2.92-2.55 m | 4H | 2 (ArCH\(_2\))
| 1.99-1.35 m | 6H | 3 (CH\(_2\))\(_2\)

I.R. \( \nu_{\text{max}} \) (Nujol) 1683(CO), 1606 and 1240 cm\(^{-1}\)

** ** ** **

3-Phenylcyclohepta(b)pyrrol-8-one(141)

m.p. 188-189°C

\( ^{13}C \) N.M.R. (CDCl\(_3\)) \( \delta \) (multiplicity)

\[
176.4(s), 138.4(s), 136.6(d), 133.8(d), 133.4(s), 132.0(d), 129.3(d^*), 128.5(d^*), 126.9(d), 126.8(s), 126.2(s), 125.2(d), 123.5(d) \text{ p.p.m.}
\]

*-Two overlapping resonances.
Photolysis of 3-phenylcyclohepta(b)pyrrol-8-one (141)

3-Phenylcyclohepta(b)pyrrol-8-one (141) (0.44 g) in methanol (900 ml) was irradiated for 10 hrs in the usual way as described for the compound (38). Removal of the solvent gave a light brown polymeric material, from which nothing could be isolated.

1-Methyl-3-phenylcyclohepta(b)pyrrol-8-one (281)

3-Phenylcyclohepta(b)pyrrol-8-one (141) (0.66 g) in 1,2-dimethoxyethane (DME) (60 ml) was heated under reflux for 10 hrs with methyl iodide (0.42 g) and sodium hydroxide (0.15 g). After 20 hrs further methyl iodide was added and the mixture allowed to reflux for 20 hrs. Progress of the reaction was observed by using t.l.c. The mixture was cooled and the DME removed under reduced pressure. Water was added and the aqueous solution extracted with chloroform. The combined extracts were dried over anhydrous sodium sulphate and then the solvent evaporated off under reduced pressure to give a brown gum, which was chromatographed on p.l.c. plates (toluene-ethyl acetate, 90:10) to give the pure compound (281) (0.45 g, 63%) as pale brown solid.

m.p. 109-110°C

Analysis C<sub>16</sub>H<sub>13</sub>NO

<table>
<thead>
<tr>
<th>Found</th>
<th>Required</th>
</tr>
</thead>
<tbody>
<tr>
<td>C 81.93%</td>
<td>C 81.70</td>
</tr>
<tr>
<td>H 5.76%</td>
<td>H 5.53</td>
</tr>
<tr>
<td>N 6.06%</td>
<td>N 5.95</td>
</tr>
</tbody>
</table>
Photolysis of 1-methyl-3-phenylcyclohepta(b)pyrrol-8-one(281)

1-Methyl-3-phenylcyclohepta(b)pyrrol-8-one(281)(0.33 g) was irradiated in methanol by the procedure described before. Monitoring of the photolysis by t.l.c. and $^1$H N.M.R. examination showed decreasing amounts of starting material with the formation of only polymeric material, until finally after 9 hrs irradiation only the latter remained.

** ** *** **
**Cycloheptanone phenylhydrazone**

Cycloheptanone (74 g) and phenylhydrazine (71 g) were heated together on a water-bath for 10 minutes and then cooled, the pale yellow product solidified and then crystallised from ethanol to give colourless product (128 g, 96%), as needles.

m.p. 72-73 °C

Lit. 72°C

**5,6,7,8,9,10-Hexahydrocyclohept(b)indole (153)**

A mixture of cycloheptanone phenylhydrazone (18 g), water (360 ml) and concentrated sulphuric acid (20 ml) was heated on a water-bath for 45 minutes, with frequent shaking. The product gradually separated out and was practically pure. It was washed during filtration with water, and purified by crystallisation from ethanol to give the compound (153) (11 g, 74%) as shiny colourless plates.

m.p. 146-147 °C

Lit. 125 144 °C

**5-Ethyl-6,7,8,9,10-hexahydrocyclohept(b)indole (282)**

A mixture of compound (153) (5.6 g), ethyl p-toluenesulphonate (6.1 g) and NaH (1 g) in xylene was heated under reflux for 15 hrs. The mixture was cooled, filtered and the filtrate washed with ether. The solvent was evaporated off under reduced pressure to give the crude product, which was crystallised from ethanol to give the pure compound (282) (6.2 g, 97%) as yellow prisms.

m.p. 61-62 °C

Analysis: $C_{15}H_{19}N$

Found: C 84.32%  H 8.99%  N 6.56%

Required: C 84.45%  H 8.98%  N 6.57%
5-Ethyl-6,7,8,9-tetrahydrocyclohept(b)indol-10(5H)-one (283)

2,3-Dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) (11 g) in 100 ml of tetrahydrofuran was added dropwised to an ice-cooled solution of the compound (282) (5.2 g) in 275 ml of 90% aqueous tetrahydrofuran with stirring. The reaction was carried out under a nitrogen atmosphere. The reaction mixture first turned blue, after few minutes it changed to a brownish-red colour. The stirring was continued for 2 hrs, then the solvent evaporated off under reduced pressure. The remaining residue was extracted with ethyl acetate, and purified by passing through an alumina column (IV) to give almost pure product. The product was further purified by crystallisation from cyclohexane to the compound (283) (4.5 g 81%) as pale yellow crystals.

m.p. 97-98 °C

Analysis \( \text{C}_{15}\text{H}_{17}\text{NO} \)

<table>
<thead>
<tr>
<th></th>
<th>Found</th>
<th>Required</th>
</tr>
</thead>
<tbody>
<tr>
<td>C</td>
<td>79.19%</td>
<td>79.26</td>
</tr>
<tr>
<td>H</td>
<td>7.51%</td>
<td>7.54</td>
</tr>
<tr>
<td>N</td>
<td>6.39%</td>
<td>6.16</td>
</tr>
</tbody>
</table>
Bromination was carried out, as described for the compound (246), from the ketone (283) (2 g) and phenyltrimethylammonium tribromide (6.4 g) in anhydrous tetrahydrofuran (300 ml). The combined filtrates were evaporated off in vacuo to give a gummy material, which was chromatographed on alumina (IV), eluting with benzene-petroleum ether (10:90). The product (284) (3.1 g, 91%) was crystallised from chloroform-petroleum ether (40:60), as pale yellow crystals.

\[ \text{m.p.} \quad 124-125 \, ^{\circ}\text{C} \]

\[ \text{Analysis} \quad C_{15}H_{15}Br_2NO \]

\[ \text{Found} \quad C \quad 47.07\% \quad H \quad 3.83\% \quad N \quad 4.01\% \]

\[ \text{Required} \quad C \quad 46.77\% \quad H \quad 3.92\% \quad N \quad 3.63\% \]
The dibromoketone (284) (3.3 g) was dehydrobrominated with lithium chloride (1.4 g) in boiling dimethylformamide (300 ml) in the usual way giving the indolotropone (285) (1.85 g, 96%), which was crystallised from chloroform-petroleum ether (90:10) as shiny yellow prisms.

m.p. 117-118 °C

Analysis C₁₅H₁₅NO

Found C 80.88% H 5.70% N 6.15%

Required C 80.69% H 5.87% N 6.27%

1H N.M.R. (100 MHz, CDCl₃) δ

9.10-8.99 m 1H H on C1 J₁,₂=7.3 Hz
7.58-6.82 m 7H Other protons
4.47-4.29 q 2H NCH₂ J =8 Hz
1.45-1.33 t 3H CH₃

I.R. νmax (CHCl₃) 1635(CO), 1565 and 1480 cm⁻¹

U.V. λmax (log₁₀ ε) (EtOH) 241 (4.34), 295 (4.33), 378 (3.96) n.m.
Photolysis of 5-ethylcyclohept(b)indol-10(5H)-one (285)

5-Ethylcyclohept(b)indol-10(5H)-one (285) (0.45 g) was irradiated in methanol (800 ml) by procedure described before. Monitoring of the photolysis by t.l.c. and $^1$H N.M.R. examination showed decreasing amounts of starting material with formation of only polymeric material, until finally after 7 hrs irradiation only the latter remained.

5-Methyl-6,7,8,9,10-hexahydrocyclohept(b)indole (286)

This compound prepared (11.3 g, 95%), as described for the compound (282), from the compound (153) (11 g), methyl p-toluenesulphonate (11 g) and sodium hydride (2.8 g) in xylene. The crude was crystallised from ethanol to give the pure compound (286) as yellow prisms.

\[
\begin{align*}
\text{Found} & : \quad \text{C} \ 84.30\% \quad \text{H} \ 8.33\% \quad \text{N} \ 7.04\% \\
\text{Required} & : \quad \text{C} \ 84.37\% \quad \text{H} \ 8.60\% \quad \text{N} \ 7.03\%
\end{align*}
\]
5-Methyl-6,7,8,9-tetrahydrocyclohept(b)indole-10(5H)-one (287)

Oxidation was carried out, as described for the compound (283), from the compound (286) (4 g) and DDQ (10.9 g) in 275 ml of 90% aqueous tetrahydrofuran. The product (3.5 g, 82%) was further purified by crystallisation from ethanol.

- m.p. 132-134°C Lit\textsuperscript{100} 132-134°C
- I.R. \( \nu_{\text{max}} \) (Nujol) 1635(CO), 1615 and 1605 cm\(^{-1}\)

9,9-Dibromo-6,7,8,9-tetrahydro-5-methylcyclohept(b)indol-10(5H)-one (288)

Bromination was carried out, as described for the compound (246), from the ketone (287) (2.13 g) and phenyltrimethylammonium tribromide (7.5 g) in tetrahydrofuran (400 ml). The pure dibromoketone (288) (2.9 g, 78%) was crystallised from methanol.

- m.p. 173-174°C Lit\textsuperscript{51} 173°C

5-Methylcyclohept(b)indol-10(5H)-one (289)

The dibromoketone (288) (1.9 g) was dehydrobrominated with lithium chloride (0.85 g) in boiling dimethylformamide (250 ml) in the usual way giving the indolotropone (289) (0.52 g, 89%), which was crystallised from methanol.

- m.p. 169-170°C Lit\textsuperscript{51} 169-170°C

Photolysis of 5-methylcyclohept(b)indol-10(5H)-one (289)

The indolotropone (289) (0.42 g) in methanol (900 ml) was irradiated for 7 hrs in the usual way as described for the compound (38). Removal of the solvent gave a light brown polymeric material, from which nothing could be isolated.
6,7,8,9-Tetrahydrocyclohept(b)indol-10(5H)-one (154)

Oxidation was carried out, as described for the compound (283), from the compound (153) (5 g) and DDQ (12 g) in 297 ml of 90% aqueous tetrahydrofuran. The product (154) (4.8 g, 90%) was further purified by crystallisation from ethanol.

m.p. 220-221 °C

I.R. v_max (Nujol) 3155 and 1600 (CO) cm⁻¹

9,9-Dibromo-6,7,8,9-tetrahydrocyclohept(b)indol-10(5H)-one (290)

Bromination was carried out, as described for the compound (246), from the ketone (154) (2 g) and phenyltrimethylammonium tribromide (7.5 g) in tetrahydrofuran (350 ml). The pure dibromoketone (290) (3 g, 87%) was crystallised from methanol.

m.p. 183-184 °C

Cyclohept(b)indol-10(5H)-one (8)

The dibromoketone (290) (1.8 g) was dehydrobrominated with lithium chloride (0.84 g) in boiling dimethylformamide (200 ml) in the usual way giving the indolotropone (8) (0.94 g, 97%), which was crystallised from methanol as yellow prisms.

m.p. 285-286 °C

Photolysis of cyclohept(b)indol-10(5H)-one (8)

The indolotropone (8) (0.5 g) was irradiated in methanol (1000 ml) for 8 hrs in the usual way as described for the compound (38). Removal of the solvent gave a light brown polymeric material, from which nothing could be isolated.

** *** **** ** **
2-Furlylacryyaldehyde(291)

2-Furaldehyde(34.5 g) and acetaldehyde(101.2 g) were added to a solution of sodium hydroxide(10 g) and water (2000 ml). The mixture was heated on a water-bath to 40 °C, then after 5 minutes cooled to 25 °C, and extracted with chloroform. The combined extracts were dried over magnesium sulphate and distilled under reduced pressure to yellow oil. Distillation of the residue under vacuo gave the pure product(291)(30.8 g, 70%), which was crystallised from benzene-petroleum ether, as yellow needles.

m.p. 52-53 0°C

1H N.M.R. (CDCl3) δ
9.62-9.48 d 1H CHO
7.54 m 1H H on C5
7.46-6.30 m 4H Other protons

I.R. vmax (CHCl3) 1675(CO), 1630, 1550 and 1120 cm⁻¹

Lit 103 53°C

Ethyl S-(2-furyl)pentadienoate(292)

The aldehyde(291)(61 g) in dried ethyl acetate (98 g) was added slowly to the ice-bath cooled mixture of sodium wire (11.2 g) in ethyl acetate (196 g). The mixture was left with occasional shaking at room temperature for 24 hrs. The mixture was cooled and a mixture of glacial acetic acid (30 g) and water was added and the aqueous solution extracted with dichloromethane. The combined extracts were dried over sodium sulphate and then the solvent removed, and the residue distilled under vacuo to give the pure ester(292)(69 g, 72%).

b.p. 120 °C/0.5 mm Hg Lit 104 145-150 °C/10 mm Hg
Ethyl 5-(2-furyl)valerate (293)

This compound (293) prepared in 88% yield, as described for the compound (238), from hydrogenation of the ester (292) (25 g).

b.p. 100-110 °C/2 mm Hg Lit105 77-78 °C/1 mm Hg

Ethyl 5-(2-furyl)valerate (293)

The mixture of ester (293) (23 g), sodium hydroxide (9.2 g), methanol (60 ml) and water (23 ml) was heated under reflux for 3 hrs. The mixture was cooled and then acidified with HCl. The aqueous solution extracted with ether, and the combined extracts were dried over sodium sulphate, then the solvent
removed, and the residue was distilled under vacuo to give the acid (15.7 g, 85%) which was solidified and then crystallised from petroleum ether.

\[
\text{m.p.} \quad 43-44 \, ^\circ\text{C} \quad \text{Lit}^{105} 44-45 \, ^\circ\text{C}
\]

\[
\begin{array}{ccc}
1H \text{ N.M.R. (CDCl}_3) & \delta \\
10.1 & s & 1H \text{ CO}_2\text{H} \\
7.28-7.25 & m & 1H \text{ H on C5} \\
6.30-6.20 & m & 1H \text{ H on C3} \\
6.00-5.92 & m & 1H \text{ H on C4} \\
2.80-2.20 & m & 4H \text{ ArCH}_2 \text{ and CH}_2\text{CO}_2 \\
1.90-1.50 & m & 4H \text{ CH}_2\text{CH}_2 \\
\end{array}
\]

I.R. \( \nu_{\text{max}} \) (Nujol) 1705(CO) and 1590 cm\(^{-1}\)

5-(2-Furyl)valeryl chloride (180)

Thionyl chloride (6.37 g) was added to an ice-bath cooling solution of the acid (9.1 g) in dried ether (50 ml). The mixture was heated under reflux for 5 hrs. The excess of thionyl chloride and ether was removed under nitrogen atmosphere. The residue was distilled under vacuo to give the valeryl chloride (180) (5.84 g, 58%).

b.p. \( 65-70 \, ^\circ\text{C/0.1 mm Hg Lit}^{105} 95 \, ^\circ\text{C/3 mm Hg} \)

\[
\begin{array}{ccc}
1H \text{ N.M.R. (CDCl}_3) & \delta \\
7.30-7.25 & m & 1H \text{ H on C5} \\
6.32-6.22 & m & 1H \text{ H on C3} \\
6.06-5.02 & m & 1H \text{ H on C4} \\
3.00-2.45 & m & 4H \text{ ArCH}_2 \text{ and CH}_2\text{CO}_2 \\
1.90-1.50 & m & 4H \text{ CH}_2\text{CH}_2 \\
\end{array}
\]

I.R. \( \nu_{\text{max}} \) (Neat) 1800(CO) and 1600 cm\(^{-1}\)
5,6,7,8-Tetrahydro-4H-cyclohepta(b)furan-4-one (181)

The valeryl chloride (180) (4.84 g) in carbon disulfide (15 ml) and freshly distilled tin tetrachloride (3.4 ml) in carbon disulfide (15 ml) were simultaneously and separately dropped into boiling stirred carbon disulfide (150 ml, 60°C). The mixture was boiled at 60°C for a further 1 hr when the addition had reached completion. The excess of tin tetrachloride and carbon disulfide was distilled off (80°C), to 10 ml of its volume. Ice-water was added to the residue (10 ml), and then extracted with ether. The combined extracts were dried over sodium sulphate, and then the solvent removed, and the residue was distilled under vacuo the cycloheptafuranone (181) (2.3 g, 59%).

b.p. 65-70°C/0.2 mm Hg
m.p. 42-43°C

^H N.M.R. (CDCl3) δ
7.20-7.08 d 1H H on C2 J2,3 = 2 Hz
6.66-6.65 d 1H H on C3
3.10-2.54 m 4H ArCH2 and 2H on C5
2.12-1.76 m 4H 4H on C6 and C7

I.R. v_max (Neat) 3120, 2930, 1725 (CO), 1660
1580 and 1420 cm⁻¹

5,5-Dibromo-5,6,7,8-tetrahydro-4H-cyclohepta(b)furan-4-one (182)

Bromination was carried out, as described for the compound (283), from the cycloheptafuranone (181) (2.1 g) and phenyltrimethylammonium tribromide (21 g) in tetrahydrofuran (200 ml). The pure dibromoketone (182) (2.5 g, 59%) was crystallised from methanol.
m.p. 112-113 °C  Lit\(^6^2\) 113-114 °C

\(^1\)H N.M.R. \((\text{CDCl}_3)\) δ

7.30-7.20  d  1H  H on C2  \(J_{2,3}=2\) Hz
6.80-6.70  d  1H  H on C3
3.20-2.88  m  4H  4H on C6 and C8
2.40-2.04  m  2H  2H on C7

\(\text{I.R. } \nu_{\text{max}} \ (\text{CCl}_4) \)  1670 cm\(^{-1}\)

**4H-Cyclohepta(b)furan-4-one (9)**

The dibromoketone (182) (1.54 g) was dehydrobrominated with lithium carbonate (1.5 g) in boiling dimethylformamide (100 ml) in the usual way giving the furotropone (9) (0.36 g, 50%), which was distilled in bulb-tube.

\(m.p. 38-39 °C\) \ Lit\(^6^2\) 39-41 °C

\(^1\)H N.M.R. \((\text{CDCl}_3)\) δ

7.70  d  1H  H on C2  \(J_{2,3}=2\) Hz
7.48  dd  1H  H on C8  \(J_{7,8}=11\) Hz,\(J_{6,8}=1\) Hz
7.25  m  1H  H on C6
7.22  d  1H  H on C3
7.15  dd  1H  H on C5  \(J_{5,6}=12\) Hz,\(J_{5,7}=1.5\) Hz
6.85  m  1H  H on C7

\(\text{I.R. } \nu_{\text{max}} \ (\text{CCl}_4) \)  1630 and 1595 cm\(^{-1}\)

**Photolysis of 4H-cyclohepta(b)furan-4-one (9)**

The furotropone (9) (0.3 g) in methanol (800 ml) was irradiated for 7 hours in the usual way, as described for the compound (38). Removal of the solvent gave a light brown polymeric material, from which nothing could be isolated.
Chapter 6

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