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CHEMICAL TRANSFORMATIONS OF THE PHOTOCHEMICAL 1,3-ADDUCTS OF BENZENE AND ANISOLE TO CYCLOBUTENES

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Abstract—The photochemical 1,3-adduct of benzene to *cis*-3,4-dichlorocyclobutene has been transformed in four steps to 2,5-*endo*-10-oxotricyclo[4.3.1.$0^{2,5}$]deca-3,8-diene **1**. The key reaction is the acid catalyzed addition of water to the photoadduct **2** which gives the 3,4-dichloroalcohol **3** corresponding to **1**. Similarly the photochemical 1,3-adduct of benzene to cyclobutene has also been cleaved with acid. A more convenient synthesis of **1** is provided by the photochemical 1,3-addition of anisole to *cis*-3,4-dichlorocyclobutene and the treatment of the adduct with acid. The 3,4-dichloro derivative of **1** is thereby obtained directly. Probable mechanisms for these transformations are discussed.

The photochemical 1,3-addition of benzene to olefins is known to be a reaction applicable to a variety of olefins.[1] In this work, it is shown that the 1,3-adducts of benzene and anisole to cyclobutene and *cis*-3,4-dichlorocyclobutene can be transformed to derivatives of the tricyclic ketone, $C_{10}H_{10}O$, **1**. These reactions extend the synthetic utility of the photochemical 1,3-addition.[2] The ketone **1** is a possible precursor to $C_{10}H_{10}$ hydrocarbons which are of current interest.[3]

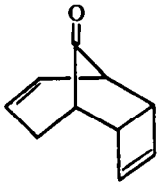
RESULTS

Irradiation of benzene and *cis*-3,4-dichlorocyclobutene[4] at 254 nm gave the adduct **2**, m.p. 77–78°, which could be conveniently isolated by column chromatography.[5-8] Treatment of **2** with hydrochloric acid in refluxing dioxane furnished an alcohol **3**, m.p. 118–119°, and an oily mixture.* The NMR spectrum (220 MHz) of the alcohol **3** exhibited resonances at δ 5·79 (m, 2H, protons at C-7 and C-8), 4·47 (broad s, 2H, protons at C-3 and C-4), 4·22 (s, 1H, proton at C-10) and 1·88 (s, 1H, –OH) among other absorptions. The mass spectrum revealed the characteristic cluster of ions at 220, 218 (M^+), 185 and 183 (M–Cl) corresponding to the molecular formula $C_{10}H_{12}Cl_2O$.

The protons derived from the benzene part of the alcohol **3** could be identified by comparing its NMR spectrum to that of the deuterioalcohol **3a** which was obtained by treatment of the photoadduct from hexadeuteriobenzene and dichlorocyclobutene with HCl. **3a** showed NMR signals at δ 1·88 (s, 1H, –OH, exchangeable in D_2O), 2·54 (b, 1H, proton at C-9), 3·31 (b, 2H, protons at C-2 and C-5), and 4·22 (m, 2H, protons at C-3 and C-4). The protons at C-1, C-6 through C-10 could therefore be identified as those originating from benzene. The *endo* attachment of the cyclobutane ring in **3** is suggested by the magnitude of the coupling between the protons at C-1 and C-2. In the case of norbornanes, the coupling constant between the protons at C-1 and the 2-*exo* position is of the order of 3–5 Hz while between the proton at C-1 and the 2-*endo* proton, it is ~0 Hz.[9-11] The width of the broad multiplet (δ 3·34) at half-height (W_H) for the protons at C-2 and C-5 in **3** is about 10 Hz whereas in the partially deuteriated compound, **3a** in which there is no proton at C-1, the W_H for the same pair of protons is 5 Hz. This suggests that this pair of protons is significantly coupled in **3**, and therefore the stereochemistry of the ring must be *endo*.† The same conclusion regarding the stereochemistry of **3** can be reached by comparing its spectra with those of the alcohols that were obtained by treating the photoadducts of benzene to cyclopentene.[1b,12] In the latter

*This fraction contained some of the starting adduct **2** and probably the trichloro compound.

†The X-ray structure of the *p*-nitrobenzoate of **3** has been determined. (S. La Placa and J. Weidenborner, to be published.) It is in full agreement with the stereochemical representation displayed here.



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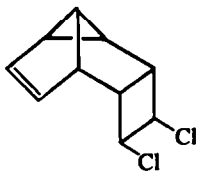

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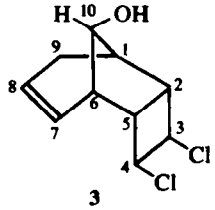

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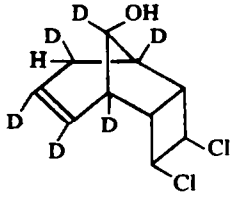
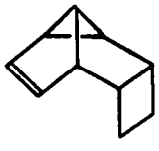


3a



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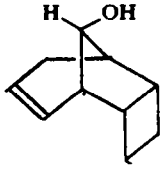

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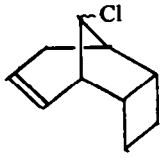

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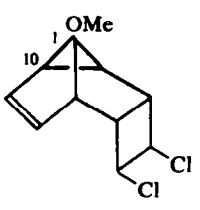
instance, double irradiation and europium shift reagents were used extensively to establish the structures.*

Photoadduct **4** which was prepared from benzene and cyclobutene,[5-7] on hydration in the presence of acid gave two major fractions. One of these contained the alcohol **5** whose structure was substantiated by physical data. GLC separation of the second fraction afforded a mixture of chloro-compounds **6** whose mass spectra confirmed the molecular formula, $C_{10}H_{13}Cl$. The NMR spectrum (60 MHz) of **6** showed olefinic protons at δ 5·75 and a proton adjacent to the chlorine atom at δ 4·3. **6** could not be dehydrohalogenated either with potassium t-butoxide in t-butanol or with 1,5-diazabicyclo[4.3.0]non-5-ene (DBN) in benzene. This suggested that the chlorine atom must be situated at the C-10 position where dehydrohalogenation would result in a product containing an exceedingly strained double bond.

Photolysis of anisole and *cis*-3,4-dichlorocyclobutene led to the adduct **7**, m.p. 80–81°, whose NMR spectrum revealed resonances for the olefinic protons at δ 5·93, for the protons at C-3 and C-4 adjacent to the chlorine atoms



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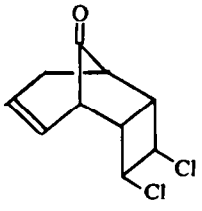

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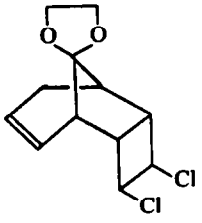

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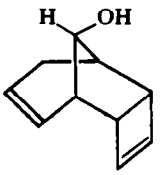
at 4·61 (broad t, J = 6·5 Hz, 1H) and 4·13 (broad d, J = 6·5 Hz, 1H) and the methoxyl protons at 3·31. Treatment of **7** with acid furnished the ketone **8**, m.p. 112–113°, which was found to be identical to the product that was obtained on oxidation of the alcohol **3** with Jones reagent. The structure of the bridged ketone **8** is supported by IR bands† at μ 5·5 (weak), 5·75 (strong) and 5·86 (weak) and the NMR spectrum.

8 was converted to the ketal **9** in the presence of ethylene glycol and *p*-toluene sulphonic acid in benzene and then to **1**, m.p. 94–95° by successively reacting with sodium naphthylide in dimethoxyethane[14] and hydrochloric acid in acetone. **1** had a carbonyl absorption in its IR spectrum at 5·75 μ and NMR absorptions for the four olefinic protons at δ 6·17 (δ, J = 2·5 Hz, 1H), 6·04 (d, J = 2·5 Hz, 1H) and 5·59 (m, 2H).

The tricyclic alcohol **3** could be dehalogenated with lithium amalgam in benzene or sodium and t-butanol in THF[13] to the alcohol, **10**.



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DISCUSSION

The photochemical 1,3-additions that are described here illustrate two features which seem quite common to these reactions, viz the orientational specificity of the reaction which places the substituent on the benzene ring at the C-1 position in the adduct[6,12] and the preference for the *endo* orientation of the substituents on the double bond of the olefin. Both these characteristics fit well with the "sandwich" model for the exciplex that has been proposed earlier.[12]

The acid-catalysed cleavage of the cyclopropane ring of the adduct **2** may be initiated through corner protonated cyclopropanes[15] **11** and **12** or preferably by protonation of the double bond to give a cyclopropylcarbinyl cation[16,17] **13** leading to the rearranged olefinic alcohols (Scheme 1). If the initial protonation of double bond occurs, cleavage of C-2–C-10 bond (path a) in the cation **13** results in the homoallylic cation **14** whereas cleavage of C-1–C-10 bond (path b) leads to the formation of ion **15** which can collapse to the alcohols **16** and **3**. Since the ketone **8** obtained from the oxidation of alcohol **3** was found to be identical with the product of acid-catalysed cleavage of the anisole-dichlorocyclobutene adduct **7**, the alcohol was assigned the structure **3**. The geometry of the cyclopropylcarbinyl cation **13** might be favourable for the orbitals of the C-1–C-10 σ bond to effectively overlap with the vacant *p*-orbital of the carbonium ion during the cleavage. It is well known that homoallylic cations such as **15** can be stabilized by interaction with the neighbouring π-cloud.[18] Attack by water on the ion **15** might occur from the less hindered side, i.e. opposite to the π face, leading to the *anti*-alcohol **3**.

Acid catalysed cleavage of the anisole-dichlorocyclobutene adduct **7** may be expected to occur at the C-1–C-10 bond since C-10 is an allylic position. This constitutes the second example[2] of the synthesis of a bicyclo[3.2.1]octan-8-one derivative from the photoaddition of anisole to a cyclic olefin. This reaction seems to be of considerable synthetic utility.

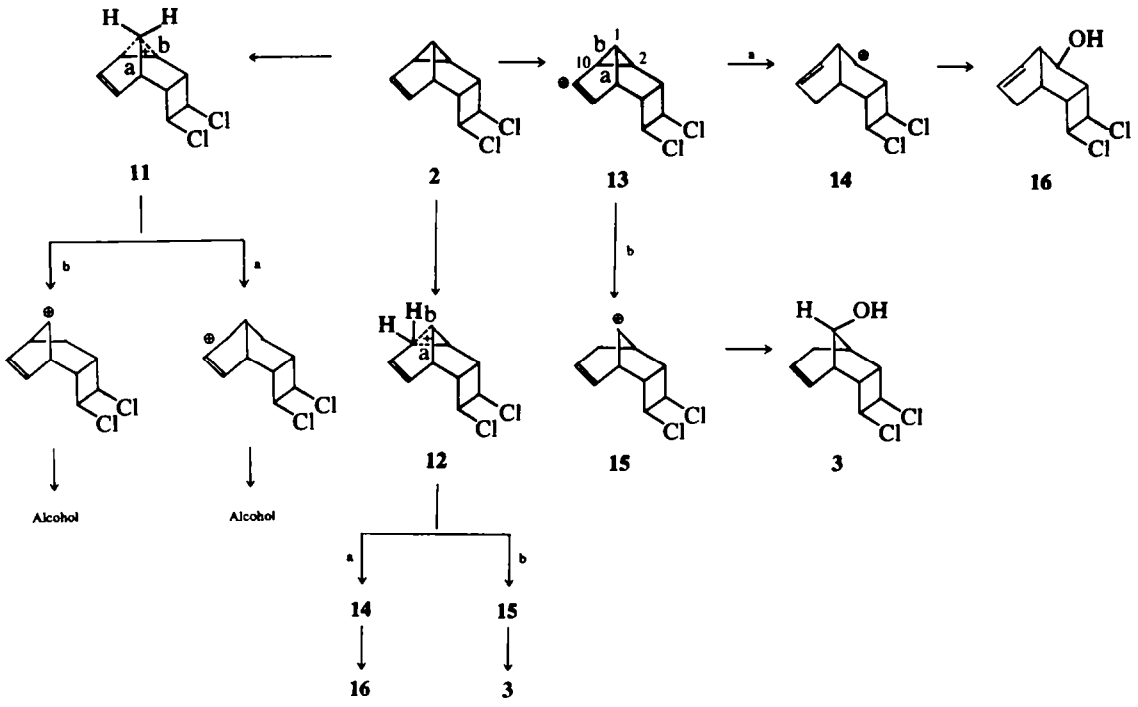
EXPERIMENTAL

IR spectra were recorded on a Perkin-Elmer infracord spectrophotometer, mass spectra on a Hitachi Perkin-Elmer RMS-4 mass spectrometer, UV spectra on a Cary 14 spectrophotometer and NMR spectra at 60 and 220 MHz on a JEOL Minimar and a Varian HR-220 spectrometer respectively. The latter was operated by the consortium at the Rockefeller University in New York. GLC separations were made on an F&M model 500 gas chromatograph fitted with a silicone column (8 ft; UCON-550x). High pressure liquid chromatography was performed on Waters Associates liquid chromatograph model ALC-2021R-40/W on a corasil column (1/8 in diameter and 4 ft length) employing isooctane as solvent. Microanalyses were carried out by Schwarzkopf Microanalytical Laboratories, Woodside, N.Y. Alumina (80–200 mesh) supplied by Fischer Scientific Co was used for column chromatography. Petroleum ether refers to fraction boiling at 30–60°.

2,5 - endo - 3,4 - cis - *Dichloro* - anti - 10 - *hydroxy-tricyclo*[4.3.1.$0^{2,5}$]*dec* - 8 - *ene* **3**. To a soln of benzene-dichlorocyclobutene photoadduct **2** (1·9 g) in dioxan (40 ml) was

*The structure of the alcohol[1b] obtained from the hydration of the benzene: cyclopentene adduct has been revised, *J. Am. Chem. Soc.* in press.

†cf Bicyclo[2.2.1]hept-2-en-7-one shows IR bands at μ 5·37 (m), 5·58 (s), and 5·62 (m).[13]



Scheme 1. Acid catalysed cleavage of 2.

added water (8 ml) and conc. HCl (1·6 ml) and refluxed for 75 min. The reaction mixture was cooled, K_2CO_3 soln (30 ml, 10%) added and extracted with CH_2Cl_2. The extract was washed with water and the solvent removed. The residue was chromatographed over alumina and the pet ether fraction gave an oil (0·9 g), which on addition of pet ether and cooling slowly deposited the starting adduct 2 (0·45 g). High pressure liquid chromatography[24] of this fraction indicated the presence of four components. The ether fraction gave a solid residue (803 mg) which on crystallisation from CCl_4 afforded colourless feathery needles (534 mg), m.p. 118–119°; IR (Nujol): 3μ; MS: *m/e* 220, 218, 183, 165, 127, 125, 104, 106, 79 and 77; NMR (220 MHz) ($CDCl_3$): δ 1·88 (1H, exchangeable with D_2O), 2·13–2·68 (4H), 3·34 (m, 2H), 4·22 (b, 1H), 4·47 (b, 2H) and 5·79 (m, 2H) (Found: C, 54·54; H, 5·54; Cl, 32·15. Calcd. for $C_{10}H_{12}Cl_2O$: C, 54·82; H, 5·52; Cl, 32·36%).

p-*Nitrobenzoate* m.p. 162–163° (ether); IR (nujol): 5·82μ; MS: *m/e* 367, 332, 217, 200 and 150; NMR (220 MHz) ($CDCl_3$): δ 2·27–3·18 (4H), 3·41 (m, 2H), 4·54 (b, 2H), 5·29–5·39 (m, 1H), 5·88 (m, 2H) and 8·06–8·31 (4H) (Found: C, 55·23; H, 4·15; Cl, 19·40. Calcd. for $C_{17}H_{15}Cl_2NO_4$: C, 55·43; H, 4·07; Cl, 19·29%).

2,5 - endo - 1,6,7,8,9,10 - *Hexadeuterio* - 3,4 - cis - *dichloro* - anti-10 - *hydroxytricyclo*[4.3.1.$0^{2,5}$]*dec* - 8 - *ene* **3a** was prepared as above starting from the photoadduct of benzene-d_6 and dichlorocyclobutene, IR (nujol): μ 3·1 and 4·6; NMR (see text).

2,5 - endo - anti - 10 - *Hydroxytricyclo*[4.3.1.$0^{2,5}$]*dec* - 8 - *ene* **5**. The photolysate (4 g) from benzene-cyclobutene irradiation was hydrated as described earlier in dioxan and HCl. The product was chromatographed over alumina and the pet ether fraction gave an oil (1·4 g) from which two major oily compounds **6** could be separated by GLC, IR (neat): 6·1μ; MS: *m/e* 168, 133, 132, 105, 91, 79, 78, 77 and 51. The ether fraction furnished an oil **5** (802 mg) which was further purified by chromatography over alumina, IR (neat): 3·1μ; NMR ($CDCl_3$) (60 MHz): δ, 5·75 (olefinic protons).

5 was converted to its p-nitrobenzoate and purified by column chromatography. The solid, obtained from 2:8 benzene–pet ether fraction, was crystallised from EtOH, m.p. 73–76°; IR (nujol): μ 5·82; MS: *m/e* 299, 149 and 133; NMR (220 MHz) (CCl_4): δ 1·1–3·4 (10H), 5·09–5·22 (m, 1H), 5·45–5·9 (m, 2H) and 7·72–8·5 (4H) (Found: C, 68·35; H, 5·54; N, 4·90. Calcd. for $C_{17}H_{17}NO_4$: C, 68·22; H, 5·72; N, 4·68%).

Attempted dehydrohalogenation of **6**. (a) To t-BuOK, prepared from K (172 mg) and t-BuOH (3 ml) was added the mixture of chloro compounds **6** (362 mg) in t-BuOH (2 ml) under nitrogen and stirred for 16 hr at room temp and then refluxed for 4 hr. The mixture was poured into water and extracted with CH_2Cl_2. The extract was washed with water and the solvent removed to recover the starting material. (b) To 1,5-diazabicyclo[4.3.0]non-5-ene (142 mg) under N_2 was added the halide mixture **6** (185 mg) in benzene (3 ml) and refluxed for 2 hr. The mixture was poured into water (10 ml) and H_2SO_4 (1N, 2 ml) and extracted with pet ether. The extract was washed with water and the solvent removed to recover **6**.

2,5 - endo - 3,4 - cis - *Dichloro* - 7 - *oxotricyclo*[4.3.1.$0^{2,5}$]*dec* - 8-*ene* **8**. To a soln of the alcohol **5** (750 mg) in acetone (15 ml) was added Jones reagent dropwise until the orange colour persisted at 0–5°. After 10 min water (25 ml) was added and extracted with CH_2Cl_2. The extract was washed with $NaHCO_3$ aq and water and the solvent removed. The oily residue was passed through a column of alumina. Fractions eluted with 2:8 to 6:4 benzene–pet gave a solid, which on crystallisation from ether–pet afforded colourless plates (355 mg), m.p. 112–113°; IR (nujol): μ 5·52 (w), 5·75 (s), 5·83 (w); MS: *m/e* 216, 181, 153; NMR (220 MHz) ($CDCl_3$): δ 2·5–3·47 (6H), 4·68 (m, 1H), 4·81 (m, 1H) and 5·9 (d, J = 3·5 Hz, 2H).

2,5 - endo - anti - 10 - *Hydroxytricyclo*[4.3.1.$0^{2,5}$]*deca* - 3,8 - *diene* **10**. (a) To Li amalgam, prepared by stirring Li pieces (175 mg) and Mg (13 g) for 4 hr, was added the dichloroalcohol **3** (190 mg) in benzene (10 ml) and refluxed for 16 hr. The mixture was filtered through a sintered funnel and the residue was repeatedly washed with hot benzene. Evaporation of benzene and crystallisation of the residue (120 mg) from pet ether containing a few drops of CCl_4 gave a solid (80 mg), m.p. 105–110° with softening at 95°, IR (nujol): μ 3·1, 6·1; MS: *m/e* 148, 129, 130, 128, 119, 91, 80 and 70; NMR (220 MHz) ($CDCl_3$): δ 1·91–2·38 (m, 5H), 3·43–3·63 (m, 2H), 4·36 (s, 1H), 5·56 (broad d, J = 4·5 Hz, 2H), 5·81 (d, J = 2·5 Hz, 1H) and 6·0 (d, J = 2·5 Hz, 1H). (b) To sodium pieces (450 mg) in dry THF (5 ml) was added, under reflux, dry t-butanol (1 ml) under N_2. A soln of the alcohol **3** (220 mg) in THF (3 ml) was then added during 10 min and refluxed for 5 hr. The hot soln was filtered through glass wool and the residue washed with hot CH_2Cl_2. Water (30 ml) was added to the filtrate, the organic layer separated and washed with water. Removal of the solvent left a semi solid residue (120 mg) which was crystallised from pet ether containing a few drops of CCl_4 to give **10** (80 mg).

3,6 - endo - cis - 4,5 - *Dichloro* - 1 - *methoxy-tetracyclo*[5.3.0.$0^{2,10}$.$0^{3,6}$]*dec* - 8 - *ene* **7**. A soln of anisole (17·5 g) and *cis*-3,4-dichlorocyclobutene (11·1 g, 98% pure) made up to 50 ml with methyl cyclohexane was irradiated in a quartz tube with 253·7 nm radiation from four modules of a Rayonet, Type RS RPR-208 reactor. After 36 hr the solution was distilled and the distillate reirradiated. From three such successive irradiations, the residues were collected and distilled in vacuo. The fraction, distilled at 100–150° (5 nm), was passed through a column of alumina. Pet ether and 1:9 benzene–pet ether fractions eluted an oil (2·8 g) whose structure is under investigation. The latter benzene–pet ether fractions eluted the adduct **7** (6·2 g), which solidified on addition of pet ether and cooling, m.p. 80–81°; MS: *m/e* 230, 197, 195, 159, 129, 127, 117 and 115; NMR (220 MHz) ($CDCl_3$): δ 2·98 (d.d, J = 9 Hz, 1H), 2·38 (broad d, J = 0 Hz, 1H), 3·31 (s, 3H), 3·49–3·86 (m, 3H), 4·13 (broad d, J = 6·5 Hz, 1H), 4·61 (broad t, J = 6·5 Hz, 1H) and 5·93 (m, 2H).

Acid treatment of **7**. To a soln of the adduct **7** (3·25 g) in dioxan (84 ml) was added water (21·4 ml) and conc HCl (6·5 ml) and refluxed for 90 min and worked up as described previously. The crude product was passed through a column of alumina. Pet ether fractions eluted the starting adduct **7** (0·25 g). Benzene–pet ether fractions gave the ketone **8** (1·5 g), which was crystallised from ether–pet ether, m.p. and m.m.p. 112–113°. IR spectra of the foregoing ketone and **8** are superimposable.

2,5-endo-10-*Oxotricyclo*[4.3.1.$0^{2,5}$]*deca*-3,8-*diene* **1**. A soln of **8** (1·085 g), ethylene glycol (465 mg) and *p*-toluenesulphonic acid (20 mg) in benzene (60 ml) was heated in an azeotropic set for 8 hr. The reaction mixture was poured into $NaHCO_3$ aq (10%; 25 ml) and extracted thoroughly. The benzene layer was washed with water and the solvent removed. The oily product **9** (1·1 g) showed no CO band in the IR spectrum and solidified slowly, m.p. 64–66°. The crude ketal **9** was directly used for dehalogenation without further purification as below.

A 100 ml round bottomed flask fitted with a 25 ml pressure-equalizing separatory funnel and a drying tube was flame dried under a current of dry nitrogen. A soln of naphthalene (6·04 g) in dimethoxyethane (50 ml, distilled over Na) was added to the flask followed by Na pieces (552 mg) in one lot and stirred for 2 hr under N_2. To the resulting green soln of sodium naphthylide was added a soln of **9** (1·1 g) in dimethoxyethane during 1 hr. Stirring was continued for another hr. O_2 was then flushed into the green mixture to destroy the excess of the sodium naphthylide reagent when a pale orange (sometimes colourless) cloudy soln was obtained. Dimethoxyethane was removed under suction and the residue was refluxed in acetone (20 ml) with H_2SO_4 (20%, 15 ml) for 3 hr. Most of the acetone was then removed, water added to the residue and extracted with CH_2Cl_2. The extract was washed with water and the solvent removed. The residue was chromatographed over alumina, the pet ether fraction gave naphthalene. Benzene–pet ether (3:7–1:1) eluted the ketone **1** (0·52 g) which on addition of pet ether and cooling furnished a solid, m.p. 94–95°; IR (nujol): μ 5·73; MS: *m/e* 146, 118, 115 and 91; NMR (220 MHz) (CCl_4): δ 2·27–2·79 (m, 4H), 3·22 (m, 1H), 3·22 (m, 1H), 3·38 (m, 1H), 5·59 (m, 2H), 6·04 (d, J = 2·5 Hz, 1H) and 6·17 (d, J = 2·5 Hz, 1H).

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