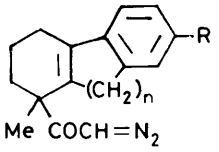
Acid-catalysed Intramolecular *C*-Alkylation in β,γ-Unsaturated Diazomethyl Ketones. Part 5.[1] Synthesis of Functionalised Hydrofluorene Derivatives *via* Novel Fragmentation Reactions

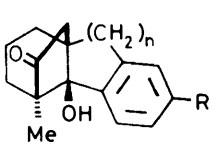
Bijali Saha, Gutta O. S. V. Satyanarayana, and Usha Ranjan Ghatak *
Department of Organic Chemistry, Indian Association for the Cultivation of Science, Jadavpur, Calcutta—700 032, India

Some transformations of the hexahydro-4a-hydroxy-4,9a-ethano-1*H*-fluoren-11-ones (**4a**) and (**4b**), derived *via* acid-catalysed alkylation-rearrangement reactions, are described. While hydrogenolysis of the demethoxyhydroxycyclopentanone (**4a**) with lithium–ammonia proceeds with retention of configuration to give the respective bridged-ketone (**6a**) exclusively, the corresponding methoxy analogue (**4b**) on the other hand gave the respective hydrogenolysed product (**6b**) in a very low yield, which however, was obtained along with its C-4a epimer (**5b**) by catalytic hydrogenolysis in the presence of perchloric acid. Formylation–oxidation of (**6a**) or the alkoxy ketones (**14**) and (**15**) gave the β,γ-unsaturated acid (**8a**); the methoxy analogue (**6b**) under similar conditions gave the respective acid (**8b**), arising through novel fragmentation reactions. Under certain conditions, (**6a**) gave the *cis*-dicarboxylic acid (**10a**) along with (**8a**). The hydroxy ketones (**4a**) and (**4b**) underwent fragmentations with ethyl formate and sodium hydride or with perchloric acid in ethanol to give the angularly functionalised esters (**18a**) and (**18b**).

In the previous paper in this series[1] we have reported some transformations of the hydroxycyclopentanones (**2a, b**) derived through acid-catalysed alkylation-rearrangement reactions of the hexahydrophenanthrene diazoketones (**1a, b**). In our earlier papers,[2,3] we described that the *C*-alkylation rearrangements of the tetrahydrofluorene diazoacetyl derivatives (**3a**) and (**3b**) with tetrafluoroboric acid in nitromethane gave the corresponding bridged hydroxycyclopentanones (**4a**) and (**4b**) in good yields. We now present in detail some interesting transformations of (**4a**) and (**4b**) to a number of functionalised hexahydro- and tetrahydro-fluorene derivatives involving fragmentation reactions.



(1) *n* = 2
(3) *n* = 1



(2) *n* = 2
(4) *n* = 1

a; R = H
b; R = OMe

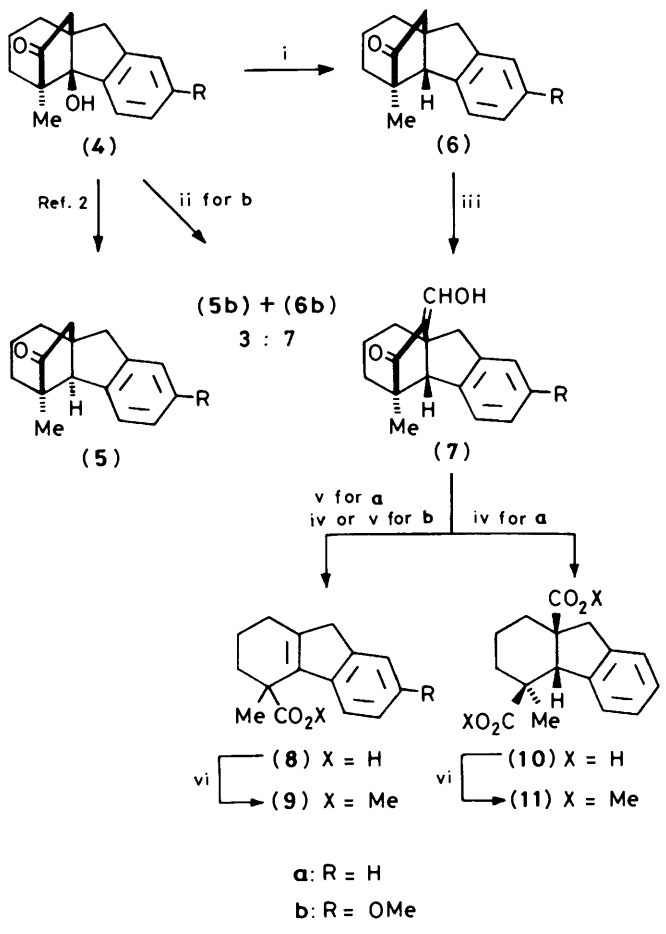
Results and Discussion

As previously reported,[2] the catalytic hydrogenations of compounds (**4a**) and (**4b**) over palladium–charcoal in the presence and the absence of perchloric acid produced the corresponding hydrogenolysed products (**5a**) and (**5b**) respectively in excellent yields, through inversion of configuration at the benzylic asymmetric centre. The reductive cleavage of (**4a**) with lithium in ammonia[1] followed by oxidation with Jones reagent gave exclusively the corresponding crystalline ketone (**6a**) in 88% yield, with *retention* of configuration, similar to that observed[1] with the related hydrophenanthrene derivatives (**2a, b**) (Scheme 1). In contrast, under identical reaction conditions, the *p*-methoxy derivative (**4b**) was recovered unchanged.† In one experiment, a large excess of lithium and a longer reaction period gave only a very low yield of the desired hydrogenolysed product (**6b**).However, hydrogenolysis of (**4b**) over palladium–charcoal in ethanol in the presence of aqueous perchloric acid produced a 7:3 mixture of the epimeric ketones (**6b**) and (**5b**) in 96% yield. The i.r. and ^{1}H n.m.r. spectral data of these ketones are in complete agreement with the assigned structures (see the Experimental section).

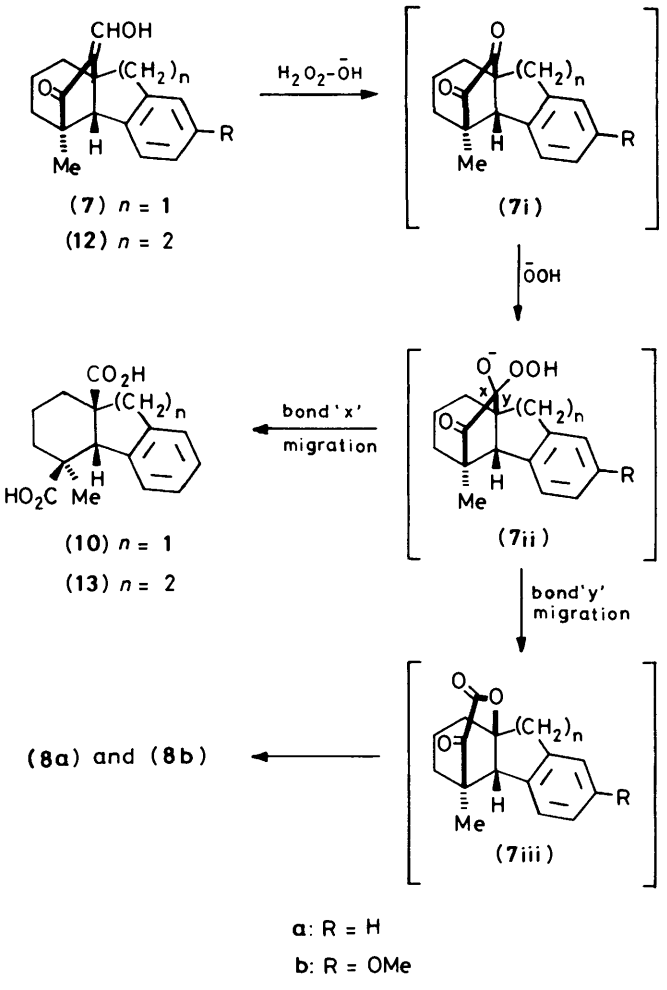
With the C-4a epimeric ketones (**5a, b**) and (**6a, b**) in hand, attention was next directed to the formation of the C-4,9a-*cis*-dicarboxylic acid functions in the *trans*- and *cis*-hexahydrofluorene entities *via* a formylation–oxidation sequence.[1,6]

In keeping with our earlier observation on the related *trans*-octahydrophenanthrene analogues,[1] attempted formylation of (**5a**) under forcing conditions with an excess of ethyl formate in the presence of sodium hydride failed to give the respective hydroxymethylene derivatives, possibly owing to the strong steric interaction between the C-2 axial methylene hydrogen and the $COCH_2$ moiety. However, condensation of the *cis*-ketone (**6a**) with ethyl formate in the presence of a large excess of sodium hydride in benzene afforded the crystalline hydroxymethylene derivative (**7a**) in 87% yield. Surprisingly oxidation of (**7a**) with alkaline hydrogen peroxide (30%) at room temperature, under the usual conditions,[1,6] produced the liquid unsaturated acid (**8a**) as the sole isolable product. This was characterised as the methyl ester (**9a**) [50% overall yield from (**7a**)] after esterification with diazomethane (Scheme 1). The spectral and analytical data of (**9a**) are consistent with the assigned structure. Repeating the oxidation of (**7a**) with alkaline hydrogen peroxide at 0—5 °C gave a mixture of (**8a**) and the dicarboxylic acid (**10a**), from which the crystalline acid (**10a**) was separated (*ca.* 29%). The corresponding dimethyl ester (**11a**) was obtained by esterification with diazomethane.

† The recovery of the *p*-methoxyhydroxy ketone (**4b**) is not surprising in view of the earlier observations by Birch,[4] who reported that in sodium–ammonia induced reactions, *o*- and *m*-methoxybenzyl alcohols were reduced to the respective methoxytoluenes; whereas *p*-methoxybenzyl alcohol suffered only ring reduction. LCAO–MO calculations[5] have shown that the ring position of the radical anion adjacent to the $-CH_2OH$ function was comparatively electron rich in the *ortho* and *meta* isomers.



Scheme 1. *Reagents:* i, Li–NH_3, Jones reagent; ii, H_2, Pd–C (10%), $HClO_4$ (70%); iii, NaH, HCO_2Et, C_6H_6; iv, NaOH (10%), H_2O_2 (30%) at 0—5 °C, HCl; v, NaOH (10%), H_2O_2 (30%) at 25—30 °C, HCl; vi, CH_2N_2–Et_2O



Scheme 2.

The formylation of the methoxy ketone (**6b**) and oxidation of the resulting hydroxymethylene derivative (**7b**) with alkaline hydrogen peroxide both at 0—5 °C or at room temperature afforded the unsaturated acid (**8b**) as the only isolable product, which was again characterised as the respective methyl ester (**9b**) [49% overall yield based on (**6b**)].

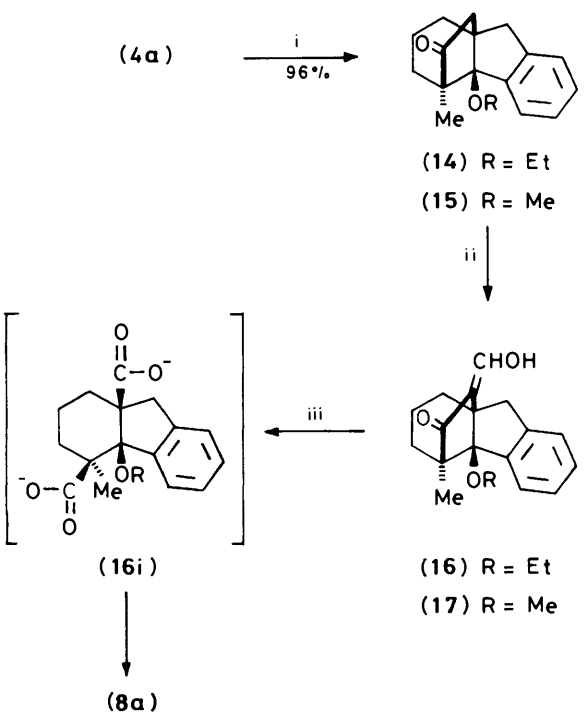
The formation of the unsaturated acids (**8a**) and (**8b**) from the respective hydroxymethylene ketones (**7a**) and (**7b**) is in sharp contrast to the similar oxidative degradation[1] of the hydrophenanthrene derivatives (**12a, b**) which produced only the respective diacids (**13a, b**) in high yields. This possibly arises due to the difference in strain in the hydrofluorene and the hydrophenanthrene substrates. Examinations of Dreiding models clearly indicate that the hydrofluorene bridged compounds (**7a**) and (**7b**) are considerably more strained in comparison to those of the hydrophenanthrene analogues (**12a, b**). The exceptional modes of peracid oxidation reaction in constrained systems is also known.[8] In the cases of the hydroxymethylene compounds (**7a, b**) and (**12a, b**), the oxidative degradation with alkaline hydrogen peroxide possibly* proceeds through the respective intermediate diketones (**7i**), whereas the subsequent cleavage of the corresponding hydroperoxide adducts (**7ii**) may involve two different modes of bond rearrangements. Thus, while the migration of bond 'x' in (**7ii**) would lead to the dicarboxylic acids (**10a**) and (**13a, b**), the bond 'y' migration would give rise to the angular oxolactone intermediates (**7iii**), finally resulting in the unsaturated acids (**8a**) and (**8b**) by a base-catalysed elimination process (Scheme 2).

Access to the unsaturated acid (**8a**) has also been accomplished through formylation–oxidation of the ethoxy- and the methoxy-cyclopentanones (**14**) and (**15**), respectively (Scheme 3). Thus, treatment of the hydroxy ketone (**4a**) with dry refluxing ethanol or methanol in the presence of a catalytic amount of perchloric acid (70%) afforded the respective crystalline ethoxy- and methoxy-ketones (**14**) and (**15**) in 96% yield. Attempted reactions with propan-1-ol and butan-2-ol failed to give the respective alkoxy derivatives. The methoxy analogue (**4b**) failed to give any exchange product with ethanol or methanol. The crude hydroxymethylene ketones (**16**) and (**17**), prepared from (**14**) and (**15**) respectively, on oxidation with alkaline hydrogen peroxide afforded (**8a**) in good yields. The formation of (**8a**) from (**16**) and (**17**) in the oxidation sequence may be rationalised as proceeding through a base-catalysed decarboxylative elimination[11] of the intermediate (**16i**) (Scheme 3).†

On attempted formylation with ethyl formate and sodium hydride (Scheme 4), the hydroxy ketone (**4a**) underwent

* It is generally accepted that hindered twinned carbonyl compounds[9] are cleaved easily by hydroperoxide anion through a Baeyer–Villiger type rearrangement.[10]

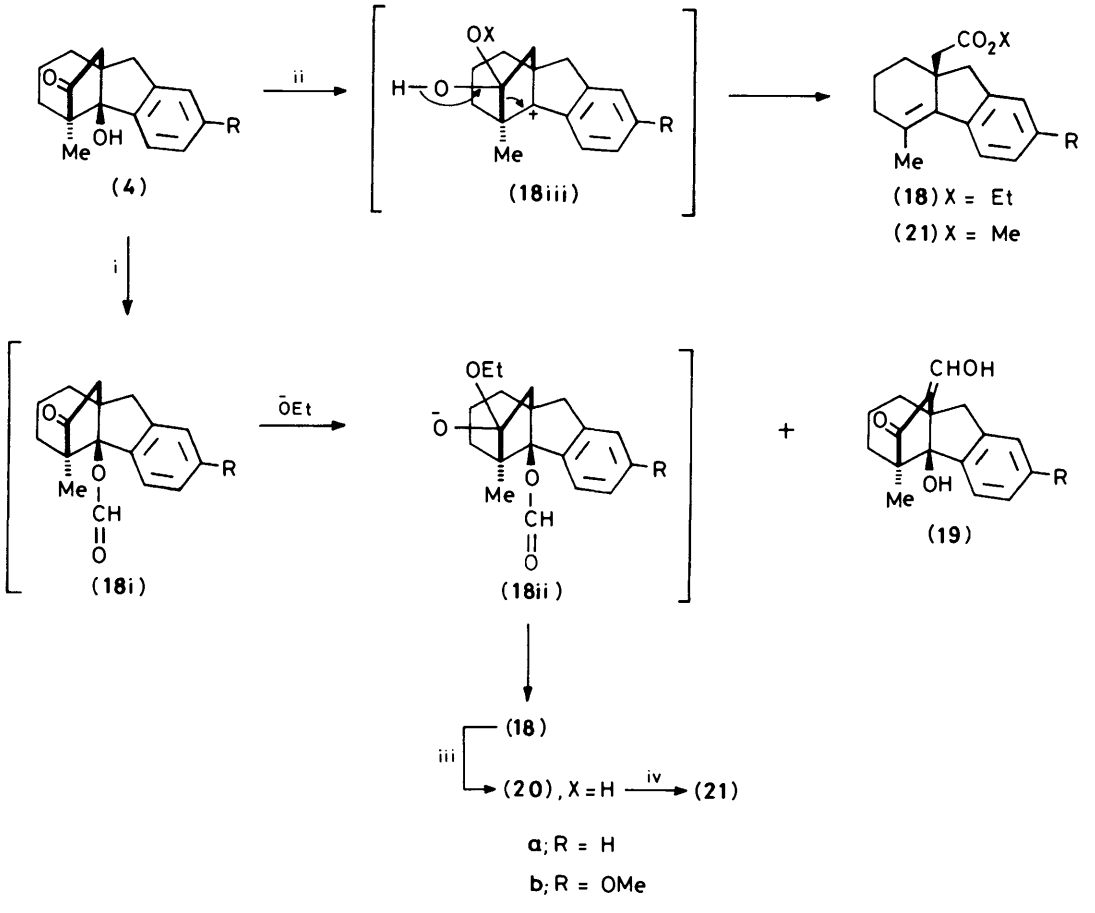
† It is possible that owing to the presence of the neighbouring alkoxy group the oxidation in the substrates (**16**) and (**17**) follow only this course of the reaction unlike those shown for (**7**) and (**12**) in Scheme 2.



Scheme 3. *Reagents:* i, EtOH or MeOH, $HClO_4$ (70%) as catalyst; ii, NaH, HCO_2Et, C_6H_6; iii, NaOH (10%), H_2O_2 (30%) at 0—5 °C or 25—30 °C, HCl

fragmentation leading to the unsaturated ester (**18a**) in 75% yield along with the hydroxymethylene ketone (**19a**) (*ca.* 7%). Oxidation of (**19a**) with alkaline hydrogen peroxide again gave (**8a**). Attempted formylation of the methoxy analogue (**4b**) again gave the respective unsaturated ester (**18b**) in 75% yield as the only isolable product. The esters (**18a**) and (**18b**) were further characterised through the respective crystalline acids (**20a**) and (**20b**). The i.r. and ^1H n.m.r. spectral data of these compounds are in complete agreement with the assigned structures (see the Experimental section). That ethyl formate plays an important role in the fragmentations of the hydroxy ketones (**4a**) and (**4b**) is evident from the recovery of the unchanged materials on treatment with refluxing sodium ethoxide or potassium hydroxide in ethanol. Possibly, *trans*-esterifications of (**4a**) and (**4b**) during attempted formylation reaction led to the formates (**18i**) which undergo a *syn*-periplanar fragmentation[12,*] through the intermediates (**18ii**) (Scheme 4). Interestingly, the hydroxy ketones (**4a**) and (**4b**) also led to the fragmented ethyl esters (**18a**) and (**18b**) respectively, in excellent yields, on prolonged refluxing with ethanol in the presence of perchloric acid (70%). Repeating the reaction with methanol gave the respective methyl esters (**21a**) and (**21b**). Acid-catalysed fragmentation of (**4a**) and (**4b**) logically proceeds through the cation (**18iii**) analogous to the well known Grob fragmentation.[13]

* This fragmentation is somewhat similar to that observed[1] in the methoxyhydrophenanthrene analogue (**2b**) during formylation reaction. In that case, however, the initially produced hydroxymethylene intermediate underwent fragmentation.



Scheme 4. *Reagents:* i, NaH, HCO_2Et, C_6H_6; ii, EtOH or MeOH, $HClO_4$ (70%); iii, KOH, EtOH; iv, CH_2N_2–Et_2O

In conclusion, the present work provides efficient synthetic routes to some functionalised hydrofluorene derivatives involving a few mechanistically interesting fragmentation reactions of the easily accessible intermediates from certain β,γ-unsaturated diazomethyl ketones.

Experimental

The compounds described are all racemates. M.p.s were measured in open capillary tubes and are uncorrected. I.r. spectra of solids (KBr) and liquids (film) were recorded on a Perkin-Elmer model 298 spectrometer. U.v. spectra were recorded on a Beckman DU or a Shimadzu UV 210A spectrometer for solutions in 95% ethanol. ^{1}H N.m.r. spectra were recorded at 60, 100, or 200 MHz (as specified) on Varian Associates T-60A, HA-100 and XL-200 spectrometers respectively, for solutions in CCl_4 or $CDCl_3$ (if specified), with $SiMe_4$ as an internal standard. Analytical g.l.c. was performed on a Hewlett-Packard model 5730A chromatograph equipped with a flame-ionisation detector employing the following columns with N_2 as the carrier gas at 190 °C:10% UCW-982 (20 ft × $\frac{1}{8}$ in) (Column A); 1.5% OV-17 (6.56 ft × $\frac{1}{4}$ in) (Column B). Elemental analyses were performed by P. P. Bhattacharya of this laboratory. Column chromatography was performed on neutral alumina (Brockman Grade I). Petroleum and light petroleum refer to fractions of b.p. 60—80 °C and 40—60 °C respectively. Ether refers to diethyl ether.

Hydrogenolysis of the 4aβ-*Hydroxycyclopentanones* (**4a, b**) *with* Li–NH_3.—(±)-4α-*Methyl*-2,3,4,4aβ,9,9a-*hexahydro*-4β,9aβ-*ethano*-1H-*fluoren*-11-*one* (**6a**). To a magnetically stirred solution of the hydroxy ketone (**4a**) (500 mg, 2.06 mmol) in dry Et_2O (15 ml) and anhydrous liquid NH_3 (250 ml), distilled over Na, was added freshly scraped Li-wire (295 mg, 42 mmol) in small portions over 3 min. Stirring was continued for a further 5 min after which an excess of powdered NH_4Cl was added and the NH_3 allowed to evaporate. The residue was carefully acidified with 6M HCl, and extracted with Et_2O. The extract was dried (Na_2SO_4) and evaporated and the resulting crude viscous gum (437 mg) ($\nu_{max.}$ 3 460, 1 730, and 1 600 cm^{-1}) was dissolved in acetone (5 ml) and oxidised with Jones reagent[14] at 10—15 °C until the colour of the reagent persisted for 10 min; the mixture was then worked up. The crude product was chromatographed on silica gel (10 g) with petroleum as eluant to afford the cyclopentanone (**6a**) (410 mg, 88%), m.p. 71—72 °C (light petroleum) (Found: C, 85.0; H, 8.0. $C_{16}H_{18}O$ requires C, 84.91; H, 8.02%), $\nu_{max.}$ 2 940, 2 920, 2 880, 2 840, 1 730, 1 600, 1 465, 1 450, 1 400, 1 370, and 1 300 cm^{-1}; δ($CDCl_3$) 1.40 (3 H, s, Me), 1.5—2.16 (8 H, m, methylenes), 2.85 (2 H, br s, $ArCH_2$), 2.99 (1 H, br s, Ar*CH*), and 7.0—7.4 (4 H, m, ArH).

(±)-7-*Methoxy*-4α-*methyl*-2,3,4,4aβ,9,9a-*hexahydro*-4β,9aβ-*ethano*-1H-*fluoren*-11-*one* (**6b**).—*Method A: Catalytic hydrogenation in the presence of acid.* To a solution of the hydroxy ketone (**4b**) (500 mg, 1.84 mmol) in ethanol (50 ml) was added 70% aqueous $HClO_4$ (1 ml). The solution was hydrogenated at room temperature and atmospheric pressure in the presence of 10% palladium–charcoal (300 mg) for 24 h after which it was cautiously neutralised with solid Na_2CO_3 and the catalyst was filtered off. Removal of the solvent from the filtrate under reduced pressure afforded a mixture of the epimers (**6b**) and (**5b**) (452 mg, 96%) in the ratio of 7:3 (^{1}H n.m.r. at 200 MHz and g.l.c. in column A) (R_t 4.4 and 3.5 min). This mixture was chromatographed on alumina (10 g) with petroleum–ether as eluant (92:8) to afford (**5b**) (130 mg, 28%) identical with an authentic sample[2] (mixed m.p., i.r., and ^{1}H n.m.r.). The subsequent eluates with petroleum–ether (90:10) gave (**6b**) (288 mg, 61%), m.p. 105—106 °C (petroleum) (Found: C, 79.4; H, 7.8. $C_{17}H_{20}O_2$ requires C, 79.65; H, 7.86%), $\nu_{max.}$ 2 980, 2 950, 2 930, 2 915, 2 890, 2 860, 2 830, 1 735, 1 615, 1 575, 1 475, 1 460, 1 445, 1 425, 1 400, 1 370, 1 340, 1 320, and 1 305 cm^{-1}; δ ($CDCl_3$; 100 MHz) 1.35 (3 H, s, Me), 1.4—2.2 (8 H, m, methylenes including $COCH_2$), 2.82 (2 H, br s, $ArCH_2$), 2.94 (1 H, br s, Ar*CH*), 3.76 (3 H, s, ArO*Me*), and 6.6—7.36 (3 H, m, ArH).

Method B: With Li–NH_3. Reduction of the hydroxy ketone (**4b**) (500 mg, 1.84 mmol) in Et_2O (15 ml) and anhydrous NH_3 (250 ml) with Li-wire (295 mg, 42 mmol) was carried out as described for compound (**4a**) with stirring for an additional 15 min. After work-up it was oxidised with Jones reagent.[14] The crude product was chromatographed on alumina (10 g) to afford (**6b**) (30 mg, 6%), m.p. 105—106 °C alone or in admixture with the sample described above.

Hydroxymethylation followed by Oxidation of the Cyclopentanones (**6a**) *and* (**6b**).—(±)-10-*Hydroxymethylene*-4α-*methyl*-2,3,4,4aβ,9,9a-*hexahydro*-4β,9aβ-*ethano*-1H-*fluoren*-11-*one* (**7a**). To a magnetically stirred suspension of NaH (350 mg, 14.6 mmol) in dry benzene (5 ml) cooled in an ice-bath under N_2, a solution of the ketone (**6a**) (250 mg, 1.11 mmol) in dry benzene (5 ml) was added, followed by a drop of dry MeOH. Stirring was continued at the same temperature for 1 h after which ethyl formate (1.25 ml, 15.5 mmol) was added to the cold stirred mixture; it was then stirred for a further 2 h and then left overnight at room temperature. The excess of NaH was decomposed by dropwise addition of MeOH followed by cold water. The neutral material was extracted with Et_2O to afford a small amount of brown gum which was not characterised further. The basic aqueous part and the washings were chilled together and acidified with 6M HCl. The organic material was extracted with Et_2O to afford the hydroxymethylene ketone (**7a**) as a light yellow solid (245 mg, 87%), m.p. 122 °C (ether–petroleum) (Found: C, 80.2; H, 7.1. $C_{17}H_{18}O_2$ requires C, 80.08; H, 7.34%), $\nu_{max.}$ 2 920, 2 850, 1 670, 1 600, 1 470, 1 445, 1 385, 1 370, 1 320, and 1 305 cm^{-1}; δ 1.4 (3 H, s, Me), 1.43—2.1 (6 H, m, methylenes), 2.83 (2 H, s, $ArCH_2$), 2.93 (1 H, s, Ar*CH*), 6.66—7.39 (5 H, m, ArH and =C*H*OH), and 10.23 (1 H, br s, =CHO*H*; exchangeable with D_2O).

(A) *Oxidation with* H_2O_2 *at* 25—30 °C; (±)-*Methyl* 4-*Methyl*-1,2,3,4-*tetrahydrofluorene*-4-*carboxylate* (**9a**).—The hydroxymethylene ketone (**7a**) (125 mg, 0.49 mmol) was dissolved in cooled aqueous NaOH (10 ml, 10%) and maintained at 25—30 °C (bath temperature). Aqueous H_2O_2 (5 ml, 30%) was added dropwise with stirring over 20—25 min, and stirring was continued for 1 h. A second aliquot of aqueous NaOH (10 ml, 10%) was added in one portion followed by dropwise addition of H_2O_2 (5 ml, 30%). The mixture was stirred for a further 2 h at 25—30 °C and then kept overnight. The solution was diluted with water, acidified with 6M HCl, and extracted with ethyl acetate. The extract was dried (Na_2SO_4) and evaporated to afford the unsaturated acid (**8a**) (70 mg) as a thick light brown liquid ($\nu_{max.}$ 1 690 and 1 600 cm^{-1}). This was dissolved in Et_2O (10 ml) and esterified with an excess of CH_2N_2 in Et_2O. The crude ester was purified by filtration (in petroleum) through a short packed column of alumina to afford the ester (**9a**) (59 mg, 50% overall yield) (homogeneous in g.l.c. on column **B**) (R_t 4.5 min) (Found: C, 79.2; H, 7.6. $C_{16}H_{18}O_2$ requires C, 79.31; H, 7.49%), $\nu_{max.}$ 2 910, 2 850, 1 725 (C=O), 1 605, 1 580, 1 450, 1 410, 1 350, and 1 330 cm^{-1}; $\lambda_{max.}$ 258 nm (log ε 4.06) (Styrene); δ($CDCl_3$) 1.50 (3 H, s, Me), 1.51—2.66 (6 H, m, methylenes), 3.21 (2 H, br s, $ArCH_2$), 3.57 (3 H, s, CO_2Me), and 6.73—7.42 (4 H, m, ArH).

(B) *Oxidation with* H_2O_2 *at* 0—5 °C: (±)-4α-*Methyl*-2,3,4,4aβ,9,9a-*hexahydro*-1H-*fluorene*-4β,9aβ-*dicarboxylic Acid*

(**10a**) *and the Unsaturated Acid* (**8a**).—Oxidation of (**7a**) (125 mg, 0.49 mmol) with alkaline hydrogen peroxide at 0—5 °C following the procedure described above afforded a mixture of the diacid (**10a**) and unsaturated acid (**8a**) (105 mg) in a ratio of *ca.* 3:4 as revealed by g.l.c. (on column B) (R_t 9.06 and 4.5 min) and ^{1}H n.m.r. (at 100 MHz) analyses of the corresponding methyl esters (CH_2N_2–Et_2O). From this mixture the diacid (**10a**) (40 mg, 29%) was separated, m.p. 208 °C (decomp.) (ethyl acetate–petroleum) (Found: C, 70.05; H, 6.6. $C_{16}H_{18}O_4$ requires C, 69.79; H, 6.62%), $\nu_{max.}$ 3 000, 2 960, 2 940, 1 705, 1 470, 1 455, 1 405, and 1 325 cm^{-1}.

The dicarboxylic acid (**10a**) (40 mg, 0.146 mmol) in Et_2O (15 ml) was esterified with CH_2N_2 in Et_2O and the product was purified by filtration (in petroleum) through a short packed column of alumina to give (±)-*dimethyl* 4α-*methyl*-2,3,4,4aβ,9,9a-*hexahydro*-1H-*fluorene*-4β,9aβ-*dicarboxylate* (**11a**) (36 mg, 82%) as a colourless thick liquid (homogeneous in g.l.c. on column B) (R_t 9.06 min), $\nu_{max.}$ 2 960, 2 940, 2 880, 1 725, 1 460, 1 435, 1 380, 1 345, and 1 330 cm^{-1}; δ($CDCl_3$; 100 MHz) 1.00 (3 H, s, Me), 1.20—3.48 (9 H, m, methylenes), 3.61 (3 H, s, $-CO_2Me$), 3.64 (3 H, s, $-CO_2Me$), and 7.08—7.4 (4 H, m, ArH).

(±)-*Methyl* 7-*Methoxy*-4-*methyl*-1,2,3,4-*tetrahydrofluorene*-4-*carboxylate* (**9b**).—Following the procedure described for compound (**6a**), the methoxy analogue (**6b**) (250 mg, 0.98 mmol) was converted into its hydroxymethylene derivative (**7b**) 245 mg, 88%) ($\nu_{max.}$ 1 710, 1 660, and 1 600 cm^{-1}), a thick brown liquid. The crude product gave on oxidation with alkaline H_2O_2 (30%) as described for (**7a**) at 25—30 °C the unsaturated acid (**8b**) (165 mg) as a light brown semi-solid. This was directly esterified (CH_2N_2 in Et_2O) and the resulting ester was purified by filtration (in petroleum) through a short packed column of alumina to give (**9b**) (130 mg, 49%) as a colourless thick liquid (homogeneous in g.l.c.) (Found: C, 74.8; H, 7.15. $C_{17}H_{20}O_3$ requires C, 74.97; H, 7.40%), $\nu_{max.}$ 2 910, 2 830, 1 720, 1 605, 1 580, 1 460, 1 420, 1 375, 1 345, and 1 310 cm^{-1}; $\lambda_{max.}$ 267 nm (log ε 4.12); δ ($CDCl_3$; 200 MHz) 1.55 (3 H, s, Me), 1.65—2.5 (6 H, m, methylenes), 3.28 (2 H, d, *J* 5 Hz, ArCH_2), 3.66 (3 H, s, $-CO_2Me$), 3.83 (3 H, s, ArOMe), and 6.75—7.15 (3 H, m, ArH).

Repeating the oxidation of (**7b**) at 0—5 °C gave an identical result.

Transformation of the Hydroxycyclopentanone (**4a**) *to the Alkoxycyclopentanones* (**14**) *and* (**15**).—(±)-4aβ-*Ethoxy*-4α-*methyl*-2,3,4,4a,9,9a-*hexahydro*-4β,9aβ-*ethano*-1H-*fluoren*-11-*one* (**14**). A solution of the hydroxy ketone (**4a**) (242 mg, 1 mmol) in anhydrous ethanol (30 ml) and aqueous $HClO_4$ (70%) (0.3 ml) was heated at 80—82 °C (bath temperature) for 4.5 h under N_2. The reaction mixture was neutralised with $NaHCO_3$, filtered, and evaporated under reduced pressure to afford compound (**14**) as a white solid (260 mg, 96%), m.p. 98 °C (petroleum) (Found: C, 79.7; H, 8.2. $C_{18}H_{22}O_2$ requires C, 79.96; H, 8.20%), $\nu_{max.}$ 2 970, 2 910, 1 870, 1 850, 1 735, 1 450, 1 430, 1 400, 1 365, and 1 340 cm^{-1}; δ 0.96 (3 H, t, *J* 7 Hz, CH_2Me), 1.31 (3 H, s, Me), 1.4—2.6 (6 H, m, methylenes), 1.45 (δ_A) and 2.42 (δ_B) (2 H, AB_q, *J* 18 Hz, $COCH_2$), 2.75 (2 H, br d, *J* 6 Hz, ArCH_2), 3.1 (2 H, q, *J* 7 Hz, $-CH_2Me$), and 6.9—7.5 (4 H, m, ArH).

(±)-4aβ-*Methoxy*-4α-*methyl*-2,3,4,4a,9,9a-*hexahydro*-4β,9aβ-*ethano*-1H-*fluoren*-11-*one* (**15**).—Following the procedure described for the preparation of (**14**) treatment of the hydroxy ketone (**4a**) (242 mg, 1 mmol) at 60—65 °C with dry methanol gave the methoxy ketone (**15**) as a white solid (247 mg, 96%), m.p. 78 °C (petroleum) (Found: C, 79.8; H, 8.2. $C_{17}H_{20}O_2$ requires C, 79.65; H, 7.86%), $\nu_{max.}$ 2 960, 2 940, 2 870, 2 830, 1 735, 1 465, 1 400, and 1 370 cm^{-1}; δ($CDCl_3$) 1.4 (3 H, s, Me), 1.0—2.66 (6 H, m, methylenes), 1.81 (δ_A) and 2.31 (δ_B) (2 H, AB_q, *J* 18 Hz, $-COCH_2$), 2.83 (2 H, br d, *J* 6 Hz, ArCH_2), 3.03 (3 H, s, OMe), and 7.01—7.63 (4 H, m, ArH).

Formylation–Oxidation of the Alkoxy Bridged Ketones (**14**) *and* (**15**) *to the Unsaturated Methyl Ester* (**9a**).—(A) A solution of the ethoxy ketone (**14**) (250 mg, 0.93 mmol) in benzene (5 ml) was formylated with NaH (350 mg, 14.6 mmol) and ethyl formate (1.25 ml, 15.5 mmol) was described for (**6a**) to afford the formylated product (**16**) (250 mg, 91%) as a thick brown liquid ($\nu_{max.}$ 1 670 and 1 605 cm^{-1}). The crude product was oxidised with alkaline H_2O_2 (30%) at 25—30 °C as described for (**7a**) to afford the unsaturated acid (**8a**) which was esterified (CH_2N_2–Et_2O) and purified by filtration (in petroleum) through a short packed column of alumina to afford (**9a**) (131 mg, 58%), identical (i.r., ^{1}H n.m.r., and g.l.c.) to the sample described before.

Repeating the oxidation at 0—5 °C gave an identical result.

(B) Following the procedure described for compound (**6a**), the methoxy ketone (**15**) (250 mg, 0.98 mmol) was converted into its hydroxymethylene derivative (**17**) (245 mg, 88%) as a brown liquid ($\nu_{max.}$ 1 670 and 1 605 cm^{-1}). This crude product on oxidation with alkaline H_2O_2 (30%) at 25—30 °C as described above gave the crude acid (**8a**) which was esterified (CH_2N_2–Et_2O) and purified by filtration (in petroleum) through a short packed column of alumina to give (**9a**) (130 mg, 55%), identical (i.r., ^{1}H n.m.r., and g.l.c.) to the sample described before.

Repeating the oxidation at 0—5 °C gave an identical result.

Cleavage of the Hydroxycyclopentanones (**4a**) *and* (**4b**): (±)-*Ethyl* 4-*Methyl*-2,3,9,9a-*tetrahydro*-1H-*fluoren*-9a-*ylacetate* (**18a**).—(A) *Reaction with ethyl formate and* NaH. Hydroxymethylation of compound (**4a**) (250 mg, 1.03 mmol) in benzene (5 ml) with NaH (400 mg, 16.66 mmol) in benzene (4 ml) and ethyl formate (1.25 ml, 15.5 mmol) following the procedure described for (**6a**) afforded from the neutral fraction a brown liquid which on chromatography over alumina (6 g) using petroleum as eluant afforded (**18a**) (210 mg, 75%) as a colourless liquid (Found: C, 79.8; H, 8.3. $C_{18}H_{22}O_2$ requires C, 79.96; H, 8.20%), $\nu_{max.}$ 2 930, 2 860, 1 730, 1 520, 1 500, 1 365, and 1 310 cm^{-1}; δ 1.18 (3 H, t, *J* 7 Hz, $-CO_2CH_2Me$), 1.93 (3 H, s, =CMe), 1.46—2.55 (6 H, m, methylenes), 2.59 (δ_A) and 3.34 (δ_B) (2 H, AB_q, *J* 16 Hz, ArCH_2), 3.96 (2 H, q, *J* 7 Hz, CO_2CH_2Me), and 6.82—7.52 (4 H, m, ArH).

The hydroxymethylene compound (**19**) (20 mg, 7%) was isolated from the basic aqueous fraction and washings after acidification with 6M HCl and extraction with Et_2O. The crude derivative (**19**) (43 mg, 0.16 mmol), isolated from several runs, was oxidised with alkaline H_2O_2 (30%) as described for compound (**7a**) to afford the unsaturated acid (**8a**) which was esterified (CH_2N_2–Et_2O) and chromatographed on alumina to afford the ester (**9a**) (21 mg, 55%), identical (i.r., ^{1}H n.m.r., and g.l.c.) with the sample described before.

(B) $HClO_4$-*Catalysed cleavage in ethanol.* A solution of the hydroxy ketone (**4a**) (242 mg, 1 mmol) in anhydrous ethanol (30 ml) and $HClO_4$ (70%; 1.5 ml) was heated to reflux under N_2 for 4—5 h. The reaction mixture was cooled, neutralized with $NaHCO_3$, and filtered. Removal of the solvent under reduced pressure afforded the ethyl ester (**18a**) (200 mg, 74%), identical (i.r. and ^{1}H n.m.r.) with the sample described above.

Hydrolysis of (**18a**): (±)-4-*Methyl*-2,3,9,9a-*tetrahydro*-1H-*fluoren*-9a-*ylacetic Acid* (**20a**).—A solution of compound (**18a**) (125 mg, 0.46 mmol) in ethanol (2.25 ml) was refluxed under N_2 for 2 h with a solution of KOH (250 mg, 4.46 mmol) in water (0.25 ml). After work-up, the aqueous alkaline layer was acidified with 6M HCl and the acidic material was extracted with Et_2O. The dried (Na_2SO_4) ethereal layer on evaporation left a

white solid (**20a**) (80 mg, 71%), m.p. 137—138 °C (ether–petroleum) (Found: C, 79.2; H, 7.7. $C_{16}H_{18}O_2$ requires C, 79.31; H, 7.49%), $\nu_{max.}$ 3 020, 2 940, 2 890, 2 830, 2 700, 1 685, 1 460, 1 430, 1 405, and 1 320 cm^{-1}; $\lambda_{max.}$ 258 nm (log ε 4.31).

The unsaturated acid (**20a**) (50 mg, 0.20 mmol) in Et_2O (10 ml) was esterified (CH_2N_2 in Et_2O) and purified by filtration through a short column of alumina (5 g) using petroleum as eluant to afford (±)-*methyl* 4-*methyl*-2,3,9,9a-*tetrahydro*-1H-*fluoren*-9a-*ylacetate* (**21a**) (46 mg, 87%) as a colourless thick liquid (Found: C, 79.65; H, 7.9. $C_{17}H_{20}O_2$ requires C, 79.65; H, 7.86%), $\nu_{max.}$ 2 935, 2 850, 1 730, 1 530, 1 485, 1 380, and 1 320 cm^{-1}; δ 1.93 (3 H, s, =CMe), 1.25—2.6 (8 H, m, methylenes), 2.5 (δ_A) and 3.31 (δ_B) (2 H, AB_q, *J* 16 Hz, $ArCH_2$), 3.53 (3 H, s, $-CO_2Me$), and 6.86—7.5 (4 H, m, ArH).

$HClO_4$-*Catalysed Cleavage of* (**4a**) *to the Methyl Ester* (**21a**).—Following the procedure described above for the preparation of the ethyl ester (**18a**) by acid-catalysed cleavage, treatment of the hydroxy ketone (**4a**) (242 mg, 1 mmol.) with dry methanol (30 ml) and $HClO_4$ (70%; 1.5 ml) gave the methyl ester (**21a**) (195 mg, 76%), identical (i.r. and ^1H n.m.r.) with the sample described above.

(±)-*Ethyl* 7-*Methoxy*-4-*methyl*-2,3,9,9a-*tetrahydro*-1H-*fluoren*-9a-*ylacetate* (**18b**).—(A) *Reaction with ethyl formate and* NaH. Following the procedure described for compound (**4a**), the hydroxy ketone (**4b**) (250 mg, 0.919 mmol) was converted into the ethyl ester (**18b**) (208 mg, 75%) as a colourless liquid (Found: C, 76.1; H, 8.2. $C_{19}H_{24}O_3$ requires C, 75.97; H, 8.05%), $\nu_{max.}$ 2 935, 2 855, 1 730, 1 600, 1 500, 1 340, and 1 310 cm^{-1}; δ 1.18 (3 H, t, *J* 7 Hz, $-CH_2Me$), 1.85 (3 H, br s, =CMe), 1.43—2.6 (8 H, m, methylenes), 2.56 (δ_A) and 3.30 (δ_B) (2 H, AB_q, *J* 16 Hz, $ArCH_2$), 3.71 (3 H, s, ArOMe), 3.95 (2 H, q, *J* 7 Hz, $-CH_2Me$), and 6.33—7.30 (3 H, m, ArH).

(B) $HClO_4$-*Catalysed cleavage in ethanol.* Following the procedure described for the preparation of the ethyl ester (**18a**) by acid cleavage, the hydroxy ketone (**4b**) (272 mg, 1 mmol) on treatment with dry ethanol (30 ml) and $HClO_4$ (70%; 1.5 ml) gave the ethyl ester (**18b**) (225 mg, 75%), identical (i.r. and ^1H n.m.r.) with the sample described above.

Hydrolysis of (**18b**). (±)-7-*Methoxy*-4-*methyl*-2,3,9,9a-*tetrahydro*-1H-*fluoren*-9a-*ylacetic Acid* (**20b**).—The ester (**18b**) (125 mg, 0.41 mmol) was hydrolysed to the acid (**20b**) (86 mg, 76%) by following the procedure described for compound (**18a**), m.p. 153 °C (ethyl acetate–petroleum) (Found: C, 74.8; H, 7.4. $C_{17}H_{20}O_3$ requires C, 74.97; H, 7.40%); $\nu_{max.}$ 2 990, 2 960, 2 820, 2 800, 2 760, 2 720, 1 690, 1 610, 1 575, 1 480, 1 460, 1 450, and 1 430 cm^{-1}; $\lambda_{max.}$ 264 nm (log ε 4.25).

The unsaturated acid (**20b**) (50 mg, 0.18 mmol) was esterified (CH_2N_2–Et_2O) to (±)-*methyl* 7-*methoxy*-4-*methyl*-2,3,9,9a-*tetrahydro*-1H-*fluoren*-9a-*ylacetate* (**21b**) (46 mg, 88%) as a colourless thick liquid (Found: C, 75.4; H, 7.9. $C_{18}H_{22}O_3$ requires C, 75.49; H, 7.74%), $\nu_{max.}$ 2 940, 2 850, 1 730, 1 600, 1 580, 1 480, 1 430, 1 330, and 1 310 cm^{-1}; δ 1.86 (3 H, s, =CMe), 1.0—3.36 (8 H, m, methylenes), 2.50 (δ_A) and 3.16 (δ_B) (2 H, AB_q, *J* 16 Hz, $ArCH_2$), 3.50 (3 H, s, $-CO_2Me$), 3.73 (3 H, s, ArOMe), and 6.33—7.33 (3 H, m, ArH).

$HClO_4$-*Catalysed Cleavage of* (**4b**) *to the Methyl Ester* (**21b**).—Following the procedure described for the preparation of the ethyl ester (**18a**) by acid-catalysed cleavage; treatment of (**4b**) (272 mg, 1 mmol) with methanol (30 ml) and $HClO_4$ (70%; 1.5 ml) gave the methyl ester (**21b**) (210 mg, 73%), identical (i.r. and ^1H n.m.r.) with the sample described above.

Acknowledgements

Financial support from the Science and Engineering Research Council/D.S.T. Scheme under Grant No. 23(3p-8)/81-STP/II is gratefully acknowledged.

References

1 Part 4, B. Saha, S. C. Roy, G. O. S. V. Satyanarayana, U. R. Ghatak, A. Seal, S. Ray, R. Bandyopadhyay, M. Ghosh, B. Das, and B. S. Basak, *J. Chem. Soc., Perkin Trans. 1*, 1985, 505.
2 S. C. Roy, G. O. S. V. Satyanarayana, and U. R. Ghatak, *J. Org. Chem.*, 1982, **47**, 5361.
3 U. R. Ghatak, B. Sanyal, G. O. S. V. Satyanarayana, and S. Ghosh, *J. Chem. Soc., Perkin Trans. 1*, 1981, 1203.
4 A. J. Birch, *J. Chem. Soc.*, 1945, 809.
5 H. E. Zimmerman, *Tetrahedron*, 1961, **16**, 169.
6 (*a*) U. R. Ghatak and S. Chakrabarty, *J. Org. Chem.*, 1976, **41**, 1089; (*b*) U. R. Ghatak, S. Ghosh, and B. Sanyal, *J. Chem. Soc., Perkin Trans. 1*, 1980, 2881.
7 U. R. Ghatak, R. Dasgupta, and J. Chakravarty, *Tetrahedron*, 1974, **30**, 187.
8 H. Miura, K. Hirao, and O. Yonemitsu, *Tetrahedron*, 1978, **34**, 1805; and references cited therein.
9 (*a*) H. O. House, 'Modern Synthetic Reactions,' W. A. Benjamin, New York, 1965, p. 327; (*b*) Y. Ogata, Y. Sawaki, and H. Shimizu, *J. Org. Chem.*, 1978, **43**, 1760; (*c*) R. D. Temple, *ibid.*, 1970, **35**, 1275; (*d*) M. B. Hocking, K. Bhandari, B. Shell, and T. A. Smyth, *ibid.*, 1982, **47**, 4208.
10 (*a*) N. M. Weinshenker and R. Stephenson, *J. Org. Chem.*, 1972, **37**, 3741; (*b*) B. M. Trost and M. J. Bogdanowicz, *J. Am. Chem. Soc.*, 1973, **95**, 5321.
11 H. O. House, 'Modern Synthetic Reactions,' W. A. Benjamin, New York, 1965, pp. 651 and 661.
12 (*a*) H. L. Brown, G. L. Buchanan, and J. O'Donnell, *J. Chem. Soc., Perkin Trans. 1*, 1979, 1740; (*b*) R. D. Sands, *J. Org. Chem.*, 1969, **34**, 2794.
13 (*a*) C. A. Grob and P. W. Schiess, *Angew. Chem., Int. Ed. Engl.*, 1967, **6**, 1; (*b*) J. S. Yadav, D. G. Patil, R. R. Krishna, H. P. S. Chawla, and S. Dev, *Tetrahedron*, 1982, **38**, 1003; and references cited therein.
14 A. Bowers, T. G. Halsall, E. R. H. Jones, and A. J. Lemin, *J. Chem. Soc.*, 1953, 2548.

Received 19*th May* 1986; *Paper* 6/949