

## THE PHOTOCHEMISTRY OF 7,11-DIMETHYLDODECA-1,6,10-TRIEN-3-ONE

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**Abstract**—Direct irradiation of 7,11-dimethyldodeca-1,6,10-trien-3-one (13) has been shown to give the isomeric bicyclo[2.2.1]hexanes (24) and bicyclo[3.2.0]heptanes (14). The reduced ketone (22) was isolated when the irradiation was performed in pentane solution.

INTRAMOLECULAR cyclisation of an isolated double bond with a suitably placed, photochemically excited conjugated diene system has provided new and ingenious routes to ring systems of great synthetic potential. Crowley found that irradiation of myrcene (1) produced the cyclobutene 2 and, in smaller amount  $\beta$ -pinene (3).<sup>1</sup> Another minor product was shown to be the bicyclo[2.2.1]hexane 4, resulting from an alternative mode of interaction of the diene chromophore with the isolated double bond.<sup>2</sup> Hammond<sup>3</sup> found that 4 is the main product of the sensitised irradiation of myrcene (1); a process thought to involve a discrete 1,4-diradical intermediate (5), which cyclises specifically to form a five membered ring.

Subsequent extension of this work to the photolysis of  $\beta$ -farnesene (6) had greater synthetic potential, since the analogous photoproduct to  $\beta$ -pinene (3), namely 7, has the structure assigned to the naturally occurring sesquiterpene bergamotene. Unfortunately, two groups of workers were unable to achieve this transformation.<sup>4,5</sup> Direct irradiation of  $\beta$ -farnesene (6) produced a mixture containing the cyclobutene 9 and the bicyclo[3.2.0]heptane 10. Also, sensitised irradiation gave results analogous to the myrcene case in that the main products were the isomeric bicyclo[2.1.1]hexanes 11 and 12.

We sought to introduce greater selectivity into the cyclisation leading to structures such as 7 and 8 by using the trienone 13 as the substrate for irradiation, rather than  $\beta$ -farnesene (6). Since the  $n-\pi^*$  transition of a conjugated ketone occurs at  $\sim 320$  nm it should be possible to selectively excite this portion of the trienone (13) without interfering with the two isolated double bonds. The definitive work of Corey<sup>6</sup> would seem to support the formation of structures 7, 8 and 14 by an intramolecular photochemical process. In the synthesis of 13 it was decided to have the *trans* configuration of the  $\Delta^{6,7}$  double bond, hoping that this would be reflected in the stereochemistry of the photoproducts.

### *Synthesis of 7,11-dimethyldodeca-1,6,10-trien-3-one (13)*

The desire to preserve the *trans* configuration of the central double bond in 13 placed certain restrictions on the synthetic methods to be used. Geraniol (15) was chosen as the obvious precursor of such a synthesis, but in order to activate the

geranyl unit for subsequent elaboration it was necessary to prepare geranyl chloride (16). Although 16 cannot be formed free from isomers by thionyl chloride treatment of geraniol (15), we were able to achieve this transformation using  $\text{Ph}_3\text{P}/\text{CCl}_4$  under carefully controlled conditions to give 16, which was pure by glc analysis. Pure geranyl chloride (16) has recently been made by Corey<sup>7</sup> and Stork<sup>8</sup> by other methods.

The next step in the sequence was the conversion of geranyl chloride (16) to the aldehyde 17, using the method of Wittig.<sup>9</sup> This involved alkylation of the lithio salt of the imine 18 derived from acetaldehyde and cyclohexylamine followed by mild acid hydrolysis of the alkylated imine. Purification of the aldehyde 17 was effected by chromatography over silica rather than alumina, which caused it to undergo aldol condensation.

Reaction of 17 with ethynylmagnesium bromide in THF gave the corresponding propargyl alcohol (19), which was reduced to the vinyl alcohol (20) by LAH. Oxidation of 20 with  $\text{MnO}_2$  or Jones reagent afforded the required trienone (13), which had the expected spectral properties for such a structure. Although 13 is a vinyl ketone it was found to be stable at room temperature for several days. Chromatography over neutral alumina, however, gave a polymeric product, which showed strong carbonyl absorption at 1705 in the IR corresponding to a saturated carbonyl group.

#### *Ultraviolet irradiation of trienone (13)*

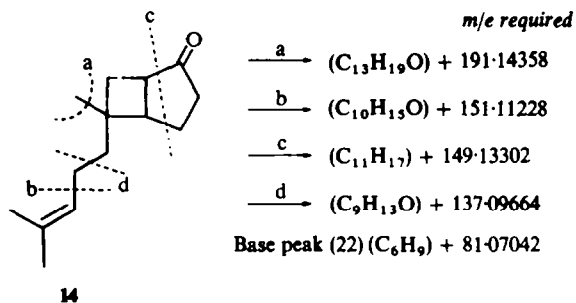
Irradiations of the trienone 13 were performed in a number of solvents ( $\text{Et}_2\text{O}$ , pentane,  $\text{C}_6\text{H}_6$ ) at various wavelengths (250, 310 and 350), with and without benzophenone as sensitiser. As expected, the most useful conditions were 310 nm, 0.1% solution in pentane or  $\text{C}_6\text{H}_6$ , without added sensitiser. This implies the intermediacy of the  $n-\pi^*$  transition of the enone system in 13. The progress of the photolysis was followed by glc and the irradiation stopped when the trienone (13) had been completely transformed into ten volatile products. Chromatography of the crude product allowed the isolation of three main constituents A (3%), B (2%), C (5%), to which structures could be assigned on spectroscopic evidence.

Component A exhibited IR absorption at  $1730\text{ cm}^{-1}$  and important NMR peaks at  $5\tau$  (H, broad, olefinic), 8.32 (S, 3H), 8.39 (S, 3H), 8.73 (S, 3H). The NMR data indicated the presence of an isopropylidene residue and a Me group attached to a saturated centre and the IR absorption is in good agreement with the carbonyl absorption of (21), which was found at  $1735\text{ cm}^{-1}$ .<sup>10</sup> This evidence would be consistent with structure 14 for A, which was supported by a study of the mass spectral fragmentation. The mass spectrum contained the molecular ion expected for 14 at 206.17093 ( $\text{C}_{14}\text{H}_{22}\text{O}$  requires 206.16706). Major fragmentations were observed at 191.14115, 151.11019, 149.13317, 137.09674, 81.06976 (base peak), all of which can be rationalised on the basis of the following fragmentations. (Scheme 1).

A (14) arises from interaction of the  $\Delta^{6,7}$  double bond with the enone chromophore in an analogous fashion to that involved in the formation of 10 from  $\beta$ -farnesene (6).

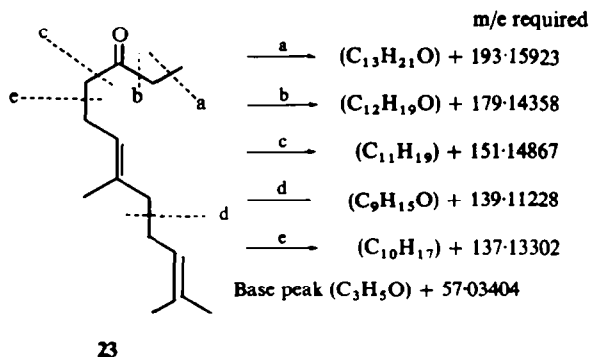
The second component, B, isolated showed IR absorption at  $1705\text{ cm}^{-1}$  and the NMR of B indicated the presence of two olefinic protons, an isopropylidene and Et group. This evidence together with the accurate mass of the parent ion at 208.18260 ( $\text{C}_{14}\text{H}_{24}\text{O}$  requires 208.18271) suggested that the enone (13) had abstracted hydrogen from the pentane solvent during irradiation to give the saturated ketone 23. This

SCHEME 1



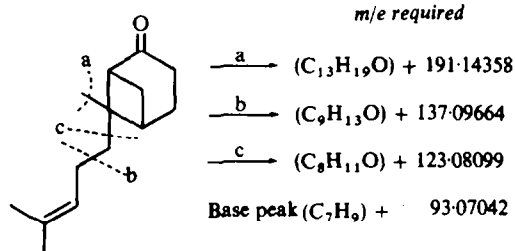
product was not observed when C<sub>6</sub>H<sub>6</sub> was used as solvent. Structure **23** was supported by the following fragmentations at *m/e* 193.16111, 179.14168, 151.14766, 139.11171, 137.13004 and 57.03222.

SCHEME 2



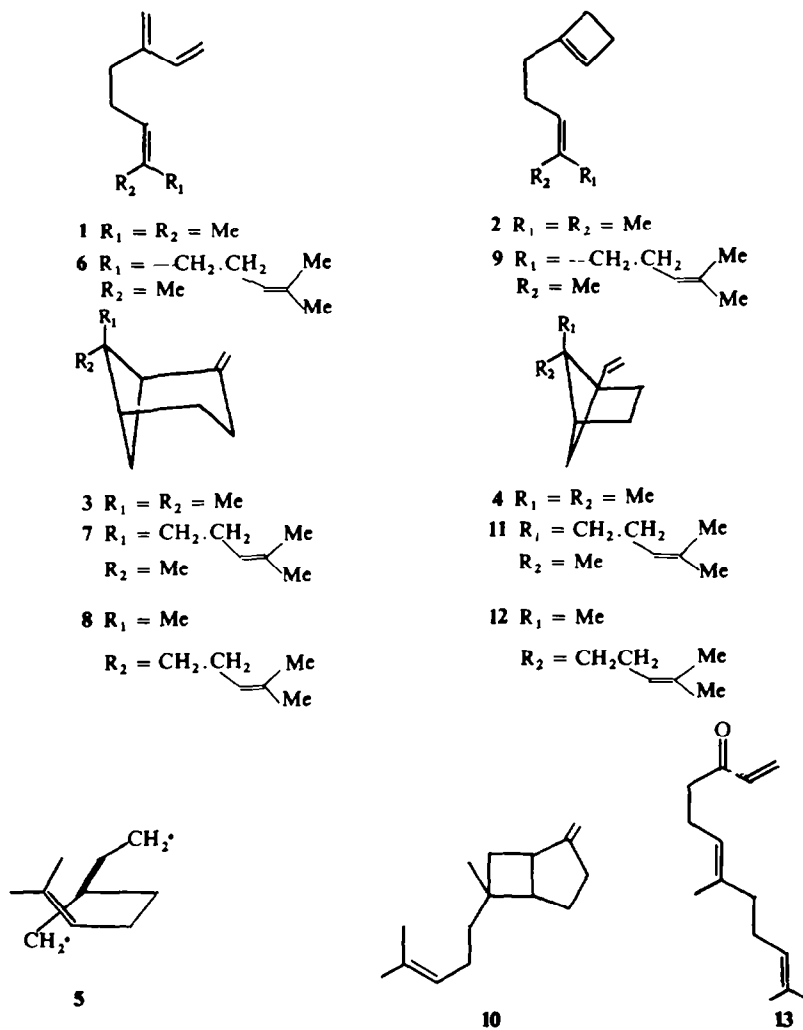
The third volatile component from the photolysis, C exhibited IR absorption at 1705 cm<sup>-1</sup> and the NMR spectrum 5τ (H, broad, olefinic), 8.33 (S, 3H), 8.40 (S, 3H), 9.4 (S, 3H), suggested the presence of one olefinic proton, an isopropylidene and a Me group attached to a saturated carbon centre. By analogy with nopinone (**24**) [*v*<sub>max</sub> 1705 cm<sup>-1</sup>; NMR 8.68 τ (S, 3H), 9.17 (S, 3H)]; this spectral evidence is consistent with structure **25** for C. In support of this was the accurate mass of the parent ion at 206.16538 (C<sub>14</sub>H<sub>22</sub>O requires 206.16706) and the following fragmentations at *m/e* 191.14451, 137.09620, 123.08060 and 93.07050. The formation of the photolysis product C (**24**) is analogous to the production of β-pinene (**3**) on irradiation of myrcene (**1**). Thus, both modes of interaction of the Δ<sup>6,7</sup> double bond with the enone system are operable during irradiation of the trienone (**13**). Although C (**25**) has a structure which could be elaborated to *trans* or *cis* bergamotene (**7** or **8**), this was not

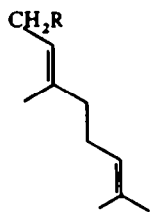
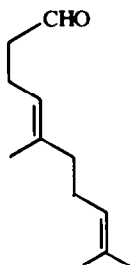
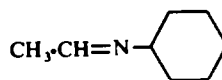
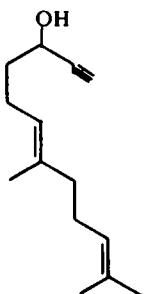
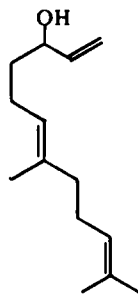
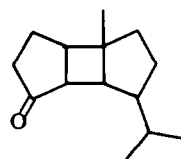
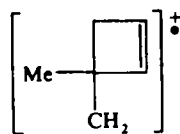
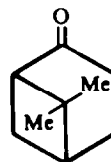
SCHEME 3



25

possible due to the low yield and difficult isolation of products resulting from the photolysis.



**15** R = OH**16** R = Cl**17****18****19****20****21****22****24**

## EXPERIMENTAL

UV spectra were measured for EtOH solutions with a Unicam S.P. 800 spectrophotometer. IR spectra were determined (liquid films) with a Unicam S.P. 200 spectrophotometer. NMR spectra ( $\text{CDCl}_3$ ) were obtained with a Varian HA-100 or A-60 spectrometer. Analytical glc was carried out with a Perkin-Elmer F11 using a 25 ft  $\times$  0.03 in packed capillary of 10% carbowax 20 M on chromosorb W. Mass spectra were measured on AEI MS 902 or MS 12. Complete high resolution accurate mass listings and elemental composition listings were produced by a MS 902/Argus 500 system. Chromatography was over kieselgel (Merck 70-325 mesh) or alumina (Merck neutral) deactivated with the requisite amount of water.

Geraniol was supplied by Bush-Boake Allan Ltd. Petroleum ether refers to the fraction bp 40-60°C. The photolyses were carried out using an Hanovia medium pressure mercury vapour lamp (254, 265, 297, 366 nm) enclosed in a pyrex jacket. The lamp was water-cooled and placed in the centre of the reaction solution.

**Geranyl chloride (16).** A solution of geraniol (15) (92.4 g) and triphenylphosphine (157.2 g) in dry "Analar"  $\text{CCl}_4$  (300 ml) was carefully heated with continuous stirring for 2 hr; the temperature of the water bath being carefully controlled within the range 75-80°C. The solvent was then removed *in vacuo* and the residue extracted with petroleum ether and filtered through celite. The filtrate was concentrated *in vacuo* and distilled under  $\text{N}_2$  to give geranyl chloride (56.4 g, 54%) an almost colourless liquid b.p. 68°/0.8;  $\nu_{\text{max}}$  1665, 840, 660  $\text{cm}^{-1}$ ; NMR  $\tau$  4.60 (H, t, olefinic), 4.95 (H, m, olefinic), 5.95 (2H, d), 7.93 (4H), 8.30-8.41 (9H, m); glc showed one peak on 50 in p.e.g.s. column 100 C. 15 psi. (Found: C, 69.40; H, 9.68.  $\text{C}_{10}\text{H}_{17}\text{Cl}$  requires C, 69.53; H, 9.92%).

*Ethylidene cyclohexylamine* (18). Ice-cold acetaldehyde (33.0 g) was added dropwise to cyclohexylamine (74.2 g) at 0° (gentle stirring). After 0.5 hr the solution was warmed to room temperature. KOH (40 g) added and the solution allowed to stand for 1 hr. The water which had separated out was absorbed by the addition of anhyd  $\text{Na}_2\text{SO}_4$  and the decanted liquid was distilled ( $\text{N}_2$ ) to give a colourless liquid (62.0 g, 66%) b.p. 51–54°/18 mm;  $\nu_{\text{max}}$  1660  $\text{cm}^{-1}$ .

5.9-Dimethyldeca-4.8-dienal (17). An ether solution of MeLi (0.174 moles; 184 ml 0.948 g) was added slowly to a solution of diisopropylamine (17.6 g) in dry ether (100 ml) at 0°. After standing for 0.25 hr at 0°, the solution was cooled to –15°, freshly distilled ethylidene cyclohexylamine (21.7 g) added and the solution allowed to attain room temperature. To this was added geranyl chloride (30.0 g) and the solution stirred continuously for 20 hr. A solution of oxalic acid (60 g) in  $\text{H}_2\text{O}$  (300 ml) was then added and the two-phase system stirred for 75 min. The ethereal layer was separated, washed several times with  $\text{H}_2\text{O}$  and dried over anhyd  $\text{Na}_2\text{SO}_4$ . After filtration the ether was removed *in vacuo* to give the crude reaction product (32.8 g).

This was chromatographed over silica (500 g). Elution with 5% ether in petroleum ether afforded an oil, which was distilled to give the pure aldehyde (17) (11.3 g, 36%) as a volatile colourless liquid b.p. 80–82°/0.66 mm;  $\nu_{\text{max}}$  2690, 1715  $\text{cm}^{-1}$ ; NMR  $\tau$  0.20 (H, CHO), 4.88 (2H, broad), 7.57 (4H), 7.99 (4H), 8.37 (9H); glc showed one peak on 50' S.E. 30 170', 15 psi. Mass spectral parent ion at  $m/e$  180. (Found: C, 79.75; H, 11.26.  $\text{C}_{12}\text{H}_{20}\text{O}$  requires C, 79.94; H, 11.18%).

7.11-Dimethyldodeca-6,10-dien-1-yn-3-ol (19). A solution of EtMgBr was prepared from clean, dry Mg turnings (4.68 g), dry EtBr (21.2 g) and dry THF (390 ml). Dry THF (950 ml) was saturated with dry, acetone-free acetylene and the EtMgBr solution added dropwise over 5 hr; the slow passage of acetylene through the solution being maintained throughout. To the resulting orange homogeneous solution was added 5.9-dimethyldeca-4.8-dienal (12.0 g) in dry THF (100 ml) over 1 hr. After stirring for 16 hr the Grignard complex was destroyed on addition of saturated  $\text{NH}_4\text{OH}$  aq and the organic layer separated. The bulk of the solvent was removed *in vacuo* and the residue extracted with ether. This ethereal extract was washed with  $\text{H}_2\text{O}$  and dried over anhyd.  $\text{Na}_2\text{SO}_4$ . Removal of the solvent afforded the crude ethynyl alcohol which was distilled to give 19 (12.0 g, 94%) as a colourless oil b.p. 108°/0.55 mm,  $\nu_{\text{max}}$  3330, 3290, 2100, 1660, 840  $\text{cm}^{-1}$ ; NMR  $\tau$  4.85 (2H, m), 5.60 (H, m), 7.53 (H, d), 7.70–7.95 (7H, multiplet 6H on  $\text{D}_2\text{O}$  shake), 8.05–8.38 (11H, complex); Mass spectral parent ion at  $m/e$  206 (Found: C, 81.36; H, 10.65.  $\text{C}_{14}\text{H}_{22}\text{O}$  requires C, 81.50; H, 10.75%).

7.11-Dimethyldodeca-1.6,10-trien-3-ol (20). LAH (0.88 g) was slowly added to the ethynyl alcohol 19 (4.80 g) in ether (50 ml) and the solution stood 16 hr at room temperature. The complex was decomposed by saturated aqueous Rochelle salt, the solution extracted several times with ether and the combined ether extracts dried ( $\text{Na}_2\text{SO}_4$ ). Removal of solvent and distillation under  $\text{N}_2$  afforded the vinyl alcohol 20 (3.1 g, 65%) as a colourless oil b.p. 103–105°/0.5 mm;  $\nu_{\text{max}}$  3300, 925  $\text{cm}^{-1}$ ; NMR  $\tau$  4.18 (H, octet), 4.90 (4H, m), 5.90 (H, q), 8.00 (6H, broad), 8.34 (12H, broad  $\rightarrow$  11H on  $\text{D}_2\text{O}$  shake); Mass spectral parent ion at  $m/e$  208; glc showed one peak on carbowax at 120°, 20 psi. (Found: C, 80.39; H, 11.84.  $\text{C}_{14}\text{H}_{24}\text{O}$  requires C, 80.71; H, 11.61%).

7.11-Dimethyldodeca-1.6,10-trien-3-one (13). Method (a); The vinyl alcohol (20) (1.2 g) in pentane (70 ml) was stirred with freshly prepared  $\text{MnO}_2$  (12.0 g) for 2 hr. The  $\text{MnO}_2$  was removed by filtration and the solvent concentrated *in vacuo* to yield the vinyl ketone 13 (0.86 g, 72%) as a pale yellow oil.  $\nu_{\text{max}}$  1680  $\text{cm}^{-1}$ ; NMR  $\tau$  3.78 (2H, m), 4.23 (H, m), 4.93 (2H, broad), 7.33–7.95 (8H, complex), 8.33 (9H);  $\lambda_{\text{max}}$  225 nm  $\epsilon$  9000; glc showed one peak in carbowax at 130°, 20 psi. Mass spectral parent ion at  $m/e$  206 (Found: C, 81.53; H, 11.00.  $\text{C}_{14}\text{H}_{22}\text{O}$  requires C, 81.50; H, 10.75%).

Method (b); Jones reagent (2.5 ml) was added to a rapidly stirred solution of the vinyl alcohol 20 (1.04 g) in acetone (10 ml). After 10 min the solvent was removed *in vacuo* and  $\text{H}_2\text{O}$  added. Ether extraction followed by washing with  $\text{H}_2\text{O}$  and drying ( $\text{Na}_2\text{SO}_4$ ) afforded the vinyl ketone 13 (955 mg, 92%).

Irradiation of 7.11-dimethyldodeca-1.6,10-trien-3-one (13). The vinyl ketone 13 (600 mg) was dissolved in pentane (600 ml) and  $\text{O}_2$ -free  $\text{N}_2$  passed through the solution for 0.5 hr. Irradiation was then commenced at room temperature and a slow stream of gas passed through the solution throughout the photolysis. The reaction was monitored by glc and completed by distillation of solvent *in vacuo* to give the crude product (500 mg) which was chromatographed over kieselgel (50 g) and the individual fractions rechromatographed under the same conditions. Elution with 5% EtOAc in  $\text{C}_6\text{H}_6$  gave A (20 mg, 3%) as an oil.  $\nu_{\text{max}}$  ( $\text{CHCl}_3$ ) 1730  $\text{cm}^{-1}$ ;  $\lambda_{\text{max}}$  nil; NMR  $\tau$  5.0 (H, m), 8.32 (S, 3H), 8.39 (S, 3H), 8.73 (S, 3H); glc on carbowax at 130°, 20 psi showed two peaks R, 3.8 and 5.0 min; Mass spectral parent ion at  $m/e$  206.17093. fragmentation pattern showed on Scheme 1.

Further elution with 5% EtOAc in  $C_6H_6$  afforded B (13 mg, 2%),  $\nu_{max}$  ( $CHCl_3$ ) 1705  $cm^{-1}$ ;  $\lambda_{max}$  nil; NMR  $\tau$  5.0 (2H, m), 8.33 (3H, S), 8.4 (3H, S), 8.94 (3H, t = 7 cps); glc showed one peak on carbowax at 130°, 20 psi,  $R_f$  8.0 min; Mass spectral parent ion at  $m/e$  208.18160, fragmentation pattern shown on Scheme 2.

Further elution with 5% EtOAc in  $C_6H_6$  gave C (29 mg, 5%) as an oil  $\nu_{max}$  ( $CHCl_3$ ) 1705  $cm^{-1}$ ;  $\lambda_{max}$  nil; NMR  $\tau$  5.0 (H, m), 8.33 (3H, S), 8.40 (3H, S), 9.40 (S, 3H); glc on carbowax at 130°, 20 psi showed one peak  $R_f$  9.1 min; Mass spectral parent ion at 206.16538, fragmentation pattern shown on Scheme 3.

Finally, elution with EtOAc gave a viscous gum (400 mg)  $\nu_{max}$  ( $CHCl_3$ ) 3450, 1705  $cm^{-1}$ ; NMR  $\tau$  5.0 (2H, m), 8.32 (3H, S), 8.39 (S, 3H).

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