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PHOTOCHEMICAL BEHAVIOUR OF ENOLIC β-DIKETONES TOWARDS CYCLOOLEFINS

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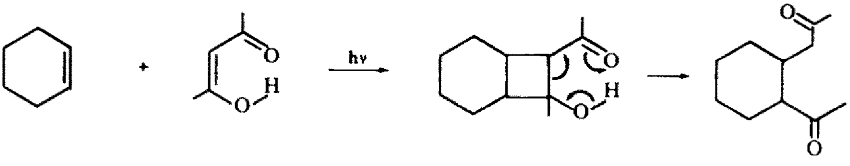
Abstract—Mechanistic studies have indicated that the triplet of acetylacetone is the active species in the photochemical cycloaddition to cyclohexene (the de Mayo reaction). The reaction of acetylacetone can be extended to cycloolefins such as 1,5-cyclooctadiene or 1,5,9-cyclododecatriene, but not to conjugated dienes. Similar cycloaddition of 2-acetylcycloalkanones to cycloolefins yields δ-diketones which can be cyclized by dehydration condensation to α,β-unsaturated ketones having three or more condensed rings.

THE de Mayo reaction of an enolic β-diketone[1] involves the photochemical cycloaddition to an olefin and the subsequent, thermal retroaldolization of the intermediary 2-acylcyclobutanol, which affords a δ-diketone. We have examined the nature of the active species involved in the photocycloaddition, and succeeded to extend the reaction to several 2-acetylcycloalkanones.

The active species in the cycloaddition. UV irradiation of acetylacetone (I) in cyclohexene solution gives δ-diketone II in high yield. It seems, however, that no convincing evidence has been obtained with respect to the exact nature of the excited state, especially the electronic configuration.* The reaction was conducted under various conditions and the results were shown in Fig. 1.† Irradiation of a mixture of I, cyclohexene and cyclohexane (1:10:10 mole ratio) through a Pyrex filter gave the diketone II in yields as shown by curve a. Substitution of cyclohexane by piperylene completely suppressed the formation of II, and I was recovered unchanged almost quantitatively (curve b). This fact should be ascribed to the quenching effect of piperylene on the diketone I in its triplet state.‡ The curve c indicates the results when a cyclohexene solution of I (10:1 mole ratio) was irradiated through an aqueous $CuSO_4$ layer as a filter transmitting above 350 mμ light. Acetylacetone has feeble absorptions in this region and slowly afforded the diketone II. Addition of acetophenone (2 mole ratio to I) remarkably accelerated the formation of II (curve d). The presence of benzophenone, on the other hand, did not show such rate enhancement, but produced 3,3′-bicyclohexenyl as a major product. Since the incident light



I
II

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* An $n \rightarrow \pi^*$ excitation has been proposed in view of the efficacy of long-wave incident light. See Ref. 2.

† The light source was 200W high pressure Hg arc throughout all experiments in this paper.

‡ For piperylene as an efficient triplet quencher, see Ref. 3.

in the runs d and e was almost exclusively absorbed by the added sensitizers, the acetophenone effect should be ascribed to the transfer of the triplet energy ($E_T = 74$ kcal/mole). The failure of benzophenone sensitization must be reasonably accounted for by assuming that its triplet energy (69 kcal/mole) is insufficient to activate I. Benzophenone triplet abstracts allylic hydrogen of cyclohexene and induces radical coupling. All these facts indicate that a triplet of acetylacetone is the active species in the cycloaddition and its triplet energy should have a value between 69 and 74 kcal/mole.

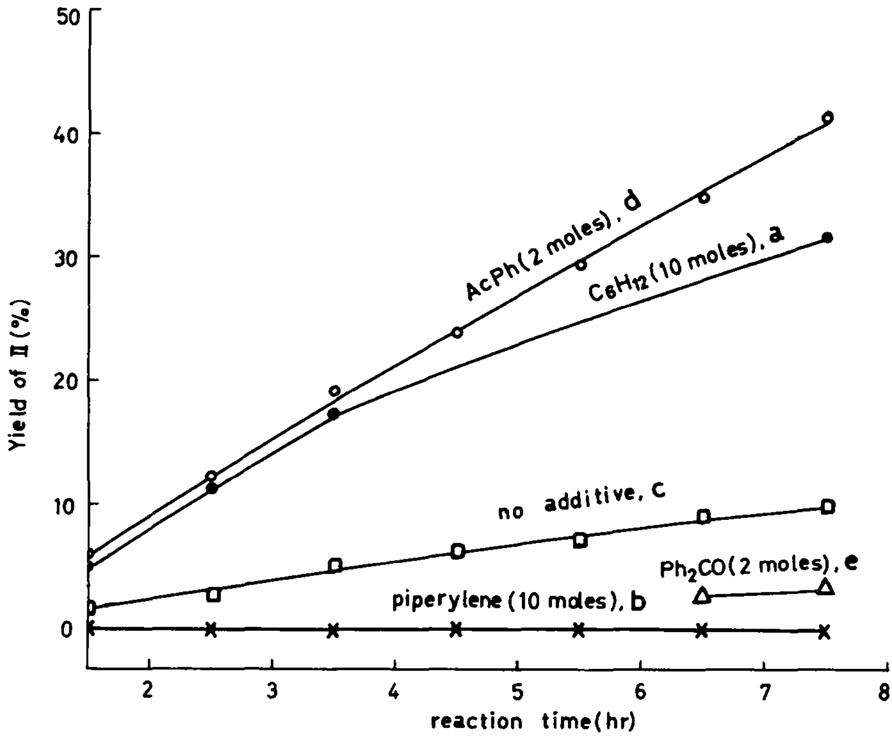

Fig. 1. Photochemical cycloaddition of acetylacetone to cyclohexene (1 : 10 mole ratio). (a, b: Pyrex filter; c, d, e: aq $CuSO_4$ filter).

Photoreaction of acetylacetone with some cycloolefins. Irradiation of acetylacetone in *cis,cis*-1,5-cyclooctadiene yielded a normal 1,2 addition product III in a 40% yield* and products arising from well-known transannular radical reaction[4] could not be isolated. Catalytic hydrogenation of III gave the corresponding saturated diketone IV which was found to be identical with the one obtained by the de Mayo reaction of I and *cis*-cyclooctene. *cis,trans,trans*-1,5,9-Cyclododecatriene gave oily addition product(s) V in a 71% yield,* which absorbed 2 moles of hydrogen to give a crystalline saturated δ-diketone VI.* The assigned structures of III–VI were supported by elemental analyses and spectrometric evidence. Attempted photoaddition

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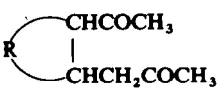
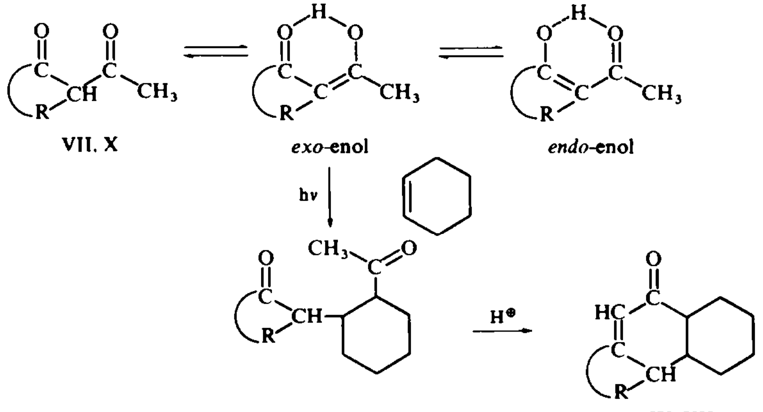
* The stereochemistry is open to researches in the future.



III: R = $\text{—CH}_2\text{CH}_2\text{CH=CHCH}_2\text{CH}_2\text{—}$
IV: R = $\text{—(CH}_2)_6\text{—}$
V: R = $\text{—CH}_2\text{CH}_2\text{CH=CHCH}_2\text{CH}_2\text{CH=CHCH}_2\text{CH}_2\text{—}$
VI: R = $\text{—(CH}_2)_{10}\text{—}$

of I to styrene resulted in recovery of the starting materials. 1,3-Cyclooctadiene also did not afford the expected adduct.* These could be explained by assuming the quenching effect of the conjugated olefins.† ‡

The de Mayo reaction of 2-acetylcycloalkanones. β-Diketones previously subjected to this photoreaction have been restricted to those having such symmetrical structures as acetylacetone or dimedone. It has been discovered that certain 2-acetylcycloalkanones do react in the expected manner. These β-diketones enolize to give an equilibrium mixture of the corresponding enols with *exo*- and *endo*cyclic double bonds as indicated by NMR.[8] Irradiation of 2-acetylcyclopentanone (VII)‡ in 10% cyclohexene solution gave an oily mixture of 1:1 adducts in a 40% yield. Isolation of VIII failed because of the extremely facile cyclization to the corresponding unsaturated ketone IX. Treatment with hydrochloric acid gave IX†† in a 74% yield based on the adduct mixture. Other products could not be isolated pure. Similarly,



VII, X — *exo*-enol — *endo*-enol

VIII, XI — IX, XII

VII, VII, IX: R = $\text{—(CH}_2)_3\text{—}$ X, XI, XII: R = $\text{—(CH}_2)_4\text{—}$

exposure to light was effected on a 10% cyclohexene solution of 2-acetylcyclohexanone (X)§ to afford 1:1 adducts(s) in a 61% yield. In this case, the ketone XI was again not isolated and treatment with hydrochloric acid yielded the condensation product XII in an 81% yield, which was identified by comparison with the authentic specimen.[9] No other products could be isolated.

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[*] Starting materials were slowly consumed, but hydrogenation of the photolysate did not give the δ-diketone IV.

[†] For styrene as an efficient triplet energy acceptor, see Ref 5. The triplet energy has been estimated as 62 kcal/mole (Ref 6).

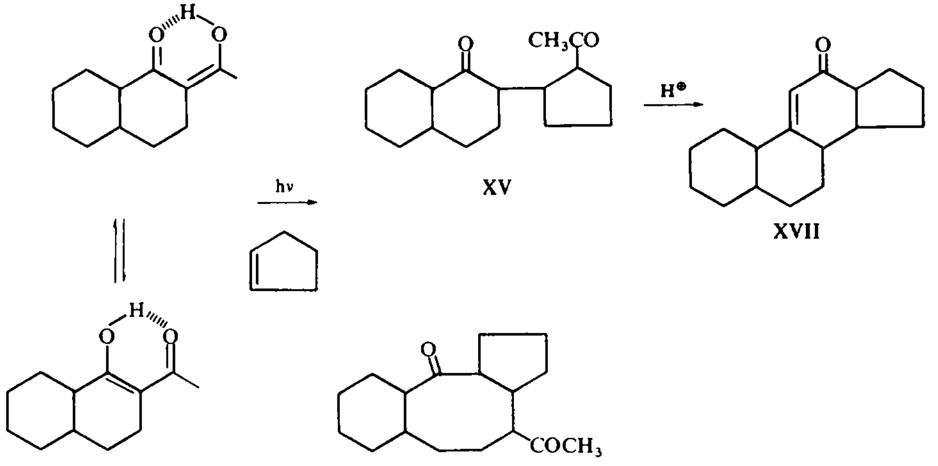
[‡] Ready energy transfer from carbonyl derivatives ($E_T > 65$ kcal/mole) to 1,3-cyclooctadiene has recently been reported. See Ref. 7.

The diketone VII exists 60% in enol form (10% CCl_4 soln). The *endo/exo* ratio is 0·43 (in benzene) (cf. Ref 8).

[††] The stereochemistry has not been determined.

[§] The diketone *X* exists 95% in enol form (10% CCl_4 soln). The *endo/exo* ratio is 2·34 (in benzene) (cf. Ref 8).[4]

Finally, this photochemical reaction was applied to 2-acetyl-1-decalone (XIV)* obtained by acetylation[10] of morpholine enamine of 1-decalone. A 7% cyclopentene solution of the diketone XIV was irradiated for 7 days to yield an oily mixture of 1 : 1 adducts in an 83% yield. Treatment with hydrochloric acid followed by chromatographic separation gave an oily unsaturated ketone, 18,19-bisnor-$\Delta^{9(11)}$-androsten-12-one (XVII), in a 30% yield.† The structure was established by elemental analyses and spectrometric evidence. The precursory diketone should be represented as XV, an adduct of cyclopentene and XIV in the *exo*-enol form. In addition to XVII, a solid



XIV XV XVI XVII

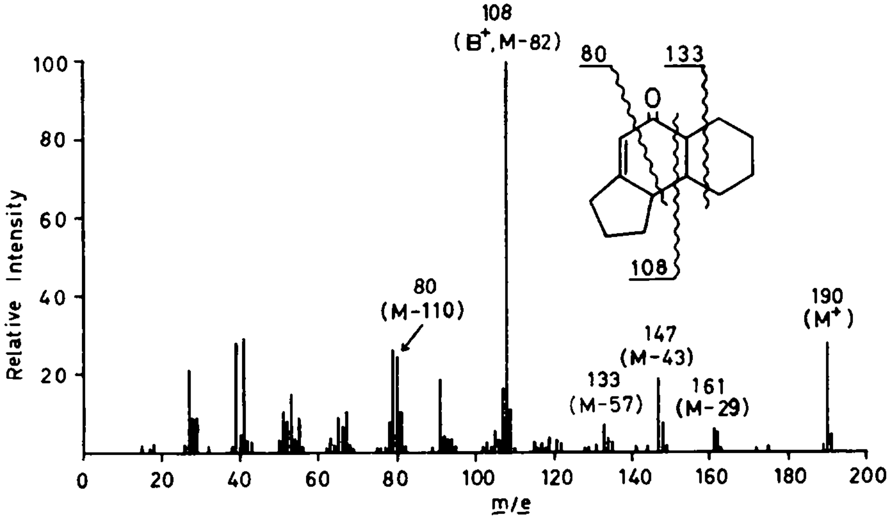


FIG. 2. Mass spectrum of IX

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* In 10% CCl_4 soln 85% of XIV exists in the enol form. The *endo/exo* ratio, however, could not be determined.

† The stereochemistry has not been determined.

diketone of broad m.p. range was obtained. This probably consisted of stereoisomers, and the structure was tentatively assigned to be XVI. Inertness to the acidic treatment suggests that these isomers arise from the *endo*-enol of XIV.

The mass spectra of unsaturated ketones IX, XII and XVII (Figs. 2–4) showed fragmentation patterns of striking similarity. The eminent peaks were explained by assuming common cleavages as indicated in the figures. Naturally, the mass spectrum of the saturates diketone XVI (Fig. 5) was completely different and was consistent with the structure given.

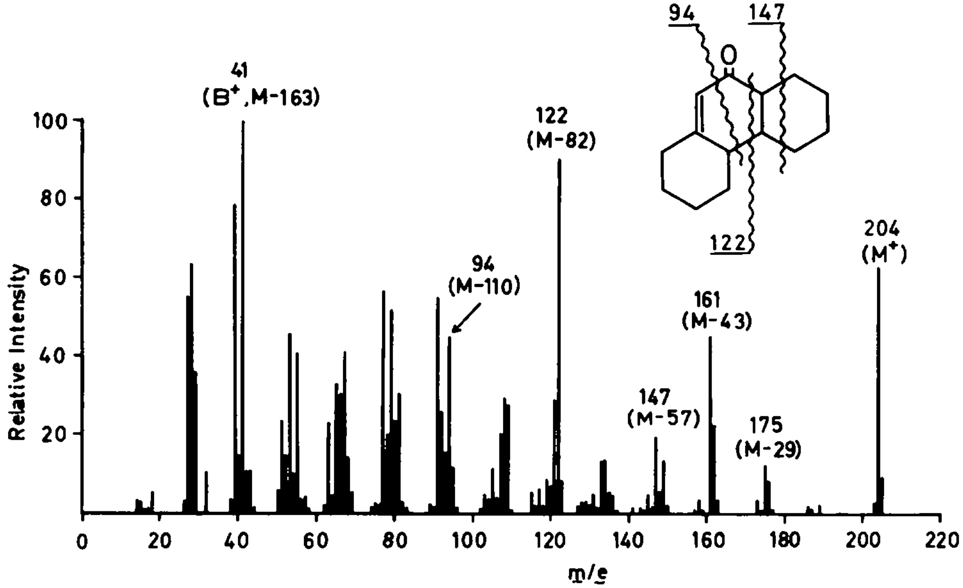

FIG. 3. Mass spectrum of XII

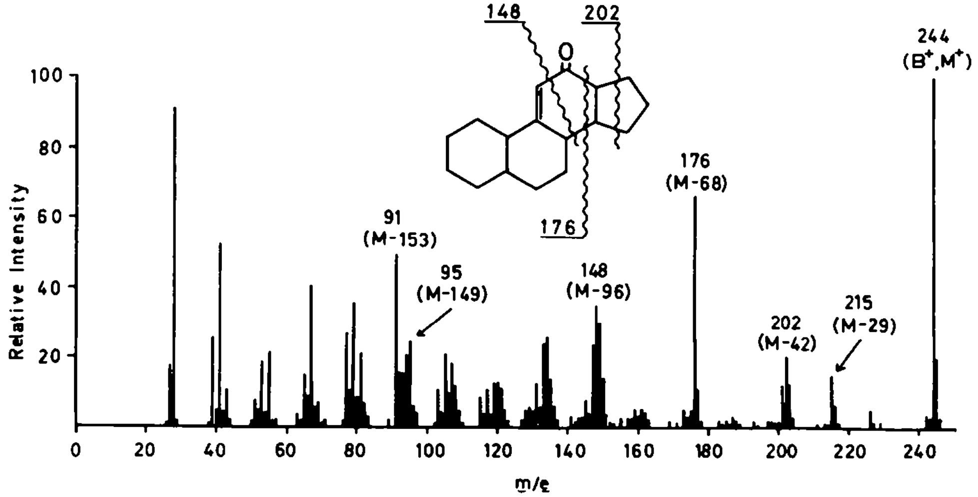

FIG. 4. Mass spectrum of XVII

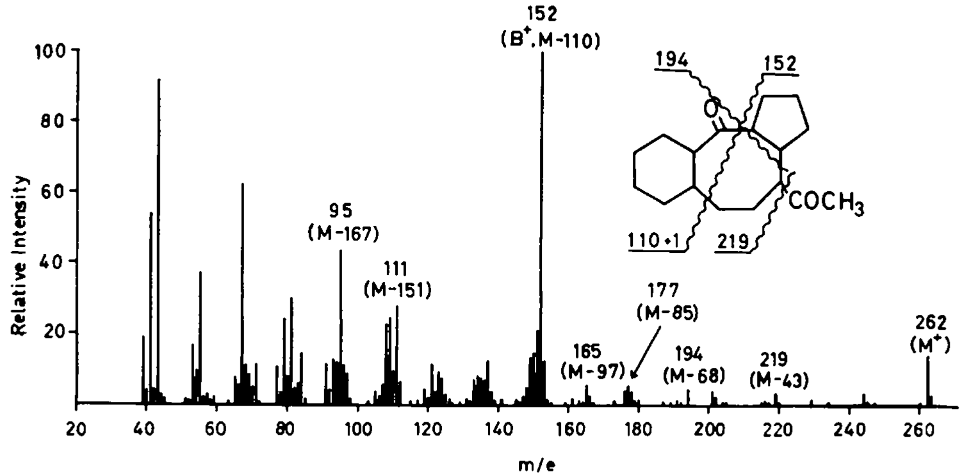

Fig. 5. Mass spectrum of XVI

EXPERIMENTAL

All m.ps and b.ps are uncorrected. NMR spectra were taken in CCl_4 soln with Varian A60 and JEOL C-60-H apparatus and chemical shifts were given in ppm unit from TMS internal standard. Mass spectra were taken on Hitachi Mass Spectrometer RMU 6D at a probe temp of 165°. Unless otherwise stated, irradiation was effected externally by means of a 200W high press Hg arc from a distance of 3 cm under N_2 atmosphere at room temp.

Photochemical reaction of acetylacetone (I) *and cyclohexene under varying reaction conditions* (Fig. 1). In runs a and b, a mixture of I, cyclohexene and cyclohexane (or piperylene) (1:10:10 mole ratio) was placed in a Pyrex tube (0·8 cm diam and 6 cm length) and irradiated externally with Hg arc. In the cases of d and e, a mixture of I and cyclohexene and a sensitizer (1:10:2 mole ratio) was irradiated in a Pyrex tube (0·8 cm × 4 cm) through a 1·0 cm thick 10% $CuSO_4$ soln. The run c was carried out similarly as d and e in the absence of a sensitizer. The course of the reaction was monitored by GLC (silicone gum SE-30 (10%) on Chromosorb W, 2m, 175°). 3,3′-Bicyclohexenyl formed in the presence of benzophenone was identified by GLC separation and comparison with the authentic specimen.[11]

Photolysis of acetylacetone (I) *in eight-membered cyclic olefins.* A soln of I (4·5 g, 0·045 mole) in freshly distilled *cis*-cyclooctene (9·9 g, 0·090 mole) was irradiated for 7 days. Vacuum distillation of the photolysate yielded *1-acetonyl-2-acetylcyclooctane* (IV) as a colourless oil (5·0 g, 51% yield), b.p. 112–116°/5 mm. A strong IR band (neat) was observed at 1715 cm^{-1}. NMR gave acetyl methyl signals at δ 2·05 and 2·02. (Found: C, 74·0, H, 10·5. $C_{13}H_{22}O_2$ requires: C, 74·2; H, 10·5%.)

Similar phototreatment was effected on a mixture of I (5·0 g, 0·050 mole) and *cis,cis*-1,5-cyclooctadiene (10·9 g, 0·10 mole) for 4 days. Distillation of the mixture *in vacuo* gave *5-acetonyl-6-acetylcyclooctene* (III) as a colourless oil (4·4 g, 40% yield), b.p. 90–100°/4 mm. IR absorptions (neat) appeared at 1715 (carbonyl) and 730 cm^{-1} (*cis* double bond). (Found: C, 74·9; H, 9·6. $C_{13}H_{20}O_2$ requires: C, 75·0; H, 9·7%.)

Hydrogenation of the unsaturated diketone III on 10% Pd-C afforded IV in an 85% yield, which was identified by comparison of IR spectra.

Photolysis of acetylacetone (I) *in* cis,trans,trans-1,5,9-*cyclododecatriene.* A mixture of I (50·0 g, 0·50 mole) and the triene (130 g, 0·80 mole) was irradiated by means of an immersion type 200W Hg lamp for 7 days. Vacuum distillation of the photolysate gave *9-acetonyl-10-acetylcyclododeca-1,5-diene* (V) as a viscous oil (40·0 g, 71% yield based on the consumed triene), b.p. 120–130°/0·1 mm. The recovered 1,5,9-triene fraction (ca. 95 g) was found to consist of all-*trans* (17%), *cis,trans,trans* (78%) and *cis,cis,trans* isomers (5%).* The adduct(s) V showed strong IR bands (neat) at 1710 (carbonyl), 970 (*trans* double bond) and 700 cm^{-1} (*cis* double bond), suggesting that the addition occurred mainly at the *trans* double bond of triene. NMR multiplet at δ 5·27 indicated the presence of 4 vinylic protons. (Found: C, 77·8; H, 10·0. $C_{17}H_{26}O_2$ requires: C, 77·8; H, 10·0%.)

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* For such photoisomerization, see Ref 12.

An ethanolic soln of V was shaken with a small amount of 10% Pd-C catalyst under H_2 atmosphere to give the corresponding saturated diketone, *1-acetonyl-2-acetylcyclododecane* (VI) as a semisolid in a 90% yield, b.p. 120–130°/0·1 mm. Recrystallizations from EtOH gave colourless needles with a 50% recovery, m.p. 64–65°, whose IR spectrum was practically identical with one obtained before the recrystallizations. NMR gave a sharp methyl signal at δ 2·02 (6H). (Found: C, 76·9; H, 11·1. $C_{17}H_{30}O_2$ requires: C, 76·6; H, 11·4%.)

Photochemical reaction of 2-*acetylcyclopentanone* (VII) *with cyclohexene*. NMR spectrum of VII[13] (10% CCl_4 soln) showed a signal of hydrogen-bonded proton at δ 11·53, indicating that VII enolized to the extent of ca 60%. A soln of VII (6·3 g, 0·050 mole) in purified cyclohexene (41·0 g, 0·50 mole) was irradiated for 10 days. Concentration of the reaction mixture followed by vacuum distillation gave a 1:1 adduct, *2-(2′-acetylcyclohexyl)cyclopentanone* (VIII) as a pale yellow oil (4·2 g, 40% yield), b.p. 70–80°/10^{-4} mm. IR spectrum (neat) showed strong absorptions at 1740 and 1710 cm^{-1} in approximately equal intensities. (Found: C, 74·7, H, 9·4. $C_{13}H_{20}O_2$ requires: C, 75·0, H, 9·7%.)

To a soln of the photoadduct (3·2 g, 0·015 mole) in EtOH (30 ml) was added conc HCl (1·5 ml) and the mixture was heated at reflux for 1·5 hr. The reaction mixture was treated with water and extracted with ether. The extracts were washed, dried (Na_2SO_4) and concentrated *in vacuo*. Distillation of the residual oil afforded *5-oxo-Δ^4-decahydrobenz*[e]*indene* (IX; 2·1 g, 74% yield), b.p. 100–110°/3 mm. This formed a viscous oil, and slowly crystallized on standing. Recrystallization from MeOH yielded an analytical sample, m.p. 62–64°. IR spectrum (Nujol) gave a strong absorption at 1670 cm^{-1} characteristic of conjugated CO group, while UV (EtOH) at 240 (log ε 4·12) and 295 mμ (1·91). An NMR signal which appeared as a diffused multiplet centred at δ 5·72 supported the existence of one olefinic proton. Mass spectrum (Fig. 2) gave the parent peak at *m/e* 190 and isotope abundances were P + 1 14·5% and P + 2 1·3%, respectively. (Found: C, 81·9; H, 9·8; $C_{13}H_{18}O$ requires: C, 82·1; H, 9·5%.)

Photochemical reaction of 2-*acetylcyclohexanone* (X) *with cyclohexene*. NMR spectrum of X[10] (10% CCl_4 soln) showed a signal due to hydrogen-bonded OH proton at δ 13·89, indicating that X enolizes to the extent of ca. 90%. Irradiation of a soln of X (15·0 g, 0·11 mole) in freshly distilled cyclohexene (72·0 g, 0·88 mole) was effected for 15 days. After removal of the solvent, the residual oil was fractionated *in vacuo* to yield a mixture of 1:1 adducts (14·5 g, 61% yield), b.p. 80–90°/10^{-4} mm. This would be mainly composed of *2-(2′-acetylcyclohexyl)-cyclohexanone* (XI). IR spectrum (neat) showed a strong band at 1710 cm^{-1}. NMR spectrum indicated the absence of olefinic protons. (Found: C, 75·6; H, 10·2. $C_{14}H_{22}O_2$ requires: C, 75·6; H, 10·0%.)

A mixture of the photoadducts (5·4 g, 0·024 mole), conc HCl (2·1 ml) and EtOH (40 ml) was heated under reflux for 1·5 hr. The reaction mixture was treated with water and extracted with ether. The combined extracts were washed with water, dried (Na_2SO_4) and concentrated. Distillation *in vacuo* gave XII as a semisolid (4·0 g, 81% yield), b.p. 120–130°/6 mm. Purification by passing through a silicagel column and subsequent recrystallization from MeOH yielded an analytical sample, m.p. and m.mp. 90° (lit.[9] 89°). IR spectrum (Nujol) showed a characteristic band at 1660 cm^{-1}. NMR spectrum gave a broad singlet centred at δ 5·68 due to one olefinic proton. Mass spectrum (Fig. 3) showed the parent peak at *m/e* 204 and isotope abundances were P + 1 15·2% and P + 2 1·4%, respectively. (Found: C, 82·0; H, 10·1. Calc. for $C_{14}H_{20}O$: C, 82·3; H, 9·9%.)

Preparation of 1-*morpholino-Δ^1-octalin* (XIII). A mixture of 1-decalone (228 g, 1·5 moles), morpholine (387 g, 4·5 moles), *p*-toluenesulphonic acid (2·0 g) and anhyd toluene (600 ml) was heated under reflux in a flask attached to a Dean-Stark moisture trap. After 40 hr heating, the solvent and excess morpholine were removed by distillation. Vacuum fractionation of the residual oil gave *1-morpholino-Δ^1-octalin* (XIII) as a colourless oil (249 g, 75%), b.p. 117–120°/2 mm. Strong IR band (neat) was observed at 1645 cm^{-1}. (Found: C, 75·8; H, 10·5. $C_{14}H_{23}NO$ requires: C, 76·0; H, 10·5%.)

Preparation of 2-*acetyl*-1-*decalone* (XIV). To a mixture of the enamine XIII (148 g, 0·67 mole), Et_3N (81·7 g, 0·81 mole) and $CHCl_3$ (870 ml) was added a soln of acetyl chloride (58 g, 0·74 mole) in $CHCl_3$ (340 ml) in the course of 1·5 hr at 35° under stirring. Then the mixture was kept at the same temp for an additional 2 hr. After standing overnight at room temp, the mixture was treated with 6N HCl (350 ml) and heated at reflux for 6 hr under stirring. After cooling the organic layer was separated. The pH of the aqueous layer was adjusted to a value of 5–6 with NaOHaq and then extraction with $CHCl_3$ was repeated. The combined extracts were washed with water, dried (Na_2SO_4) and concentrated *in vacuo*. Fractional distillation of the residual oil gave 1-decalone (67 g) arising from unreacted enamine XIII, b.p. up to 80°/1 mm, and a fraction boiling at 90–110°/1 mm (33 g). Redistillation of the latter through a Vigreux column gave *2-acetyl-1-decalone* (XIV) as a colourless oil (28 g, 63% yield based on the consumed enamine), b.p. 94–95°/1 mm. IR spectrum (neat) showed a broad band at 1610 cm^{-1} characteristic of enolized β-diketone. NMR spectrum (10% CCl_4 soln) showed signals at δ 16·23 and 16·03 (hydrogen-bonded protons), indicating that XIV enolizes to the extent of ca. 85%. (Found: C, 74·0; H, 9·5. $C_{12}H_{18}O_2$ requires: C, 74·2; H, 9·3%.)

Photolysis of 2-acetyl-1-decalone (XIV) *in cyclopentene.* A soln of XIV (19·4 g, 0·10 mole) in freshly distilled cyclopentene (300 ml) was irradiated by means of a 200W immersion type Hg lamp at room temp under N_2 atmosphere. After 7 days irradiation, the enol band at 1610 cm^{-1} disappeared. Concentration of the photolysate followed by vacuum distillation yielded a mixture of 1:1 adducts as a viscous oil (21·8 g, 83% yield), b.p. 110–115°/10^{-3} mm. IR absorption (neat) showed a broad CO band near 1715 cm^{-1}. (Found: C, 78·0; 9·8. $C_{17}H_{26}O_2$ requires: C, 77·8; H, 10·0%.) This mixture was subjected to the following acid treatment.

A mixture of the adducts (13·1 g, 0·05 mole), conc HCl (8 ml) and EtOH (120 ml) was heated at reflux for 2·5 hr. After cooling, the reaction mixture was treated with water and extracted with ether, dried (Na_2SO_4) and concentrated *in vacuo*. The residual oil was taken up in a small amount of n-hexane and chromatographed on a silicagel column. Elution with benzene afforded *18,19-bisnor-*$\Delta^{9(11)}$*-androsten-12-one* (XVII) as a viscous oil (3·7 g, 30% yield), b.p. 123–125°/0·01 mm. TLC (silicagel G, benzene–EtOAc (10:1)) gave a single spot. IR absorptions (neat) were observed at 1660 and 1620 cm^{-1} while UV (EtOH) at 243 (log ε 4·13) and 296 mμ (2·46). NMR spectrum showed a poorly resolved multiplet centred at δ 5·55 due to one olefinic proton. Mass spectrum (Fig. 4) gave the parent peak at *m/e* 244 and isotope abundances were P + 1 19·5% and P + 2 2·2%, respectively. (Found: C, 83·4; H, 9·8. $C_{17}H_{24}O$ requires: C, 83·6; H, 9·9%.) *2,4-Dinitrophenylhydrazone* of XVII formed red prisms, m.p. 196–197° (from MeOH-benzene mixture). (Found: C, 65·0; H, 6·6. $C_{23}H_{28}N_4O_4$ requires: C, 65·1; H, 6·7%.)

Elution with benzene–ether mixture (2:1) yielded *2-oxo-11-acetyltricyclo*[10.3.0.0^{3,8}]*pentadecane* (XVI; 4·2 g, 32% yield) which formed colourless crystalline mass, m.p. 100–120°. Repeated recrystallization from MeOH failed to afford a sample of sharp m.p. TLC (silicagel G, benzene–EtOAc, 10:1) gave a diffused spot. IR (Nujol) gave a strong band at 1715 cm^{-1}. NMR spectrum showed a Me signal at δ 2·06. Mass spectrum (Fig. 5) gave the parent peak at *m/e* 262 and isotope abundances were P + 1 19·7% and P + 2 2·0%, respectively. (Found: C, 77·6; H, 10·2. $C_{17}H_{26}O_2$ requires: C, 77·8; H, 10·0%.)

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