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THE THERMAL MICHAEL REACTION—III[1]
THE SCOPE OF THE REACTION

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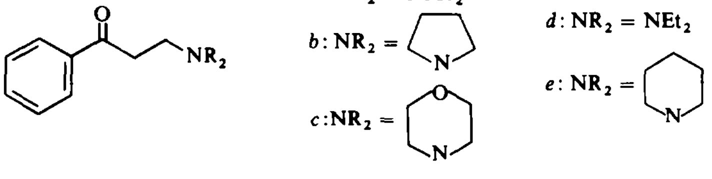
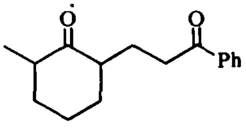
Abstract—The thermal reaction of several types of Mannich bases with a variety of ketones, has been studied to establish the yield and structure of the product in each case. An attempt has been made to define the optimum reaction conditions.

IT HAS been shown[2] that the thermal condensation of some Mannich bases with ketones affords 1,5-diketones by a Michael-type reaction (the thermal-Michael), which is mechanically distinct from the conventional process. This paper is concerned with its scope, as a prelude to formulating its mechanism.

In normal practice, the thermal-Michael reaction involves heating a Mannich base in a 3-fold excess of ketone at ca. 160–180° for ½–1 hr. If a lower temperature is used, the reaction becones less efficient. Thus when Ia was reacted with 2-methylcyclohexanone at 165° for 30 min, the product (76%) contained II, III and IV in the ratio 85, 10 and 5% respectively. The last product arises from cyclohexanone (ca. 5%) contaminating the starting material. At 130° for 1 hr, the same reaction gave a crude yield of 62% and at 110° for 2½ hr, the crude yield was 25%. In each of these cases, GLC analysis showed the ratio II:III was as before, but the relative abundance of IV *rose* as the efficiency dropped. The significance of this observation will be discussed later. Mannich bases which incorporate amines other than dimethylamine are also less efficient. In the same reaction under standard conditions, I*b*–*e* gave crude yields of 67, 53, 48 and 35% respectively, although the product distribution (II–IV) did not appear to differ from normal.





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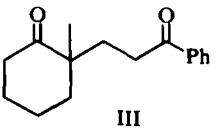

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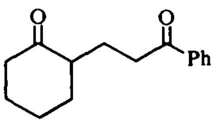
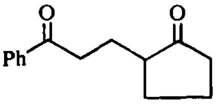
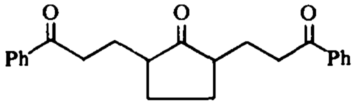


IV

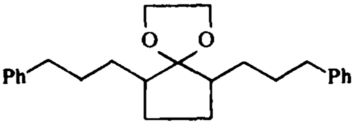
Although it is convenient[2, 3] to use a three-fold excess of ketone, it is possible to conserve precious material by use of a diluent. The reaction of equimolar amounts of Ia and cyclopentanone in ethylene glycol at 160° afforded V in 40% yield, together with a small amount (ca. 6%) of VI. When a 2;1 (molar) ratio of Mannich base to ketone was employed, the yield of V dropped to 19% whilst that of VI rose to 42%. Even under standard reaction conditions the thermal-Michael reaction usually gives rise to di-condensation products in trace amounts[4, 5] and although their structure might be guessed from the orientation rules recently established,[2] no firm evidence has been offered. In the present instance, the expected structure VI has been confirmed by an examination of the mass spectral fragmentation of the ketal VII, prepared from VI. The appearance (Experimental) of fragments at m/e 364, 273, 259 and 217, which are derived as shown in Scheme 1, can only be accommodated by the 2,5-disubstituted isomer.



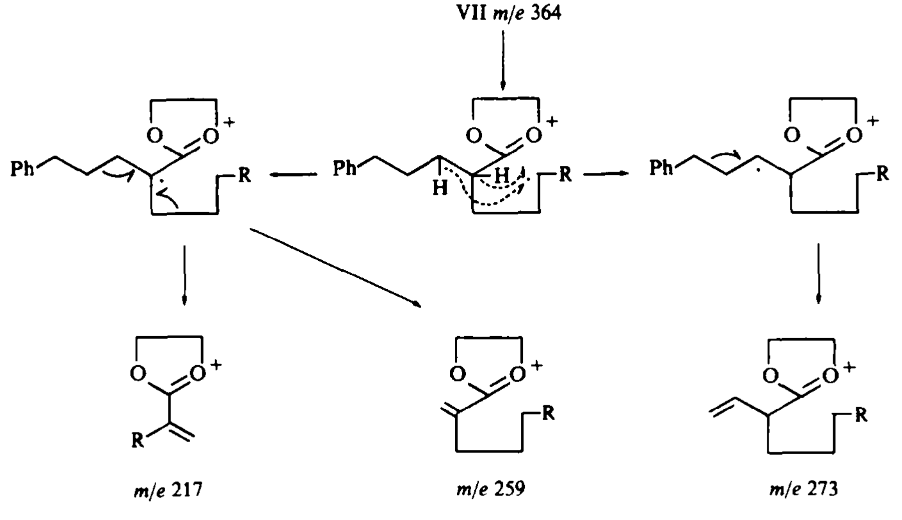
V



VI

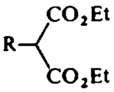


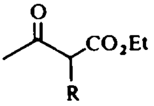
VII

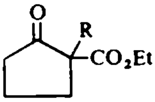


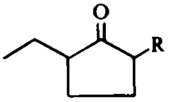
Scheme 1, (R = $CH_2CH_2CH_2Ph$)

The thermal condensation of Ia with a variety of substrates has been investigated. Aside from those already reported,[2, 3] the compounds VIIIa–XIVa, XVIIa and XVIIIa afforded the products VIIIb–XIVb, XVIIb and XVIIIb respectively and in the percentage yields shown in parenthesis. Structural evidence for each product is presented in the Experimental section, but some special comments are necessary here. (i) The yield recorded here for Xb, is in *addition* to some 13% of the dione V, isolated as a by-product. Since V must be derived from Xb, the reaction efficiency is about 65%. (ii) The structure of XIb was established by the mass-spectral cracking pattern of the ketal XVI prepared from XIb. (ii) In two cases (XVII and XVIII) it was not possible to isolate a purified specimen of the product, and so the structure assignments rest solely on mass spectral data. The results are included here because of their mechanistic significance.


VIII (42)


IX (68)


X (52)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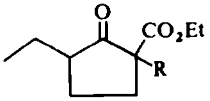
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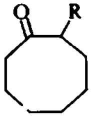
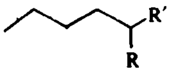
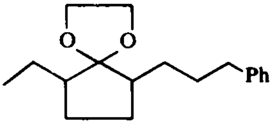
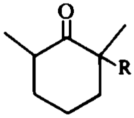
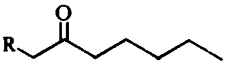

XIII (56)


XIV: R′ = CHO (77)
XV: R′ = CO_2H

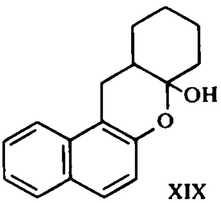

XVI

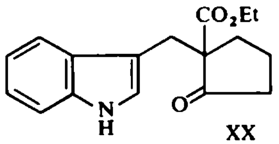

XVII (13)

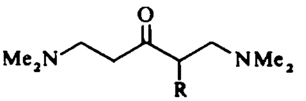

XVIII (48)

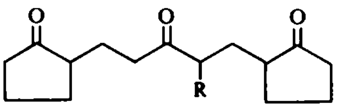
a: R = H *b*: R = $CH_2{\cdot}CH_2{\cdot}CO{\cdot}Ph$

Under thermal conditions, the Mannich base of phenylacetylene did not react with cyclohexanone, but the base prepared from 2-naphthol yielded XIX, whose preparation from a cyclohexanone enamine was recently described.[6] The heterocyclic Mannich base gramine, also reacted smoothly with XIa under thermal-Michael conditions, yielding XX and the bis-Mannich bases XXI and XXII yielded XXIII and XXIV.

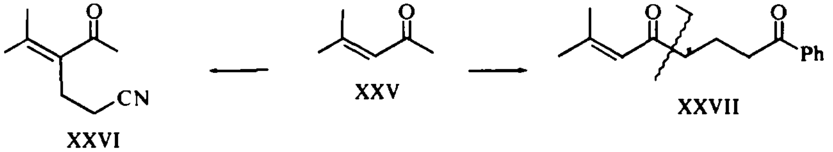

XIX


XX


XXI: R = H
XXII: R = Me

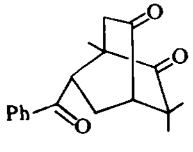

XXIII: R = H
XXIV: R = Me

Mannich bases also react with αβ-unsaturated ketones under thermal conditions, yielding novel products, but their isolation from the reaction mixture is frequently difficult, and the synthetic potential of the reaction is correspondingly reduced. Whilst the reaction of αβ-unsaturated ketones as *donors* in the classical (i.e. base-catalysed) Michael leads to substitution at the α-position[7, 8] e.g. mesityl oxide (XXV) → XXVI[8], it reacts with Ia under thermal-Michael conditions to give XXVII (~ 70%). The structure of this product can be assigned from its mass spectrum, which shows a fragment at *m/e* 83 corresponding to the α-cleavage indicated in XXVII. It is confirmed by the presence of a 1H singlet at τ 3·84 and only two 3H singlets located at τ 7·86 and 8·15, in the NMR spectrum. With isophorone, the result is less well defined.

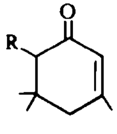


XXVI XXV XXVII

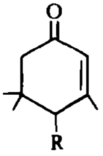
In our initial experiments we accidentally used an aged (peroxidised) specimen of isophorone, which gave[9] the unusual product XXVII as a crystalline solid. The only major by-product in this reaction was an oil, which must be formulated as XXIX or XXX, since its NMR spectrum showed the presence of one vinylic proton, one vinylic Me and two tertiary Me functions. When the reaction was re-run on purified isophorone, no solid product was observed, and effective separation of the other products proved to be too difficult. In contrast to the results above, the octalone XXXI (R = H) gave one major product (XXXI), which showed no vinylic absorption in the NMR.



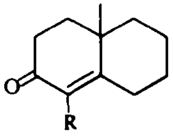
XXVIII



XXIX



XXX



XXXI

R = $CH_2 \cdot CH_2 \cdot CO \cdot Ph$

EXPERIMENTAL

IR spectra were recorded on a Unicam SP 100 double beam instrument, UV spectra on a Unicam SP 800 (in ethanol) and NMR spectra on a Perkin–Elmer R10 (60 m/c) spectrometer in $CDCl_3$ with TMS as internal reference. GLC analyses were carried out on a Perkin–Elmer F11 instrument and mass spectra were recorded on an A.E.I. MS12, but combined GC-MS work was done on an L.K.B. 9000A instrument provided by S.R.C. grant No. B/SR/2398.

Effect of reaction temperature

(a) The Mannich base (Ia; 5·4 g) and 2-methylcyclohexanone (9·5 g) were heated at 130° for 1 hr. Following the described[2, 3] work up, distillation yielded 4·5 g (62%) of product, shown by GLC to contain II, III and IV.

(b) The same reaction, carried out at 110° for 2½ hr, yielded 1·8 g (25%) of product, with the same composition.

β-(N-)*pyrrolidinopropiophenone hydrochloride*

A mixture of acetophenone (4·8 g) paraformaldehyde (2·0 g) and pyrrolidine hydrochloride (4·5 g) in EtOH (12 ml) containing two drops of conc HCl was refluxed for 2½ hr, then filtered hot and allowed to cool. The resultant crystalline mass was recrystallized from EtOH to give 6·8 g (87%) of product as white prisms, m.p. 158–159°. (Found: C, 64·94; H, 7·55; N, 5·83. $C_{13}H_{18}NOCl$ requires: C, 65·09; H, 7·56; N, 5·84%). The free base (Ib) was liberated by alkali.

Condensation of β-*aminopropiophenones* (I) *with* 2-*methylcyclohexanone*

(a) A mixture of Ib (1·1 g; 0·006 m) and 2-methylcyclohexanone (1·85 g; 0·017 m) was refluxed for 30 min at 165°. After the usual work-up procedure, distillation afforded 880 mg (67%) of a pale yellow oil, b.p. 155–160°/0·3 mm. GLC analysis on 5% QF1 at 200° showed the presence of 3 components with R_T 5·55, 6·0 and 7·57 mins. in the proportions, 85:10:5% respectively. By GLC comparison with previous work[2] these were identified as II, III and IV.

(b) A mixture of Ic[10] (1·54 g) and 2-methylcyclohexanone (2·24 g) was refluxed for 30 min at 165°. After the normal work-up, distillation yielded 868 mg (53%) of a pale yellow oil, b.p. 155–160°/0·25 mm. GLC analysis on 5% QF1 at 200° and 45 ml/min showed a similar product distribution to that found above.

(c) A mixture of Id[11] (2·05 g) and 2-methylcyclohexanone (3·36 g) was refluxed for 30 min at 165°. After cooling and the usual work-up, the product was obtained by distillation as a pale yellow oil, 1·41 g (48%), b.p. 150–155°/0·2 mm. This again showed a similar product distribution to the earlier examples by GLC analysis but with an enhanced proportion of IV.

(d) A mixture of Ie[12] (1·53 g) and 2-methylcyclohexanone (2·24 g) was refluxed for 30 min at 165°. After the usual work-up, distillation gave 580 mg (35%) of an oil, b.p. 150–155°/0·2 mm. GLC analysis showed the same distribution of products as observed above.

Dilution studies

(a) Compound Ia (10·5 g), cyclopentanone (5 g) and ethylene glycol (30 ml) were heated with stirring for 45 min at 150–160°. The mixture was neutralized with glacial AcOH and extracted with ether. A crystalline solid separated out of soln on addition of the ether, m.p. 115–116° from benzene, light petroleum; yield 6% (Found: C, 79·37; H, 6·99. $C_{23}H_{24}O_3$ requires: C, 79·28; H, 6·94%), $\nu_{C=O}^{CCl_4}$ 1687, 1732 cm^{-1} (2:1), NMR τ 6·89 (4 × H, tr, $J = 7$ Hz), τ 7·6–8·7 (10 × H, m), τ 1·9–2·8 (10 × H, m). This data is consistent with a di-condensation product (VI).

Extraction of the remaining mixture with ether, yielded a discoloured oil. Distillation gave 5·04 g (40% yield) of V b.p. 160°/0·15 min, identical (IR) with an authentic specimen.[13]

(b) Dimethylaminopropiophenone (10·5 g), cyclopentanone (2·5 g) and ethylene glycol (30 ml) were heated together at 160° for 90 min. The same work-up gave 4·5 g (42% yield) of the crystalline disubstituted product VI, and 2·5 g (19%) of the mono-substituted product (V).

Ketal (VII)

The crystalline product VI (500 mg), and 5% Pd/C (100 mg) in 15 ml EtOH containing 1 drop conc HCl was shaken in a H_2 atm at room temp and press, for 24 hr. After filtration and removal of solvent, the oily residue was dissolved in ether, washed with $NaHCO_3$ aq and recovered by evaporation. The crude product ($\nu_{CO}^{CCl_4}$ 1738 cm^{-1}) (300 mg) in ethylene glycol (1 ml), triethyl orthoformate (2 ml) and toluene-*p*-sulphonic acid (60 mg) was simmered on a hot plate for 1 hr, diluted with $NaHCO_3$ aq and extracted into ether. This soln was washed with water, dried and evaporated. TLC analysis of the product showed the presence of one major product, which was isolated from a preparative plate and submitted directly for mass spectral analysis. The spectrum showed the following peaks (% relative abundance): 364 (35), 273 (60), 259 (50), 217 (48), 113 (100), 99 (42), 91 (75), 55 (23) and 44 (20).

Diethyl β-*benzoylethylmalonate* (VIIIb)

A mixture of β-dimethylaminopropiophenone (3·5 g) and diethyl malonate (9·5 g) was heated for 1 hr at 140°, then neutralised with AcOH, taken up in ether and washed with water. Distillation afforded 2·47 g (42%) of a clear oil, b.p. 150–155°/0·3 mm. GLC analysis showed this to consist of essentially a single component, $R_t = 24$ min on 5% QF1 at 175° and 45 ml/min. (Found: C, 65·03; H, 6·71. $C_{16}H_{20}O_5$ requires: C, 65·74; H, 6·90%), $\gamma_{C=O}^{CCl_4}$ 1693, 1737 and 1754 cm^{-1}, NMR, τ 1·95–2·60 (5 H, m); τ 5·81 (4H, qu); τ 8·87 (6 H, tr).

Ethyl 6-phenylhexan-2,6-dione-3-carboxylate (IXb)

A mixture of Ia (1·9 g) and acetoacetic ester (4·2 g) was heated for 45 min at 180°. The above work-up procedure yielded, on distillation, 1·92 g (68%) of a clear oil, b.p. 144–150°/0·05 mm. GLC analysis indicated the presence of one major product, greater than 90% of the total, R_t = 3·5 min on 5% QF1 at 200° and 45 ml/min on 1% SE 30 at 175° and 45 ml/min. A sample of enhanced purity, obtained by preparative TLC showed $\gamma_{C=O}^{CCl_4}$ 1692, 1720 and 1748 cm^{-1}; NMR, 7·73 τ (3H, s) and 8·73 τ (3H, tr, J = 7 Hz); *m/e* 262. It gave a positive ferric chloride test and its structure was proved by synthesis, as follows.

Phenyl vinyl ketone (1·43 g) in dry ether was added dropwise at 0° to a mixture of acetoacetic ester (2·85 g) and ethanolic KOH (from 500 mg KOH and 2·5 ml EtOH) in ether (10 ml) and stirred at room temp for 2 hr. The mixture was poured on to ice, acidified (HCl) and taken up in ether. This soln was washed, dried and evaporated, yielding the diketo ester 1·95 g (69%) m.p. 112° (benzene) [Found: C, 68·16; H, 6·90. $C_{15}H_{18}O_4$ requires: C, 68·69; H, 6·92%] which proved to be identical (GLC, NMR) with the product of (a) above.

Ethyl 1-(β-benzoylethyl)-2-oxocyclopentane carboxylate (Xb)

A mixture of Ia (1·89 g) and 2-carbethoxycyclopentanone (5·0 g) was heated for 30 min at 160°. The usual work-up procedure[1, 2] gave 1·95 g (65%) of a pale yellow oil, b.p. 150–155°/0·1 mm, shown by GLC to consist of two products, in the ratio 1:4, R_t = 3·6 and 11·75 min on 1% SE 30 at 175° and 45 ml/min and 7·00 and 20·75 min on 5% QF1 at 200° and 40 ml/min. Analysis by gas chromatography/mass spectrometry showed the respective mol wts to be 216 and 288, and from previous experience,[2] these were assumed to be V and Xb respectively. The former was identified by comparison (GLC and IR) with an authentic sample,[3, 13] and the latter by the following synthesis.

Phenyl vinyl ketone (900 mg) in dry ether (7·5 ml) was added dropwise to a mixture of 2-carbethoxycyclopentanone (2·12 g) and ethanolic KOH (from 200 mg KOH in 2·5 ml EtOH) in dry ether (7·5 ml) at 0°, and the mixture stirred at room temp for 2 hr. Work-up as before[2] yielded 1·3 g (66%) of an oil, b.p. 155–160°/0·2 mm which showed a single peak in GLC analysis, R_t = 20·75 min on 5% QF1 at 200° and 40 ml/min. (Found: C, 70·74; H, 7·28. $C_{17}H_{20}O_4$ requires: C, 70·81; H, 6·99%). The IR spectrum showed $\gamma_{C=O}^{CCl_4}$ 1690, 1732 and 1744 cm^{-1} and was otherwise identical with that of the product described above.

2-(*β-Benzoylethyl*)-*5-ethylcyclopentanone* (XIb)

The base Ia (8·9 g; 0·05 mole) and 2-ethylcyclopentanone (5·6 g; 0·05 mole) in ethylene glycol (30 ml) were heated at 160° for 1 hr. neutralized with AcOH and extracted with ether. After washing the ethereal soln was evaporated and yielded 9·35 g (77%) b.p. 150–154°/0·25 mm R_t 16·25 min on 5% QF1 at 200° (Found: C, 78·72; H, 8·31. $C_{16}H_{20}O_2$ requires: C, 78·65; H, 8·25%); IR $\nu_{C=O}^{CCl_4}$ 1732 and 1687 cm^{-1}.

Hydrogenolysis, followed by ketalisation by the method described above for VII, afforded the ketal XVI, isolated by preparative TLC (Found: C, 78·64; H. 9·51. $C_{18}H_{20}O_2$ requires: 78·79; H, 9·55%). The mass spectrum showed the following peaks (% relative abundance) 274 (30), 217 (20), 183 (40), 169 (35), 127 (100), 113 (65), 99 (55), 91 (60), 55 (28) and 44 (40). The occurrence of fragments of mass 217, 183, 169 and 127 *m/e* establishes the orientation of XIb.

When the β-keto-ester XIIa was heated with Ia, under standard conditions, there was virtually no evolution of dimethylamine. The standard work-up gave an oil which was shown (GLC) to be a mixture of only XIa and XIIa.

2-(*β-Benzoylethyl*)*cyclo-octanone* (XIIIb) (by Dr. A. M. Lawson)

The base Ia (8·8 g) and cyclo-octanone (19 g) was refluxed for 2 hr, cooled, neutralized and dissolved in ether. The soln was washed with $NaHCO_3$ aq, and brine, dried and distilled affording the dione (7·2 g, 56%) b.p. 160–162°/2 mm. (Found: C, 79·03; H, 8·58. $C_{17}H_{22}O_2$ requires: C, 78·38; H, 8·54%); $\nu_{CO}^{CCl_4}$ 1700, 1692 cm^{-1}.

2-*β-Benzoylethyl*)*hexanoic aldehyde* (XIVb) *and acid* (XVb)

A mixture of n-hexaldehyde (6·0 g) and β-dimethylaminopropiophenone (3·0 g) was heated under a reflux for 1 hr at 135°. Following the usual work-up, distillation yielded 3·03 g (77%) of a clear oil, b.p. 128–130°/0·1 mm, which showed $\gamma_{C=O}^{CCl_4}$ 1692 and 1728 cm^{-1}. The NMR spectrum had an aldehyde proton signal at 0·40 τ (1H, d, J = 2·5 Hz) and GLC analysis on 5% QF1 at 200° and 45 ml/min showed this to consist of a single product (R_t = 5·0 min) presumably XIVb. On standing for a few hr, the material solidified and was recrystallized from 60–80 petrol as white, feathery needles, m.p. 94°. (Found: C, 72·46; H, 8·09. $C_{15}H_{20}O_3$ requires: C, 72·55; H, 8·12%). This product showed $\gamma_{C=O}^{CCl_4}$ 1692 cm^{-1} and 1707 cm^{-1} and a broad O—H band between 3440 and 3600 cm^{-1}. The NMR spectrum showed an acid proton at $-0{\cdot}1$ τ, the remainder of the spectrum being unaltered, except for the disappearance of the aldehyde proton. The material was also base soluble and was assumed on this basis to be the corresponding acid, with R_t = 12·6 min under the above GLC conditions.

2-(β-*Benzoylethyl*)-2,6-*dimethylcyclohexanone* (XVIIb)

A mixture of Ia (2·1 g) and 2,6-dimethylcyclohexanone (4·5 g) was refluxed for 45 min 160°. After the normal work-up, distillation afforded 1·2 g (40%) of product, b.p. 157–163°/0·3 mm. GLC analysis of this on 5% QF1 at 200° and 55 ml/min showed the presence of two components, R_t = 7·8 and 9·6 min, in the ratio 1:2. Attempts to separate these by chromatographic methods were unsuccessful, but gas chromatograph/mass spectrometer analysis on 1% SE30 gave their mol wts as 258 and 264 respectively. The first corresponds to the mono-alkylated product and the other to phenyl vinyl ketone dimer

1-*Phenyldecan*-1,5-*dione* (XVIIIb)

A mixture of Ia (3·5 g) and methyl n-amyl ketone (7·0 g) was refluxed for 2 hr at 150°. Following the usual work-up procedure, distillation gave 2·8 g (57%) of a pale red oil, b.p. 165–170°/0·3 mm. GLC analysis showed this to consist of one major and two minor components, R_t = 4·3; 6·0 and 13·5 min on 1% SE30 at 175° and 45 ml/min, comprising 10; 85 and 5% of the total product respectively. GC-MS analysis showed that the last was a dimer of phenyl vinyl ketone, whereas the first two had mol wts of 246. Of these the former showed a peak at *m/e* 203 corresponding to loss of MeCO from a branched structure, but the latter (major) product showed the characteristic peaks at *m/e* 71 and 147 expected from α-cleavages of the aliphatic ketone chain in XVIIIb.

7a,8,10,11,11a,12-*Hexahydro*-9H-*benzo*[a]*xanthen*-7a-*ol* (XIX)

1-Dimethylaminomethyl-2-naphthol (10 g) in cyclohexanone (45 g) was refluxed for 2½ hr, neutralized with glacial AcOH, diluted and extracted with ether. After removal of the ether and excess cyclohexanone *in vacuo*, there remained a colourless, alkali-insoluble product (yield > 80%) m.p. 146·5–147° (light petroleum, 60–80°). (Found: C, 79·90; H, 6·92. $C_{17}H_{18}O_2$ requires: C, 79·97; H, 6·71%), mol wt 254 ($C_{17}H_{18}O_2$ requires: 254). The mass spectrum exhibited a strong peak at 235, produced by loss of water from the molecular ion. The IR spectrum showed $\nu^{CCl_4}_{O-H}$ 3595 cm^{-1}, but no CO absorptions. Addition of deuterated DMSO to the NMR sample produced a sharp singlet at 3·88 τ. These data are all consistent with structure XIX.

Ethyl 1-(β-*indolylmethyl*)-2-*oxocyclopentane carboxylate* (XX)

A solution of gramine (3·4 g) in Xa (9·4 g) was stirred at ca. 180° until the evolution of Me_2NH was complete (2 hr). The customary work-up yielded XX (4 g) b.p. 220–225°/0·8 mm. m.p. 74–75° (aq EtOH) (Found: C, 71·25; H, 6·91; N, 4·90. $C_{17}H_{19}NO_3$ requires: C, 71·56; H, 6·71; N, 4·91%); $\nu^{CCl_4}_{CO}$ 1742 and 1720 cm^{-1}; NMR, τ 6·5 (2H s).

The same compound was obtained by reaching indole with the Mannich base derived from Xa.

1,5-*Bis*(2′-*oxocyclopentyl*)*pentan*-3-*one* (XXIII)

The structure of XXI, prepared as described,[14] was verified by the NMR spectrum of its hydrochloride in D_2O which showed no MeCO signal, but a symmetrical A_2B_2 multiplet (8H) centred at τ 6·7.

The bis-Mannich base (2·6 g) dissolved in cyclopentanone (4·5 g) was refluxed until no further Me_2NH was liberated (2 hr). The mixture was neutralized with glacial AcOH, diluted, and extracted with ether. After removal of the ether and excess cyclopentanone, the residual oil (2·7 g) was chromatographed on a silica column with EtOAc light petroleum mixtures as eluant, yielding a crystalline solid (1·9 g, 51% overall yield), m.p. 50–51° (benzene-light petroleum). (Found: C, 71·82; H, 8·87. m.w. 250. $C_{15}H_{22}O_3$ requires: C, 71·97; H, 8·86%, m.w. 250); $\nu^{CCl_4}_{C=O}$ 1737 and 1712 cm^{-1}.

1,5-*Bis*(2′-*oxocyclopentyl*)-2-*methylpentan*-3-*one* (XXIV)

The base XXII, prepared as described,[15] showed a doublet C-Me signal in the NMR (τ 8·95; *J* = 6 Hz) as expected from this structure.

The base (1·6 g) in cyclopentanone (2·2 g) was refluxed for 1½ hr, and worked up as described for XXIII. Chromatography yielded 1 g (45%) of an oil which was purified by TLC. (Found: C, 72·83; H, 8·92. $C_{16}H_{24}O_3$ requires: C, 72·69; H, 9·15%), Mol wt 264 by mass spectrometry, $C_{16}H_{24}O_3$ requires: 264; $\nu^{CCl_4}_{C=O}$ 1740 (ε 873) and 1714 cm^{-1} (ε 316).

2-Methyl-8-phenyloct-2-en-4,8-dione (XXVII)

A mixture of mesityl oxide (7·1 g) and β-dimethylaminopropiophenone (4·0 g) was refluxed for 2 hr at 130°. The normal work-up procedure yielded on distillation 3·65 g (69%) of a pale yellow oil, b.p. 190–195°/0·9 mm consisting of one major product (GLC R_t = 9·0 min on 1% SE30 at 150° and 45 ml/min and 18·2 min on 5% QF 1 at 175° and 45 ml/min). Preparative TLC furnished a solid sample, m.p. 94° (MeOH). (Found: C, 78·05; H, 7·98. $C_{15}H_{18}O_2$ requires: C, 78·23; H, 7·88%); *m/e* 230 (parent), 83 (base); $\nu_{C=O}^{CCl_4}$ 1685 cm^{-1} (broad); NMR, τ 2–2·7 (5H, mult), τ 3·84 (1H), 7·86 (3H) and 8·15 (3H), all broad singlets.

Reaction with isophorone

A mixture of isophorone (7·0 g) and β-dimethylaminopropiophenone (3·0 g) was refluxed for 1 hr at 200°. Following the usual work-up, distillation of the residue yielded 3·24 g (71%) of a red oil, b.p. 200–220°/0·25 mm. GLC analysis on 5% QF1 at 200° and 45 ml/min showed the presence of two major and three minor components, R_t = 9·8, 12·1, 16·8, 20·8 and 26·5 min accounting for 15, 5, 35, 35 and 5% of the total respectively. Trituration of the crude distillate with ether yielded a white, crystalline product, m.p. 183° (MeOH), corresponding to the fourth GLC product. (Found: C, 75·71; H, 6·74. $C_{18}H_{20}O_3$ requires: C, 76·03; H, 7·09%); $\gamma_{C=O}^{CCl_4}$ 1688 and 1733 cm^{-1}; *m/e* 284; NMR three 3H singlets at τ 8·72, 8·91 and 9·01 and a sharp 1H triplet at τ 6·17 (J = 8·8 Hz.). Its structure XXVIII had already been established.[9] Separation of the other major product by preparative TLC, yielded an oil, b.p. ca. 180°/0·2 mm. (Found: C, 79·88; H, 8·15. $C_{18}H_{22}O_2$ requires: C, 79·96; H, 8·20%) whose NMR showed one vinyl proton at τ 4·18 and Me signals at τ 7·88 (3H, s) and 9·01 (6H, s) $\gamma_{C=O}^{CCl_4}$ 1668 and 1685 cm^{-1}.

Reaction with 10–methyloctalone

A mixture of 10–methyl-$\Delta^{1(9)}$–2–octalone (5·0 g) and β-dimethylaminopropiophenone (1·77 g) was refluxed for 1 hr at 200°. On work-up, there was obtained 2·1 g (61%) of product, b.p. 177–180°/0·25 mm, as a clear viscous oil. GLC analysis on 1% QF1 at 200° and 50 ml/min showed it to consist of one major and two minor products, R_t = 4·0, 9·8 and 16·3 min, accounting for 10, 75 and 15% of total respectively.

The major product, was isolated by preparative TLC, $\gamma_{C=O}^{CCl_4}$ 1684 cm^{-1}. (Found: C, 80·85; H, 8·15. $C_{20}H_{24}O_2$ requires: C, 81·04; H, 8·16%). The NMR spectrum showed signals between τ 2·0 and 3·0 (5H, m) and at τ 8·79 (3H, s) but no vinyl proton.

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