## 135. The Structure of 1,5-Diketones.

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Some aldehydes have been condensed with β-dicarbonyl compounds in molar ratio of one to two and the infrared spectra of the products have been examined. It is concluded that these bis-compounds are hydroxycyclohexanones; but this cyclic structure is only possible if there is a methyl group adjacent to a carbonyl group in the dicarbonyl compound, and in its absence the bis-compound is an acyclic 1,5-diketone. 4-Formyl-1-phenylpyrazole behaves abnormally with benzoylacetone and dibenzoylmethane, one product being 1-phenyl-3-(1-phenyl-4-pyrazolyl)prop-2-en-1-one. The reaction between some of the bis-compounds and hydrazine or phenylhydrazine has also been examined.

CONDENSATION of aliphatic or aromatic aldehydes with β-keto-esters or β-diketones, in molar ratio of one to two and in the presence of a basic catalyst, leads to bis-compounds. Various aldehydes, β-keto-esters, and β-diketones have been used (see, *e.g.*, Rabe and Elze,[1a] Horning and Field,[2] and Martin, Shamma, and Fernelius[3] for literature references). According to Knoevenagel[4,5] the general structure of these bis-compounds is (A). Rabe,[1b,6,7,8] however, believed that these compounds are hydroxycyclohexanones (B) and that eight (±)-isomers were possible; and, in the case of the benzaldehyde bis-ester (R^1 = Ph; R^2 = Me, R^3 = OEt), Rabe[6] isolated three of these (±)-forms. Further, Rabe and Elze[1a] concluded that 1,5-diketones with a methyl group attached to one carbonyl group change to cyclic alcohols under the influence of basic substances. The usual catalyst for these condensations is piperidine, and a ketone (A), which is formed first, undergoes the intramolecular aldol condensation to give (B) if allowed to remain in contact
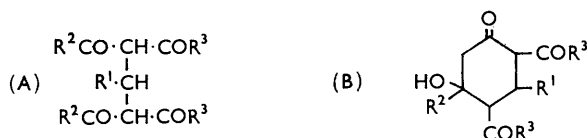
with piperidine. According to Rabe and Elze compounds (A) form dihydropyridine derivatives (with ammonia), disodium salts, and bis-pyrazolones or -pyrazoles (with hydrazine); compounds (B) form monosodium salts and mono-pyrazolones or -pyrazoles. Knoevenagel,[5] however, believed that the change of the diketo-form (A) into its corresponding keto-enol or di-enol form, or *vice-versa*, explained the effect of piperidine on 1,5-diketones and that the existence of these forms accounted for all the chemical reactions of 1,5-diketones. Furthermore, Knoevenagel believed that the use of chemical methods

[1] Rabe and Elze, *Annalen*, 1902, **323**, (a) 92, (b) 83.
[2] Horning and Field, *J. Amer. Chem. Soc.*, 1946, **68**, 384.
[3] Martin, Shamma, and Fernelius, *J. Amer. Chem. Soc.*, 1958, **80**, 5851.
[4] Knoevenagel, *Annalen*, 1898, **303**, 223.
[5] Knoevenagel, *Ber.*, 1903, **36**, 2118.
[6] Rabe, *Annalen*, 1900, **313**, 129.
[7] Rabe and Billmann, *Annalen*, 1904, **332**, 22.
[8] Rabe, *Ber.*, 1943, **76**, 979.

to elucidate the structures of these compounds was unsatisfactory. These ideas were also held by Dieckmann and Fischer [9] who also thought that reaction with hydrazine caused the acyclic to isomerise to the ring compound.

Although the preparation of these bis-compounds requires a basic catalyst, there is at least one exception. Rabe [10] showed that formaldehyde (1 mol.) condensed directly with ethyl acetoacetate (2 mol.) to form two isomers, ethyl $\alpha\alpha'$-diacetylglutarate and ethyl 2-hydroxy-2-methyl-4-oxocyclohexane-1,5-dicarboxylate, (A) and (B) respectively ($R^1 = H$, $R^2 = Me$, $R^3 = OEt$). Also the irreversible change from acyclic to cyclic structure normally requires a basic catalyst, but the above example of cyclisation is an exception, as is also the spontaneous cyclisation of ethyl 2-acetyl-5-oxo-3,4,5-triphenyl-pentanoate.[11]

In the present work the known bis-esters and -β-diketones (I—VI) have been prepared (Table 1), and 4-formyl-1-phenylpyrazole [12] has been condensed, in 1 : 2 molar ratio, with

TABLE 1. *Properties of condensation products.*

No.	R^1	R^2	R^3	M. p.	Yield (%)
(IB)	Me	Me	OEt	80—81° [a]	39
(IIB)	Me	Me	Me	108 [b]	37
(IIIB)	Ph	Me	OEt	157—158 [c]	70
(IVB)	Ph	Me	Me	168—169 [d]	71
(VB)	Ph	Me	Ph	202·5—204 [e]	49
(VIA)	Ph	Ph	Ph	157—158	51
(VIIB)	1-Ph-4-$C_3H_2N_2$	Me	OEt	177—178	81
(VIIIB)	1-Ph-4-$C_3H_2N_2$	Me	Me	146—148	72
(IXB)	1-Ph-4-$C_3H_2N_2$	Me	Ph	218—219	13
(XD)	Me	Me	OEt	265—267 [g]	90
(XIF)	Me	Me	Me	195—197	54
(XIIC)	Ph	Me	OEt	192—193 [h]	57
(XIIID)	Ph	Me	OEt	278·5—280 (dec.)	70
(XIVE)	Ph	Me	Me	182—183 [j]	49
(XVF)	Ph	Me	Me	211—212 [k]	70
(XVID)	1-Ph-4-$C_3H_2N_2$	Me	OEt	267—268	63
(XVIIF)	1-Ph-4-$C_3H_2N_2$	Me	Me	206—209	57

No.	Found (%) C	H	N	Formula	Calculated (%) C	H	N
(VIIB)	64·0	6·3	7·0	$C_{22}H_{26}N_2O_6$	63·7	6·3	6·8
(VIIIB)	67·7	6·3	7·6	$C_{20}H_{22}N_2O_4$	67·8	6·2	7·9
(IXB)	74·9	5·2	5·6	$C_{30}H_{26}N_2O_4$	75·3	5·4	5·9
(XIF)	64·7	7·9	12·6	$C_{12}H_{18}N_2O_2$	64·9	8·1	12·6
(XVID)	62·55	6·1	14·4	$C_{20}H_{22}N_4O_4$	62·8	5·8	14·7
(XVIIF)	68·5	6·3	15·6	$C_{20}H_{22}N_4O_2$	68·6	6·3	16·0

[a] Knoevenagel, *Annalen*, 1894, **281**, 104, gives m. p. 79—80°; Rabe and Billmann, *ibid.*, 1904, **332**, 26, give m. p. 80°. [b] Knoevenagel, Bialon, and Ruschhaupt, *Ber.*, 1903, **36**, 2149, give m. p. 108°. [c] Hantzsch, *Ber.*, 1885, **18**, 2583, gives m. p. 152—153°; Rabe, *Annalen*, 1900, **313**, 176, gives m. p. 149—150°. [d] Knoevenagel and Werner, *Annalen*, 1894, **281**, 81, give m. p. 166°; Schiff, *ibid.*, 1899, **309**, 206, gives m. p. 168°; Martin, Shamma, and Fernelius, *J. Amer. Chem. Soc.*, 1958, **80**, 5852, give m. p. 165—167°. [e] Knoevenagel and Erler, *Ber.*, 1903, **36**, 2131, give m. p. 195°; Martin *et al.* (ref. d) give m. p. 202—202·5°. [f] Dieckmann and Fischer, *Ber.*, 1911, **44**, 974, give m. p. 154—155°. [g] Rabe and Elze, *Annalen*, 1902, **323**, 100, give m. p. 256° (decomp.). [h] Rabe and Elze, *Annalen*, 1902, **323**, 103, give m. p. 168—171° (or 194°); Knoevenagel and Heeren, *Ber.*, 1903, **36**, 2124, give m. p. 193°. [i] Rabe and Elze, *Annalen*, 1902, **323**, 104, give m. p. 257° (decomp.). [j] Knoevenagel, *Annalen*, 1894, **281**, 83, gives m. p. 177°. [k] Rabe and Elze, *Annalen*, 1902, **323**, 111, give m. p. 220° (decomp.).

ethyl acetoacetate, acetylacetone, benzoylacetone, and dibenzoylmethane in the presence of piperidine. Ethyl acetoacetate gave the bis-compound (VIIB) even when the molar ratio of reactants was one to one. Acetylacetone behaved normally to give a bis-derivative (VIIIB), but with benzoylacetone the bis-(β-diketone) (IXB) was obtained together with

[9] Dieckmann and Fischer, *Ber.*, 1911, **44**, 966.
[10] Rabe, *Annalen*, 1904, **332**, 2; Rabe and Rahm, *ibid.*, 1904, **332**, 11.
[11] Rabe and Ehr, *Annalen*, 1908, **360**, 272.
[12] Finar and Lord, *J.*, 1959, 1819.

1-phenyl-3-(1-phenyl-4-pyrazolyl)prop-2-en-1-one (XV).[12] There is much evidence to show that the preparation of the bis-compounds involves an intermediate of the type $R^1 \cdot CH=C(COR^2) \cdot COR^3$, which then readily undergoes the Michael condensation with a second molecule of β-diketo-compound. Thus the formation of compounds (VIIIB)
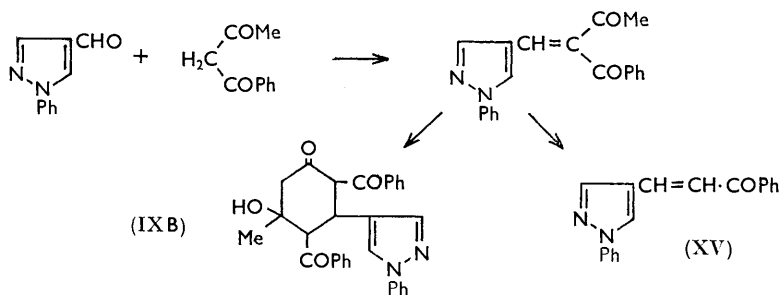
and (IXB) is normal, but at the same time some of the intermediate unsaturated compound eliminates an acetyl group.

With dibenzoylmethane, the only product isolated was the pyrazolylpropenone (as XV). Hence in this case the Michael condensation does not appear to occur, and a benzoyl group is eliminated from the intermediate. It is interesting in this connexion that condensation of acetylacetone with cinnamaldehyde,[13] 2-hydroxynaphthaldehyde,[14] and salicylaldehyde[15] does not proceed beyond the stage of the unsaturated compound, but no mention is made of an acetyl group's being eliminated.

The infrared absorption spectra of many bis-(β-diketones) have been examined by Martin *et al.*[3] who found that all their compounds gave a wine colour with methanolic ferric chloride; they state that "in the solid state, some bis-(β-diketones) of the type $R^1 \cdot CH[CH(COR^2) \cdot COR^3]_2$ may exist to an appreciable extent in the keto-form." The evidence given for this is the high-intensity carbonyl absorption in the 1733—1709 cm.$^{-1}$ region and the relatively low-intensity enol-chelate absorption near 1600 cm.$^{-1}$. It is also pointed out that most of these bis-(β-diketones) have hydroxyl stretching frequencies near 3390 cm.$^{-1}$.

An interesting point about this work is that the authors apparently do not consider at all the possibility of a cyclic structure for these compounds, and make no mention of Rabe's work. In the present work the infrared absorption spectra of the bis-compounds (I—IX) show that all except (VIA) have ring structure (B). None of these gave a colour with ferric chloride. [Among the compounds examined by Martin *et al.* are (IV) and (V), and these are stated as giving a colour with ferric chloride.] A number of enolic β-diketones have also been examined and for all there was complete absence of a true alcoholic hydroxyl group absorption near 3700 cm.$^{-1}$, and in all cases a weak band near 2700 cm.$^{-1}$ which we attribute to the chelated hydroxyl group in agreement with Rasmussen, Tunnicliff, and Brattain.[16] The compounds examined (in Nujol mull) were benzoylacetone, *m-* and *p*-nitrobenzoylacetone, *p*-methoxybenzoylacetone, dibenzoylmethane, *m*-nitrodibenzoylmethane, 3-benzoylacetyl-1,5-diphenylpyrazole,[17] octane-2,4,5,7-tetraone,[17] and 1,6-diphenylhexane-1,3,4,6-tetraone.[17] All these compounds give a colour with ferric chloride and consequently are at least partly enolic.

All the spectra of (I—IX), except that of (VIA), fall into the same general pattern (Table 2) showing a strong band between 3500 and 3324 cm.$^{-1}$. This indicates the presence

[13] Knoevenagel and Herz, *Ber.*, 1904, **37**, 4483.
[14] Knoevenagel and Schröter, *Ber.*, 1904, **37**, 4489.
[15] Knoevenagel and Arnot, *Ber.*, 1904, **37**, 4499.
[16] Rasmussen, Tunnicliff, and Brattain, *J. Amer. Chem. Soc.*, 1949, **71**, 1068.
[17] Finar, *J.*, 1955, 1205.

of a " true " hydroxyl group and not an enolic chelated hydroxyl group. For compounds (I—IV) and (VII), the hydroxyl stretching frequencies are between 3550 and 3450 cm.$^{-1}$, and this could be due to intramolecularly bonded hydroxyl group or singly linked alcohol dimer.[18a] It is suggested here that the former holds in this case since diacetone alcohol [18b]

TABLE 2. *Infrared spectra of the condensation products.*

No.	O–H stretch (cm.$^{-1}$)	tert. OH C–O stretch O–H bend (cm.$^{-1}$)	C=O stretch (cm.$^{-1}$)	C=C stretch (cm.$^{-1}$)	CH stretch of CH_2 (cm.$^{-1}$)
IB	3487s	1124m, 1393sh	1745s, 1712s	—	2926m*, 2872sh
IIB	3502s	1124m	1724s, 1706s 1695s	—	2920w, 2871w
IIIB	3484m	1124sh	1748s, 1714s	1600sh, 1500sh	2926m*, 2865w
IVB	3636s	1117w, 1389m	1724s, 1704s	1610w, 1502w	2921m, 2847sh
VB	3354s	1127w, 1395sh	1709s, 1692s	1605m, 1502s	2920m, 2847sh
VIA	—	1117w	1695s, 1681s	1600m, 1502sh	—
VIIB	3448s	1124sh, 1389s	1745s, 1724s 1709s	1605s, 1508s	2920sh,* 2872sh
VIIIB	3324s	1124sh, 1404w	1724s, 1709sh 1695s	1603w, 1508w	2921m, 2847sh
IXB	3406s	1124sh, 1399sh	1709s, 1678s	1608m, 1511w	2920m, 2877sh
a	3448m	1124m, 1393m			2926m, 2855sh
b	3600m, 3490w				2920s, 2849s

1-Methylcyclohexanol: (a) liquid capillary film, (b) 0·115M-solution in CCl_4; compensated 0·5 mm. cell.

* These compounds contain a CO_2Et group and consequently a CH_2 group.

absorbs at 3484 cm.$^{-1}$ and the carbonyl absorption [18c] occurs at 1712 cm.$^{-1}$. The influence of hydrogen bonds on certain carbonyl groups [18c] is not greater than 10 cm.$^{-1}$, and it will be seen that the carbonyl frequencies of (I—IV) and (VII) are those expected (see below). On the other hand, the hydroxyl frequencies of compounds (V), (VIII), and (IX) are in the 3400—3200 cm.$^{-1}$ region, but much closer to the former, and hence these compounds also contain some polybonded alcohol.[18a]
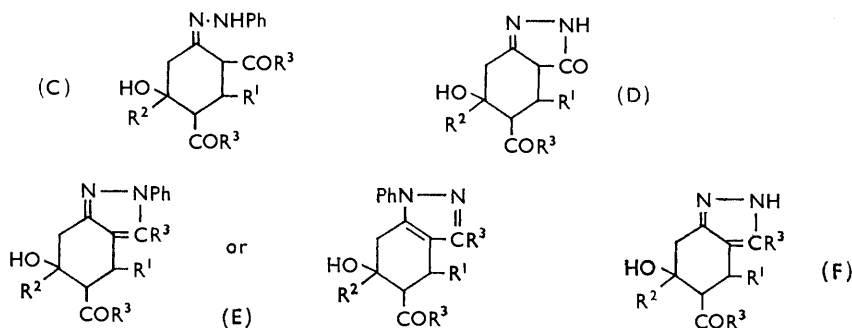
All the compounds show a peak at or near 1124 cm.$^{-1}$ and this is consistent with the C–O stretching frequency of a tertiary alcohol (near 1140 cm.$^{-1}$).[18d] Since this band could also arise from a CH in-plane deformation of a monosubstituted benzene ring (1175—1125 cm.$^{-1}$),[18e] the presence of a tertiary hydroxyl group is rendered uncertain when a monosubstituted benzene ring is known to be present. It is significant, however, that in the compounds in Table 2 this band is also present for compounds (I) and (II) in which there are no benzene rings. Further, the presence in most cases of a second band near 1393 cm.$^{-1}$ supports the argument that these compounds are tertiary alcohols, since the O–H bending frequency lies in the 1400—1300 cm.$^{-1}$ region [18f] (no similar band occurs in spectra of aromatic compounds).

All the carbonyl bands are strong and sharp and occur in the 1748—1678 region. In the spectra of the β-diketones examined above, strong broad peaks occur in the 1640—1540 cm.$^{-1}$ region, in keeping with the observation by Rasmussen *et al.*[16] Thus the bis-compounds are ketonic compounds and not chelated ketones. Further, enolic β-diketones usually absorb near 1600 cm.$^{-1}$, but since this band (and the one near 1500 cm.$^{-1}$) is characteristic of the aromatic ring,[16g] it may sometimes be difficult to differentiate between the 1600 cm.$^{-1}$ band for C=C in-plane vibration and the 1600 cm.$^{-1}$ band for a chelated carbonyl group.[16h] Table 2 shows the 1600 and 1500 cm.$^{-1}$ bands, and it is significant that both of these are absent from the spectra of ketones (I) and (II), neither of which contains an aromatic (or heterocyclic) nucleus. It is therefore concluded that no enol form is present (cf. the fact that none gave the ferric chloride reaction). Finally, all the

[18] Bellamy, " The Infrared Spectra of Complex Molecules," Methuen, London, 1958, 2nd edn., pp. (a) 102, (b) 99, (c) 136, (d) 109, (e) 82, (f) 110, (g) 69, (h) 74, (i) 15.

products except (VIA) showed two bands due to C–H stretching vibrations of the CH_2 group (2926 and 2853 $\pm$10 cm.$^{-1}$).[16i] In all the compounds other than those containing ethoxycarbonyl groups, there cannot be a CH_2 group present in form (A), but this group is present in the cyclic compounds (B). The OH and CH_2 bands of 1-methylcyclohexanol have been given in Table 2 (*a* and *b*) for comparison. Compound (VIA), in which there is no methyl group adjacent to a carbonyl group and which consequently cannot cyclise, shows no OH or CH_2 bands, but does show free CO bands.

Some of the bis-compounds were treated with an excess of phenylhydrazine or hydrazine. In all cases only one mol. of reagent was used, to give products (X—XVII). The bis-esters gave either the phenylhydrazone (C) or the hexahydroindazolone (D), and the bis-

diketones gave the tetrahydroindazole (E) or (F). The infrared spectra of these compounds were complicated, but all showed the presence of a tertiary hydroxyl group and a methylene group.

From the foregoing discussion, it is concluded that all the bis-compounds in Table 1, except (VIA), are hydroxycyclohexanones, but it appears that before the acyclic or cyclic structure can be assigned to this type of compound, the properties of each one must be studied, and a satisfactory method is by infrared spectroscopy.

EXPERIMENTAL

Preparation of Hydroxycyclohexanones (I—VIII).—Ethyl acetoacetate (0·1 mole) or the β-diketone (0·1 mole) and the aldehyde (0·05 mole) were dissolved in ethanol (25—100 c.c.), with warming if necessary; piperidine (0·5—1·0 c.c.) was added and the mixture set aside at room temperature (III, IV, V, VII, and VIII), at 0° to −5° (I and II), or at 50—60° (VI), for 1—3 days. The precipitate was collected, washed with ethanol, and recrystallised from ethanol (see Table 1). None of the hydroxycyclohexanones (I—IX), in ethanol, gave a colour with neutral ferric chloride solution.

Preparation of Hydroxycyclohexanone (IX).—4-Formyl-1-phenylpyrazole [12] (3·44 g., 0·02 mole) and benzoylacetone (6·48 g., 0·04 mole) were dissolved in hot ethanol (50 c.c.), piperidine (6 drops) was added, and the mixture left for 2 days. The yellow precipitate (4·5 g.) was collected, washed with ethanol, and then digested with cold chloroform (40 c.c.). The undissolved material was recrystallised three times from 1 : 2 chloroform–light petroleum, to give 2,4-*dibenzoyl-5-hydroxy-5-methyl-4-*(1-*phenyl-4-pyrazolyl*)*cyclohexan-1-one* (IX) (1·2 g.; see Table 1).

The chloroform filtrate (from the cold digestion) was evaporated to dryness and the residue recrystallised several times from ethanol, to give yellow needles, m. p. 181°, which were shown to be 1-phenyl-3-(1-phenyl-4-pyrazolyl)prop-2-en-1-one [12] by a mixed m. p. determination with an authentic specimen, and by conversion into 1,3-diphenyl-5-(1-phenyl-4-pyrazolyl)-pyrazoline,[12] m. p. 192°.

Reaction between 4-Formyl-1-phenylpyrazole and Dibenzoylmethane.—4-Formyl-1-phenyl-pyrazole (3·44 g., 0·02 mole), dibenzoylmethane (8·96 g., 0·04 mole), ethanol (50 c.c.), and piperidine (0·5 c.c.) were heated at 40—50° for 2 days, and then left for 1 day at room temperature. The precipitate was collected, washed with ethanol, and recrystallised from ethanol,

to give 1-phenyl-3-(1-phenyl-4-pyrazolyl)prop-2-en-1-one [12] (2·6 g., 52%), m. p. 181°, the identity of which was established as described above.

Reaction between Hydroxycyclohexanones and Hydrazine or Phenylhydrazine.—The hydroxy-cyclohexanone (0·01 mole) and hydrazine hydrate (0·02 mole) or phenylhydrazine (0·02 mole) in ethanol (30 c.c.) were heated on the steam-bath for 0·5 hr., then set aside, and the precipitate was collected and recrystallised from ethanol; compounds (XIIC) and (XIVE) were recrystallised from benzene, and (XVID) from aqueous acetic acid (see Table 1).

Infrared Absorption Spectra.—Spectra were obtained with a Perkin–Elmer model 137 fitted with sodium chloride optics or with a Grubb–Parsons model S3A fitted with lithium fluoride optics. They were taken for mulls (Nujol or Fluorolube), except 1-methylcyclohexanol (see Table 2).

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