24. *Some Substituted Phenethyl and 3-Phenylpropyl Styryl Ketones and the Corresponding Saturated Ketones.*

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Numerous αβ-unsaturated ketones have been prepared by condensing alkan-2-ones with aromatic aldehydes in alkali, reaction being assumed (and in some cases proved) to occur at the methyl group. Hydrogenation afforded the saturated ketones smoothly.

In condensations of alkyl methyl ketones with aromatic aldehydes under alkaline conditions we have obtained unsaturated ketones in the yields stated in Table 1. We did not obtain any bis-condensation products[1] although the slightly oily crude products may have contained small quantities of other materials. In conformity with general, but not universal, experience[1] we assumed condensation at the methyl group adjacent to the ketone function in our cases, and in confirmation found that the unsaturated ketones from 4-phenylbutan-2-one and 5-phenylpentan-2-one do not give a haloform test, and that the product from 4-phenylbutan-2-one and benzaldehyde is catalytically reduced to 1,5-diphenylpentan-3-one.

The unsaturated ketones were all colourless or pale yellow, except those from 4-phenylbutan-2-one, 5-phenylpentan-2-one, and amino-*p*-dimethylbenzaldehyde which were bright yellow. The methiodide of the former exception was colourless, so the yellow colour may be due to resonance between structure (I) and (II).

$$\text{(I)}\ {}^{+}\mathrm{Me_2N{:}C_6H_4{:}CH{\cdot}CH{:}CR{\cdot}O^{-}} \qquad {}^{+}\mathrm{Me_2N{\cdot}C_6H_4{\cdot}CH{:}CH{\cdot}CO{\cdot}R}\ \text{(II)}$$

The 2,4-dinitrophenylhydrazones of 1-*p*-methoxyphenyl-5-phenylpent-1-en-3-one and of 1-*o*-methoxyphenyl-6-phenylhex-1-en-3-one were dimorphic, existing in two interconvertible forms, and the *para*-analogue of the latter is probably also dimorphic. However, 1-(3,4-dimethoxyphenyl)-6-phenylhex-1-en-3-one on treatment with 2,4-dinitrophenylhydrazine gave two compounds that were not interconvertible; these may be different stereochemical forms or one of them may be a pyrazoline.

The unsaturated diaryl ketones were hydrogenated to their saturated analogues and the technique has been adapted so that up to 20 kg. of œnanthol can be reduced in one batch, this being the best route to heptan-1-ol. The dinitrophenylhydrazones of the saturated ketones were obtained in only one form.

EXPERIMENTAL

Ethyl α-Benzylacetoacetate.—Benzyl chloride (420 g.) and ethyl acetoacetate (432 g.) in alcoholic sodium ethoxide [from sodium (77 g.) and alcohol (1400 ml.)], when refluxed for 4½ hr. and left for 64 hr., gave ethyl α-benzylacetoacetate (365 g., 50%), b. p. 171°/15 mm., and αα-dibenzylacetoacetate (140 g., 14%), b. p. 237—239°/19 mm., solid at room temperatures (both b. p.s corrected). Much ethyl acetoacetate was recovered; if an excess of this reactant is used, the proportion of the monobenzyl is increased at the expense of the dibenzyl ester.

Benzylacetone.—Ethyl α-benzylacetoacetate (660 g.) and potassium hydroxide (370 g.) were left overnight in water (370 ml.) and alcohol (3 l.), then refluxed for 5 hr. Removing most of the alcohol and adding the residue to water gave benzylacetone (367 g., 82%), b. p. 118°/14 mm. [semicarbazone, m. p. 145° (Found: N, 20·6. Calc. for $C_{11}H_{15}N_3O$: 20·5%)], and, from the aqueous layer on acidification, β-phenylpropionic acid (52 g., 12%), b. p. 162—172°/25—26 mm., m. p. 46°.

Ethyl α-Phenethylacetoacetate.[1]—Phenethyl bromide (1280 g.), ethyl acetoacetate (900 g.), and alcoholic sodium ethoxide (from 159 g. of sodium and 2400 ml. of alcohol) were boiled for 15 hr., then left overnight. Fractionation afforded 5-phenylpentan-2-one (104 g., 9%), b. p. 129—136°/16 mm., ethyl α-phenethylacetoacetate (859 g., 53%), b. p. 121°/0·4 mm.,

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[1] *Inter al.*, Heilbron and Irving, *J.*, 1929, 931, 936; Heilbron, Heslop, Irving, and Wilson, *J.*, 1931, 1336.

176—184°/16—20 mm., and ethyl αα-diphenethylacetoacetate (84 g., 3·6%), b. p. 192°/0·40 mm. Ethyl α-phenethylacetoacetate gave a pale orange-yellow 2,4-*dinitrophenylhydrazone*, m. p. 92° (Found: C, 57·95; H, 5·1; N, 13·9. $C_{20}H_{22}N_4O_6$ requires C, 58·0; H, 5·3; N, 13·5%). It was not possible to obtain a crystalline dinitrophenylhydrazone from the high-boiling fraction, but its nature was inferred from hydrolysis (33·8 g.) by boiling (10 hr.) alcohol (260 ml.), water (13 ml.), and potassium hydroxide (12·3 g.) to 5-phenylpentan-2-one (3 g.), b. p. 88—94°/2·4 mm. (dinitrophenylhydrazone, m. p. and mixed m. p. 78°), 3-phenethyl-5-phenylpentan-2-one, b. p. 182—186°/2·4 mm. [*dinitrophenylhydrazone*, orange needles, m. p. 101° (Found: C, 67·6; H, 6·0; N, 12·4. $C_{25}H_{26}N_4O_4$ requires C, 67·3; H, 5·8; N, 12·6%)], and an acid (10 g.), b. p. 196—206°/5 mm., which, from its analysis (Found: C, 80·0; H, 7·3. Calc. for $C_{18}H_{20}O_2$: C, 80·6; H, 7·5%) and that of its anilide, m. p. 152° (Found: C, 84·2; H, 7·4; N, 4·0. Calc. for $C_{24}H_{25}NO$: C, 84·0; H, 7·3; N, 4·1%), was α-phenethyl-γ-phenylbutyric acid.

2,4-*Dinitrophenylhydrazones*.—The following method is superior to that of Brady. A hot solution of dinitrophenylhydrazine hydrochloride is prepared by adding concentrated hydrochloric acid drop by drop to a boiling mixture of dinitrophenylhydrazine (1 g.) in alcohol (20 ml.) until a clear solution results. The boiling solution is added to a hot solution of the aldehyde or ketone (slightly less than 1 mol.) in alcohol (10 ml. per g. of carbonyl compound). Sometimes the dinitrophenylhydrazone is precipitated immediately, sometimes during 2—3 minutes' boiling; with some simple ketones and aldehydes it may be necessary to allow the solution to cool.

5-*Phenylpentan*-2-*one*.—Ethyl α-phenethylacetoacetate (858 g.), when boiled with alcohol (3650 ml.), potassium hydroxide (450 g.), and water (450 ml.) for 5½ hr., led to 5-phenylpentan-2-one (516 g., 87%), b. p. 134°(corr.)/17 mm., and slightly impure γ-phenylbutyric acid (35 g., 6%), m. p. 46° (lit., 50°, 52°), b. p. 170—172°/17 mm. [Yellow *dinitrophenylhydrazone*, m. p. 78°, is readily soluble in hot alcohol and acetone (Found: C, 60·1; H, 5·8; N, 16·5. $C_{17}H_{18}N_4O_4$ requires C, 59·6; H, 5·3; N, 16·4%)].

Ethyl α-4-*Nitrobenzyl- and* αα-*Di*-(4-*nitrobenzyl*)-*acetoacetate*.—The product, m. p. 145°, of interaction of 4-nitrobenzyl chloride and sodioacetoacetic ester was stated by Roser [2] to be ethyl α-4-nitrobenzylacetoacetate, but Burgess [3] (using 4-nitrobenzyl bromide) showed that the more easily isolated product (m. p. 137—139°) was ethyl αα-di-(4-nitrobenzyl)acetoacetate. To produce a larger proportion of the mononitrobenzyl derivative an excess of ethyl acetoacetate has now been used. Ethyl acetoacetate (468 g., 4 mol.) was added to sodium ethoxide [from sodium (20·7 g.) and alcohol (400 ml.)], and 4-nitrobenzyl chloride (154 g., 1 mol.) was then added to the cold solution. After 30 min. at room temperature, during which it became warm, the mixture was refluxed for 3 hr., then filtered hot, most of the alcohol was evaporated, and water and dilute acid were added to the residue. The excess of acetoacetic ester (250 g.) was removed by distillation *in vacuo*. Ethyl αα-di-(4-nitrobenzyl)acetoacetate remained as colourless needles, m. p. 138—139° (27 g.), when the residue was triturated several times with cold methyl alcohol. The oil removed by the methyl alcohol was distilled in a high vacuum, ethyl α-4-nitrobenzylacetoacetate (132 g.) passing over at 178°/0·06 mm. It solidified and recrystallized from a little ethyl alcohol as pale yellow tablets (90 g.), m. p. 43°. This solvent is preferable to the benzene–ligroin mentioned in the literature. The *dinitrophenylhydrazone* forms orange-yellow needles (from alcohol), m. p. 158° (Found: C, 51·7; H, 4·0; N, 15·7. $C_{19}H_{19}N_5O_8$ requires C, 51·2; H, 4·3; N, 15·55%). The general method of formation of dinitrophenylhydrazones failed with ethyl αα-di-(4-nitrobenzyl)acetoacetate, the ester being recovered unchanged but with higher m. p. (141°). An attempt to hydrolyse ethyl α-4-nitrobenzylacetoacetate to 4-nitrobenzylacetone by methods similar to those described above was unsuccessful.

Condensation of Aldehydes with 4-*Phenylbutan*-2-*one and* 5-*Phenylpentan*-2-*one*.—Condensation of benzaldehyde with 4-phenylbutan-2-one by means of sodium ethoxide was not satisfactory. The general method adopted was a modification of that of Harries and Gollintz.[4] The ketone (0·1 mol.) was added to the aldehyde (0·1 mol.) in alcohol (280 g.) and water (400 ml.); 10% w/w sodium hydroxide solution (40 g.) was then added. A homogeneous solution usually resulted; if not, alcohol was added to remove turbidity. The solution was then left at room

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[2] Roser, *Annalen*, 1888, **247**, 136, footnote 1.

[3] Burgess, *J.*, 1927, 2017.

[4] Harries and Gollintz, *Annalen*, 1904, **330**, 185.

temperature, oil separating in 1—2 hr. Reaction was essentially complete in 48—72 hr., but occasionally the mixture was left as long as 120 hr. In many cases the oil solidified spontaneously or when shaken. In others it solidified when chilled with solid carbon dioxide. The products were isolated by filtration or sometimes by separation as oils followed by distillation.

TABLE 1.

Condensation products.

No.	Product	Yield of (%)	M. p.	B. p./mm.	Found (%)			Required (%)		
					C	H	N	C	H	N
	(*a*) R in $R\cdot CH{:}CH\cdot CO\cdot[CH_2]_2\cdot Ph$									
1	Ph	80	56° [a]							
2	p-$NMe_2\cdot C_6H_4$	34	90 [a]		81·6	8·1	4·7	81·7	7·5	5·0
3	2-Furyl	46	Oil	198°/7	79·4	6·55		79·7	6·2	
4	o-$MeO\cdot C_6H_4$	52	32°	258—278°/15	80·9	6·9		81·2	6·8	
5	p-$MeO\cdot C_6H_4$	80	89 [a]		81·2	7·0		,,	,,	
6	3,4-$CH_2O_2{:}C_6H_3$	73	128 [a]		76·8	5·8		77·1	5·7	
7	3,4-$(MeO)_2C_6H_3$	80	98	285—305°/16	76·6	6·7		77·0	6·8	
	(*b*) R in $R\cdot CH{:}CH\cdot CO\cdot[CH_2]_3\cdot Ph$									
8	Ph	64	50·5 [b]	244—266°/16						
9	p-$NMe_2\cdot C_6H_4$	31	91 [a]		82·1	7·5	5·1	81·9	7·85	4·8
10	2-Furyl	48	40	152—153°/0·2	79·7	6·7		80·0	6·7	
11	o-$MeO\cdot C_6H_4$	28	Oil	196°/0·25	81·3	7·1		81·4	7·1	
12	p-$MeO\cdot C_6H_4$	85	80° [a]		81·6	7·5		,,	,,	
13	3,4-$CH_2O_2{:}C_6H_3$	68	80 [a]		77·2	6·15		77·6	6·1	
14	3,4-$(MeO)_2C_6H_3$	61	105 [a]		77·1	7·4		77·4	7·1	

[a] From EtOH. Heilbron, Heslop, Irving, and Wilson, *J.*, 1931, 1340.

TABLE 2.

2,4-*Dinitrophenylhydrazones*

Ketone no.	M. p.	Found (%)			Formula	Required (%)		
		C	H	N		C	H	N
1	162°	65·9	4·6	13·75	$C_{23}H_{20}N_4O_4$	66·3	4·8	13·5
2	179 [a]	64·8	6·0	15·7	$C_{25}H_{25}N_5O_4$	65·3	5·4	15·3
3	195	62·1	4·7	14·2	$C_{21}H_{18}N_4O_5$	62·1	4·4	13·8
4	177	64·7	5·3	12·3	$C_{24}H_{22}N_4O_5$	64·6	4·9	12·6
5	114 [b] 170—171	64·7	5·3	12·7	,,	,,	,,	,,
6	204	62·8	4·9	12·5	$C_{24}H_{20}N_4O_6$	62·6	4·3	12·2
7	187	62·8	5·4	11·9	$C_{25}H_{24}N_4O_6$	63·0	5·1	11·8
8	183	67·3	4·8	13·7	$C_{24}H_{22}H_4O_4$	67·0	5·1	13·2
9	188—189 [a]	66·5	5·9	14·8	$C_{26}A_{27}N_5O_4$	66·0	5·7	14·8
10	186	62·9	4·8	13·2	$C_{22}H_{20}N_4O_5$	62·9	4·8	13·3
11	168 [c]	65·3	5·5	11·9	$C_{25}H_{24}N_4O_5$	65·2	5·2	12·2
	188	65·4	5·3	12·4	,,	,,	,,	,,
12	168—178 [d]	65·3	5·4	12·2	$C_{25}H_{24}N_4O_5$	,,	,,	,,
13	191—192 [e]	63·5	5·1	11·4	$C_{25}H_{22}N_4O_6$	63·3	4·6	11·8
14	172—184 [f]	63·7	5·75	11·8	$C_{26}H_{26}N_4O_6$	63·7	5·3	11·4
	172—184	64·0	5·1	11·4	,,	,,	,,	,,

Semicarbazones

Ketone no.	M. p.	Found (%)			Formula	Required (%)		
		C	H	N		C	H	N
2	179°	71·4	7·6	16·6	$C_{20}H_{24}N_4O$	71·4	7·1	16·7
4	188	70·85	6·6	13·4	$C_{19}H_{21}N_3O_2$	70·6	6·5	13·0
5	185	70·85	6·6	13·0	,,	,,	,,	,,
6	187	67·6	6·0	12·3	$C_{19}H_{19}N_3O_3$	67·65	5·6	12·5

[a] The precipitate formed when the reactants were mixed was deep orange-red, but when washed with alcohol it became purple-black. The latter form, on treatment with concentrated hydrochloric acid, re-formed the orange-red material; with sufficient alcoholic hydrochloric acid it passed into solution. Addition of 10% sodium hydroxide solution gave maroon-coloured material which was recrystallized from butyl alcohol. The free dinitrophenylhydrazones formed maroon-coloured needles, the orange-red hydrochlorides of which were readily alcoholized to the free bases. [b] Dimorphic; see text. [c] Isomer; see text. [d] ? Dimorphism; see text. [e] Highly piezoelectric. [f] Two forms; see text.

Very little organic material remained when the aqueous-alcoholic solution was evaporated, the yield of product being essentially that which could be filtered off or separated as oil. The *products* are recorded in Table 1.

The *dinitrophenylhydrazones* (Table 2) of the ketones described in Table 1 were prepared as described above; the *semicarbazones* of certain of the ketones were obtained by the usual methods although several hours' heating in alcohol was generally necessary. 1-p-*Dimethylaminophenyl*-5-*phenylpent*-1-*en*-3-*one methiodide* was prepared at room temperature (24 hr.); it crystallized from water as pale yellow leaflets, m. p. 190° (decomp.) (Found: N, 2·9. $C_{20}H_{24}INO$ requires N, 3·3%).

The dinitrophenylhydrazone of ketone no. 5 separated from ethyl acetate, on rapid cooling, as very fine orange-red needles, m. p. 114°, that changed in a few hr. to a deep red granular form, m. p. 170—171°; the latter recrystallized (as above) in the needle form.

The dinitrophenylhydrazone of ketone no. 14 crystallized from ethyl acetate in bright red, very fine needles and in a denser deep crimson form but these were formed side by side and after separation by hand crystallized from ethyl acetate without change of their distinctive forms.

The dinitrophenylhydrazone of ketone no. 12 similarly separated as a mixture of two forms (the higher- often before the lower-melting) that retained their individuality after separation by hand.

Hydrogenations.—The styryl ketones (50 g.) in ethanol (~1 l.) were stirred in hydrogen at 60°. Working on a larger scale was equally satisfactory. The products were isolated, usually in quantitative yield, by removal of the Raney nickel catalyst, evaporation, and distillation or (if crystalline) filtration, and most of them were recrystallized from alcohol. The new *products* are listed in Table 3.

The 2,4-*dinitrophenylhydrazones* (Table 4) of these ketones were usually deposited as oils

TABLE 3.

1-Aryl-5-phenylpentan-3-ones and 1-aryl-6-phenylhexan-3-ones.

No.	Aryl	M. p.	B. p./mm.	Found (%) C	Found (%) H	Formula	Required (%) C	Required (%) H
	(a) *Pentanones*							
1	Ph	10°	171°/1·4	—	—	—	—	—
2	p-$NMe_2{\cdot}C_6H_4$	76		81·4	8·4	$C_{19}H_{23}NO$	81·1	8·2
3	o-$MeO{\cdot}C_6H_4$	Oil	194°/2	80·4	7·7	$C_{18}H_{20}O_2$	80·6	7·5
4	p-$MeO{\cdot}C_6H_4$	32°	198°/11·4	80·65	7·8	,,	,,	,,
5	$3,4\text{-}CH_2O_2{:}C_6H_3$	45	208°/1·4	76·5	6·9	$C_{18}H_{18}O_3$	76·6	6·4
6	$3,4\text{-}(MeO)_2C_6H_3$	59	216°/1·4	75·8	7·4	$C_{19}H_{22}O_3$	76·4	7·4
	(b) *Hexanones*							
7	p-$MeO{\cdot}C_6H_4$	—	212°/1·7	80·5	7·9	$C_{19}H_{22}O_2$	80·85	7·8
8	$3,4\text{-}CH_2O_2{:}C_6H_3$	23—25·5	223°/2	76·7	7·0	$C_{19}H_{20}O_3$	77·0	6·75
9	$3,4\text{-}(MeO)_2C_6H_3$	55	227°/1·6	76·6	7·8	$C_{20}H_{24}O_3$	76·9	7·7

[a] Found: N, 4·9. Required: N, 5·0%.

TABLE 4.

Ketone no.	M. p.	Found (%) C	Found (%) H	Found (%) N	Formula	Required (%) C	Required (%) H	Required (%) N
	2,4-*Dinitrophenylhydrazones*							
1	117°	66·4	5·6	13·5	$C_{23}H_{22}N_4O_4$	66·0	5·3	13·4
2	165	65·3	6·0	15·6	$C_{25}H_{27}N_5O_4$	65·1	5·85	15·2
4	109	64·6	5·6	12·8	$C_{24}H_{24}N_4O_5$	64·3	5·35	12·5
5	97	61·9	4·7	12·4	$C_{24}H_{22}N_4O_6$	62·3	4·8	12·1
6	128	63·1	5·9	11·7	$C_{25}H_{26}N_4O_6$	62·8	5·5	11·7
8	104·5	62·9	5·0	11·9	$C_{25}H_{24}N_4O_6$	63·0	5·0	11·8
	Oximes							
1	92	—	—	—	—	—	—	—
2	71	77·4	8·6	9·2	$C_{19}H_{24}N_2O$	77·0	8·15	9·5
4	70—85	76·2	7·4	4·8	$C_{18}H_{21}NO_2$	76·3	7·4	4·95
5	62	73·0	6·7	4·3	$C_{18}H_{19}NO_3$	72·7	6·4	4·7
6	137	73·3	7·9	4·1	$C_{19}H_{23}NO_3$	72·8	7·4	4·5

when made by the general method but soon solidified. The oxime of 1,5-diphenylpentan-3-one had the same m. p. (92—93°) as that of the oxime of the ketone made by another route. 1-p-*Dimethylaminophenyl*-5-*phenylpentan*-3-*one methiodide*, when crystallized from water, melted partially at 115° (? solvate), then solidified and melted with decomposition at 179° (Found: C, 57·1; H, 6·2; N, 2·9. $C_{20}H_{26}INO$ requires C, 56·75; H, 6·2; N, 3·3%).

No precipitate resulted when the usual method was applied to ketone no. 2 to give the dinitrophenylhydrazone. The addition of alcoholic sodium hydroxide led to a gummy precipitate which gradually changed to an orange powder. This was crystallized from ethyl alcohol or acetate. The dinitrophenylhydrazone was so highly piezoelectric when dry that it was almost impossible to introduce it into a specimen tube.

The *oxime* of ketone no. 2 had mixed m. p. 58—67° with the ketone.

Despite repeated recrystallizations the oxime of ketone no. 4 gave a turbid liquid at 70° which only cleared at 85°. If suddenly chilled from a melt at above 85°, the solid melted sharply to a clear liquid at 62°; as the temperature was raised, some solid appeared to be present at 64° and only at 84° was the liquid quite clear again. The phenomena suggest transformation of a lower-melting, less stable into a higher-melting, more stable form.

Ethyl acetate and ethyl acetate–light petroleum were the best solvents for recrystallization of the dinitrophenylhydrazones.

5-*Bromo*-2-*methoxybenzaldehyde* 2,4-*dinitrophenylhydrazone* forms scarlet needles (from ethyl acetate), m. p. 271° (Found: C, 42·6; H, 2·95; N, 13·8. $C_{14}H_{11}BrN_4O_5$ requires C, 42·5; H, 2·8; N, 14·2%).

We thank Mrs. Jean Mamalis, Miss Pat Gunner, and Miss Alison Hagyard for the analyses

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[*Received, May* 11*th*, 1960.]