a water-bath for eight hours. The mixture was filtered free of insoluble material, and the desired ether collected and purified as described under Modification I.

Insecticidal Activity.—When tested under comparable conditions, none of the ethers described in this paper was superior to DDT as a mosquito larvicide. Two of the compounds, 3-chloroallyl *p*-chlorophenyl ether and the corresponding *p*-bromo-derivative, were approximately twice as active as DDT against the confused flour beetle. The 3-chloroallyl ethers with 2,4-dichlorophenol and *p*-benzylphenol; the *o*-chlorobenzyl ethers with *p*-chlorophenol and *p*-bromophenol and the benzyl ether with 1,2,3,4,5-pentachlorophenol were roughly equal to DDT in contact toxicity toward normal house flies.

The 3-chloroallyl ethers were more toxic toward insects than the isomeric 2-chloro compound, possibly due to a difference in their dehydrochlorination rates. The substitution of multiple chlorine atoms in the phenyl radical failed to enhance the activity of the resulting compounds except in the case of benzyl 1,2,3,4,5-pentachlorophenyl ether which was quite toxic toward houseflies. The substitution of a benzyl group for the 3-chloroallyl group in the corresponding *p*-halophenyl ethers failed to reduce their high activity. In some instances, the introduction of an *o*-chloro atom in the benzyl group yielded a more toxic molecule, notably against houseflies.

Two of the compounds, 3-chloroallyl 2,4-dichlorophenyl ether and *o*-chlorobenzyl 2,4-dichlorophenyl ether, when tested at the rate of 20 mg. of the ether and 200 mg. of DDT per sq. ft., gave considerably higher mortalities than did DDT alone against DDT-resistant flies.

Acknowledgments.—The authors are indebted to Dr. S. W. Simmons, Director, and to Dr. R. W. Fay of the Technical Development Services of the Communicable Disease Center, U. S. Public Health Service, for making available the laboratory facilities and procedures used to determine the insecticidal activity of the compounds reported here.

BATON ROUGE, LOUISIANA RECEIVED APRIL 4, 1951

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF IDAHO]

Condensation of Aldehydes with Ketones. Methylanilinomagnesium Bromide as a Condensing Agent

BY ARNOLD T. NIELSEN, CATHERINE GIBBONS[1] AND CORT A. ZIMMERMAN[1]

Ten new ketols have been prepared using the condensing agent methylanilinomagnesium bromide for the condensation of aldehydes with certain "unreactive" ketones which usually do not react using ordinary catalysts. With the present procedure the reaction was found to be limited to those ketones which do not readily self-condense in the presence of the condensing agent. Seven new diketones prepared from the ketols have been saponified and their course of cleavage studied.

In the presence of a basic catalyst such as sodium hydroxide many aldehydes have been condensed with methyl, cyclic and certain ethyl ketones to give good yields of condensation product.[2] On the other hand, some ketones are less reactive and give no reaction or very low yields of condensation product under the same conditions.[3] In such ketones the carbonyl group is generally attached to groups larger than ethyl. The present paper describes a method by which several aldehydes have been condensed with some of these "unreactive" ketones using methylanilinomagnesium bromide as the condensing agent.

Methylanilinomagnesium bromide has previously been employed in ketone–ketone condensations,[4,5,6,7] but apparently not in aldehyde–aldehyde or aldehyde–ketone condensations. In the ten examples listed in Table I nine different aldehydes and six different ketones were used. The ketols were isolated in yields of 15–88% (62–88% in seven cases). The general reaction procedure was first to add a small excess of the ketone to a freshly prepared ether–benzene solution of one mole of methylanilinomagnesium bromide and then add approximately two-thirds mole of pure aldehyde to the cold (–10°) solution.

In certain cases the condensation failed to give the desired ketol. In the attempted condensation of *n*-butyraldehyde with acetone, 3-pentanone[8] and acetophenone[8] and of propionaldehyde with 3-heptanone the ketone condensed with itself before reacting with the aldehyde. The ketols formed by the self-condensation of 3-pentanone and 3-heptanone were isolated and identified. Acetophenone was recovered, but not its ketol which decomposes on distillation.[9] Reaction of benzaldehyde with propiophenone probably gave a ketol, but attempts to distil it resulted in its decomposition into aldehyde and ketone. Attempted condensations of benzophenone with propionaldehyde and of fluorenone with isovaleraldehyde gave no aldol. The procedure was similar to Colonge's[5] by which he prepared mixed ketols when condensing benzophenone and fluorenone with various other ketones. Unreacted ketone was recovered in our experiments and the aldehyde was consumed by a side reaction to form an amine.

In most cases the unreacted aldehyde was not recovered, but removed by a side reaction involving the formation of a tertiary amine. The structure of the amine by-product was proved in two cases and it is likely that the same type of compound was formed in other instances. This side reaction occurred to the greatest extent in those cases where the least amount of aldehyde–ketone condensation

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(1) Research Corporation Fellow, 1949–1950.

(2) For a literature survey see A. T. Nielsen, Thesis, University of Washington, Seattle, 1947.

(3) *Cf.* S. G. Powell and A. T. Nielsen, THIS JOURNAL, **70**, 3627 (1948).

(4) J. Colonge, *Bull. soc. chim. France*, [5] **1**, 1101 (1934).

(5) J. Colonge, *ibid.*, [5] **5**, 90 (1938).

(6) V. V. Chelintsev and A. V. Pamaraya, *J. Gen. Chem.* (*U.S.S.R.*), **11**, 461 (1941); *C. A.*, **35**, 657 (1941).

(7) V. I. Aksenova, Uchenye Zapiski Saratov, Gosudarst, Univ. N. G. Chernyshevskogo, Sbornik, Nauch. Rabot Studentov, No. 2, 92–100 (1939); *C. A.*, **35**, 6238 (1941).

(8) Ethylanilinomagnesium bromide was used as the condensing agent.

(9) J. Colonge, *Compt. rend.*, **190**, 1414 (1933).

TABLE I

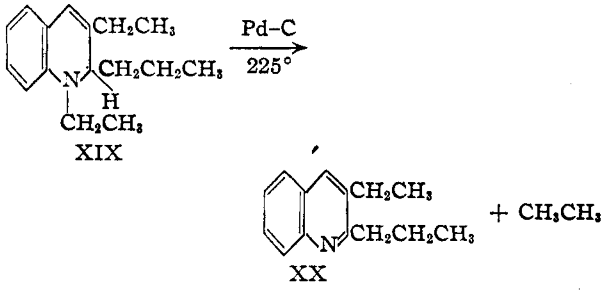
CONDENSATION OF ALDEHYDES WITH KETONES TO FORM KETOLS

$$R_1CHO + \underset{R_4}{\overset{R_3}{H\text{C}}}COR_2 \xrightarrow{C_6H_5N(CH_3)MgBr} R_1CHOH\underset{R_4}{\overset{R_3}{\text{C}}}COR_2$$

Aldehyde	Ketone	Ketol[a]	Yield,[b] %	B.p., °C.	Mm.[c]	$n^{25}D$[c]	Analyses, % Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found
n-C_3H_7CHO	$(iso\text{-}C_3H_7)_2CO$	I	81	79–80	0.22	1.4445	70.92	70.79	11.90	12.04
n-$C_4H_9CH(C_2H_5)CHO$	$(iso\text{-}C_3H_7)_2CO$	II	67	100–102	0.50	1.4520	74.32	74.49	12.48	12.54
$C_6H_5CH_2CHO$	$(iso\text{-}C_3H_7)_2CO$	III	62	112–114	0.25	1.5065	76.88	77.25	9.46	9.59
C_6H_5CHO	$(iso\text{-}C_3H_7)_2CO$	IV	80	M. 77–79		...	76.32	76.64	9.15	9.22
CH_3CHO	$(iso\text{-}C_4H_9)_2CO$	V	73	82–85	0.20	1.4433	70.92	70.74	11.90	11.92
n-$C_6H_{13}CHO$	$(iso\text{-}C_4H_9)_2CO$	VI	88	112–117	0.40[e]	1.4487	74.94	74.48	12.58	12.51
C_2H_5CHO	$(n\text{-}C_5H_{11})_2CO$	VII	15[d]	104–105	0.25	1.4518	73.63	74.01	12.36	12.34
iso-C_3H_7CHO	$C_6H_5COC_2H_5$	VIII	88	94–95	0.20	1.5210	75.69	75.84	8.79	8.91
n-$C_5H_{11}CHO$	$C_6H_5COC_3H_7$	IX	40	136–137	0.33	1.5110	77.37	77.90	9.74	9.79
CH_3CHO	$C_6H_5COC_4H_9$	X	50	103–105	0.30	1.5227	75.69	75.42	8.79	8.90
C_6H_5CHO	$C_6H_5COC_2H_5$	(ketol decomposes on distillation)								

[a] Names and empirical formulas of the new ketols are as follows: I, 5-hydroxy-2,4,4-trimethyl-3-octanone $C_{11}H_{22}O_2$; II, 6-ethyl-5-hydroxy-2,4,4-trimethyl-3-decanone, $C_{15}H_{30}O_2$; III, 5-hydroxy-6-phenyl-2,4,4-trimethyl-3-hexanone, $C_{15}H_{22}O_2$; IV, 1-hydroxy-1-phenyl-2,2,4-trimethyl-3-pentanone, $C_{14}H_{20}O_2$; V, 2-hydroxy-3-isopropyl-6-methyl-4-heptanone, $C_{11}H_{22}O_2$; VI, 6-hydroxy-5-isopropyl-2-methyl-4-dodecanone, $C_{16}H_{32}O_2$; VII, 4-butyl-3-hydroxy-5-decanone, $C_{14}H_{28}O_2$; VIII, 3-hydroxy-2,4-dimethyl-1-phenyl-1-pentanone, $C_{13}H_{18}O_2$; IX, 2-ethyl-3-hydroxy-1-phenyl-1-octanone, $C_{16}H_{24}O_2$; X, 2-propyl-3-hydroxy-1-phenyl-1-butanone, $C_{13}H_{18}O_2$. [b] These yields are calculated from the amount of aldehyde used and represent samples distilled at least once (85–95% pure). [c] Boiling point ranges and refractive indexes are reported for pure samples used for analysis and generally obtained after one redistillation. [d] The yield based on unrecovered 6-undecanone was 75%. [e] M.p. 9.5–10°.

was observed. A tertiary amine, $C_{16}H_{23}N$, was isolated from the attempted condensation of n-butyraldehyde with 3-pentanone[8] and acetophenone[8] by extracting it from the ether–benzene solution of the crude reaction products with 6 N hydrochloric acid. It had no active hydrogens, absorbed one mole of hydrogen easily, and on aromatization by heating with palladium on charcoal formed 3-ethyl-2-propylquinoline (XX) and a gas believed to be ethane. The compound is thought to be 1,3-diethyl-2-propyl-1,2-dihydroquinoline (XIX).[10]



XIX

XX

The location of the double bond in XIX was not definitely established but is probably in the 3,4-position because of the large molecular exaltation (2.5 units) of XIX and the ease of hydrogenation and aromatization.[11] Compound XX, which is known[12,13] was identified by comparison of its picrate derivative with an authentic sample.

Our experiments indicate that the use of methylanilinomagnesium bromide for the condensation of aldehydes with ketones to form ketols is probably limited to those ketones which do not readily self-condense in its presence.[14] More reactive ketones such as acetone and acetophenone cannot be used with the present procedure. At present, our data suggest no general relationship between the structure of the aldehyde and the yield of ketol and there appears to be no important limitation regarding the type of aldehyde which may be employed.

Eight of the ketols listed in Table I were oxidized to the corresponding diketones; the results are summarized in Table II. Diketone XV is known and its mono-2,4-dinitrophenylhydrazone derivative was found to be identical with an authentic sample. The other diketones were identified by cleavage with boiling concentrated sodium hydroxide solution to acids and ketones which were isolated and identified (Table III). For example, the saponification of 5-isopropyl-2-methyl-4,6-dodecanedione (XVI) gave 2-methyl-4-decanone, 18% yield, diisobutyl ketone, 66%, isovaleric acid, 22%, and heptanoic acid, 54%. In this case it is estimated that 70–80% of the cleavage occurred at the heptanoyl group. The yields of cleavage products were somewhat poorer in most of the other cases and consequently only qualitative conclusions can be made regarding the course of cleavage. In the case of the aliphatic diketones the smaller, less branched groups appear to be attacked more easily.

Ketols VIII and X were dehydrated by heating with iodine to form their corresponding α,β-unsaturated ketones XXI and XXII, respectively; the latter compounds were then hydrogenated to the corresponding saturated ketones XXIII and XXIV which were identified by comparison of their 2,4-dinitrophenylhydrazones with authentic samples. Compound XXIII was synthesized from 4-methyl-2-pentylmagnesium bromide and benzonitrile (7.8% yield); XXIV was synthesized from benzene and 2-ethylpentanoyl chloride by the Friedel–Crafts reaction (61% yield).

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(10) An amine having properties similar to XIX was isolated in an attempted condensation of n-butyraldehyde with 2-ethyl-2-hexenal using methylanilinomagnesium bromide as condensing agent.

(11) Compound XIX is very likely formed from ethylaniline and two moles of n-butyraldehyde. Although there are several plausible mechanisms for the reaction which suggest themselves, none appear to be adequately supported by the available data.

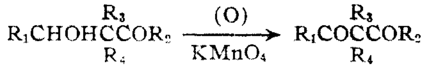
(12) M. S. Kharasch, I. Richlin and F. R. Mayo, THIS JOURNAL, 62, 494 (1940).

(13) M. Kohn, *Ber.*, 18, 3361 (1885).

(14) A study of the use of methylanilinomagnesium bromide and similar condensing agents for the self-condensation of several different ketones has been made by Colonge (ref. 4).

TABLE II

OXIDATION OF KETOLS TO 1,3-DIKETONES

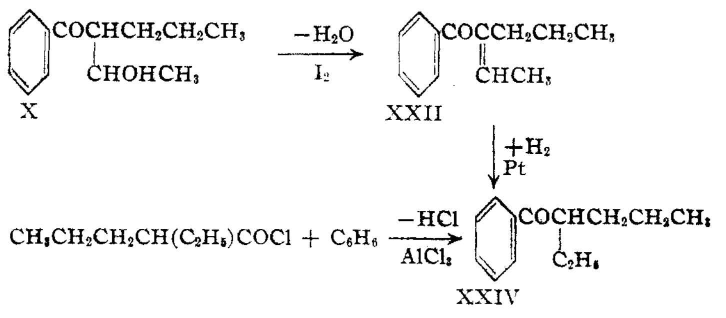


$$R_1CHOH\overset{R_3}{\underset{R_4}{C}}COR_2 \xrightarrow[KMnO_4]{(O)} R_1CO\overset{R_3}{\underset{R_4}{C}}COR_2$$

Ketol[a]	Diketone[b]	Yield,[c] %	B.p.,[d] °C.	Mm.	n^{25}D[d]	Analyses, % Carbon Calcd.	 Found	 Hydrogen Calcd.	 Found
I	XI	41	103–105	15	1.4361	71.69	71.26	10.94	11.22
II	XII	45	84–85	0.3	1.4484	74.95	74.83	11.74	12.23
III	XIII	56	121–125	0.65	1.5049	77.55	77.37	8.68	8.83
IV	XIV	52[e]	100–101	0.7	1.5124	77.03	77.16	8.31	8.61
V	XV[f]	67	111–114	20	1.4329	71.69	71.97	10.94	11.16
VI	XVI	75	122–124	1.6	1.4415	75.53	75.38	11.89	12.03
VII	XVII	(42)[g]	(96–101)[g]	0.3	(1.4453)[g]	74.28	73.07	11.58	11.85
IX	XVIII	(30)[h]	(125–128)[h]	0.45	(1.5074)[h]	78.01	76.52	9.00	8.94

[a] See Table I. [b] Names and empirical formulas of the diketones are as follows: XI, 2,2,4-trimethyl-3,5-octanedione-$C_{11}H_{20}O_2$; XII, 6-ethyl-2,4,4-trimethyl-3,5-decanedione, $C_{15}H_{28}O_2$; XIII, 1-phenyl-3,3,5-trimethyl-2,4-hexanedione, $C_{15}H_{20}O_2$; XIV, 1-phenyl-2,2,4-trimethyl-1,3-pentanedione, $C_{14}H_{18}O_2$; XV, 3-isopropyl-6-methyl-2,4-heptanedione, $C_{11}H_{20}O_2$; XVI, 5-isopropyl-2-methyl-4,6-dodecanedione, $C_{16}H_{30}O_2$; XVII, 4-butyl-3,5-decanedione, $C_{14}H_{26}O_2$; XVIII, 2-ethyl-1-phenyl-1,3-octanedione, $C_{16}H_{22}O_2$. [c] These yields represent redistilled samples having narrow boiling point ranges close to those listed. [d] Boiling point ranges and refractive indexes are for carefully purified samples used for analysis. [e] In this case it was possible to separate the unreacted solid ketol from the liquid by crystallization of the former from a petroleum ether solution of the reaction mixture (31% recovery, m.p. 75–78°). The yield of diketone based on unrecovered ketol was 76%. [f] This diketone gave a positive iodoform test. J. T. Adams and C. R. Hauser (THIS JOURNAL, **67**, 284 (1945)) report b.p. 113–115° (20 mm.). The mono-dinitrophenylhydrazones of XV and of an authentic sample generously provided by Dr. Hauser (n^{25}D 1.4345) melted at 121–121.5° alone and when mixed. *Anal.* Calcd. for $C_{17}H_{24}N_4O_5$: C, 56.03; H, 6.64. Found: C, 56.10; H, 6.9. [g] This sample, containing some impurity and available in very small amounts, was not purified further. [h] This sample contained an impurity which could not be removed by distillation (see Experimental part).

Attempts to dehydrate ketols I and V resulted in their decomposition into the original aldehyde and ketone from which they were prepared. Since these ketols have no hydrogen atom between the hydroxyl and carbonyl groups they would be expected to dehydrate less readily.



Acknowledgment.—The authors sincerely appreciate a Frederick Gardner Cottrell Grant from the Research Corporation which aided this work.

Experimental[15]

Preparation of Methylanilinomagnesium Bromide Solution.[7]—To 75 ml. of an ether solution of ethylmagnesium bromide (prepared from 40 g. (0.364 mole) of ethyl bromide and 8.0 g. (0.33 mole) of magnesium turnings) was added with cooling and stirring a solution of 32.6 g. (0.305 mole) of freshly distilled dry methylaniline in 100 ml. of dry benzene (nitrogen atmosphere maintained throughout).

Condensation of *n*-Butyraldehyde with Diisopropyl Ketone. Preparation of 5-Hydroxy-2,4,4-trimethyl-3-octanone (I).—A detailed study was made of this condensation to determine optimum reaction conditions. The best procedure finally developed after numerous runs was the following. To the above freshly prepared solution of methylanilinomagnesium bromide was added, during 10 to 15 minutes, a solution of 40 g. (0.35 mole) of dry diisopropyl ketone (b.p. 116–118° (690 mm.)) in 50 ml. of dry benzene while keeping the temperature at *ca.* 15°. After adding the ketone, the solution was allowed to stand for 30 minutes. A solution of 17 g. (0.235 mole) of freshly distilled *n*-butyraldehyde (b.p. 71–72° (690 mm.)) in 25 ml. of dry benzene was added during 30 minutes keeping the temperature at −13 to −10°. After adding the aldehyde, the solution was allowed to stand for one hour at −10° to −5°. Three hundred ml. of 3 *N* hydrochloric acid was added and the organic layer separated, washed five times with 6 *N* hydrochloric acid[16] and finally with water. After drying with anhydrous sodium sulfate and Drierite, the ether, benzene, and some of the unreacted ketone were removed by distillation at 15–30 mm. from a hot water-bath (60–70°). The residue remaining was distilled through a 25-cm. spiral packed column. After removing 5.4 g. of unreacted ketone there was obtained 25.6 g. (81.5% yield based on aldehyde) of the ketol I, b.p. 86–87° (0.7 mm.), 79–80° (0.22 mm.), 117–118° (17 mm.); for analytical data see Table I. The ketol gave a positive Fehling, Schiff and Tollens test, probably due to decomposition into butyraldehyde during the tests.

Nine other condensations were accomplished using various aldehydes and ketones, and reaction conditions similar to those described above (see Table I). In the condensation of benzaldehyde with diisopropyl ketone the crude ketol crystallized after removing the ether and benzene and most of the unreacted ketone. After recrystallization from petroleum ether there was obtained from the first and second crops an 80% yield of ketol, m.p. 76–79°; recrystallization gave white prisms, m.p. 77–79°.

Attempted Condensation of Propionaldehyde with 3-Heptanone.—Reaction of propionaldehyde, 3-heptanone and methylanilinomagnesium bromide (0.5-mole quantities of each) using conditions similar to those outlined above gave 12% of recovered ketone and 65% yield of the ketol derived from self-condensation of the ketone, b.p. 110–111° (1.6 mm.), n^{23}D 1.4479, d^{23}_4 0.8983. *Anal.* Calcd. for $C_{14}H_{28}O_2$: C, 73.64; H, 12.36; *M*D 68.39. Found: C, 73.25; H, 12.23; *M*D 68.04. A sample of this ketol was also obtained by self-condensing 3-heptanone alone using methylanilinomagnesium bromide[17]; b.p. 109–111° (1.6 mm.), n^{23}D 1.4474; d^{23}_4 0.8988. *Anal.* Found: C, 73.29; H, 12.44; *M*D 67.89.

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(15) All melting points are corrected; boiling points are uncorrected.

(16) The crude reaction product was extracted with 6 *N* hydrochloric acid to remove amine impurities formed in a side reaction. These impurities amounted to 3–8 g. in most runs of this size in this, and other condensations.

(17) A detailed study of this condensation is now in progress.

5-Ethyl-5-hydroxy-4-methyl-3-heptanone.—This ketol, formed by self-condensation of 3-pentanone, was isolated as a by-product from an attempted *n*-butyraldehyde and 3-pentanone condensation. Ethylanilinomagnesium bromide (1 mole), 3-pentanone, 86 g. (1 mole), and *n*-butyraldehyde, 216.3 g. (3 moles) reacted by a procedure similar to that above; the solution was allowed to stand 22 hours at room temperature after addition of the aldehyde. Subsequent isolation of the neutral material in the usual manner gave 42 g. of crude 5-ethyl-5-hydroxy-4-methyl-3-heptanone, b.p. 103–112° (13 mm.), n^{25}_{D} 1.4430, an unidentified fraction, 29 g., b.p. 78–98° (0.15 mm.), n^{25}_{D} 1.4496, and an undistillable residue, 14.0 g. Redistillation of the ketol gave 35 g. (41% yield), b.p. 105–107° (15.5 mm.), $n^{20.5}_{\mathrm{D}}$ 1.4440 (lit. b.p. 105° (14 mm.)[18]; $n^{20.5}_{\mathrm{D}}$ 1.4435).[4]

Dehydration of 22.5 g. of the above ketol by heating with iodine (0.2 g.) under nitrogen followed by distillation gave 1 ml. of water, a fraction, 3.2 g., b.p. 85–108° (690 mm.), n^{25}_{D} 1.3938. containing mainly 3-pentanone and 12.8 g. of an unsaturated ketone, b.p. 175–185° (690 mm.). Redistillation of the latter gave 9.5 g., b.p. 80–84° (17 mm.), n^{25}_{D} 1.4460, n^{19}_{D} 1.4480.[19] A semicarbazone prepared from it melted at 105–106° after several recrystallizations from dilute ethanol. *Anal.* Calcd. for $C_{11}H_{21}N_3O$: C, 62.52; H, 10.02. Found: C, 62.29; H, 10.2.

An authentic sample of the above ketol prepared by Colonge's procedure[4] was dehydrated with iodine in the same manner as described above. An unsaturated ketone was obtained, b.p. 178–183° (690 mm.), n^{25}_{D} 1.4440, n^{20}_{D} 1.4465.[19] The semicarbazone melted at 105–106° alone and when mixed with the sample obtained above.

1,3-Diethyl-2-propyl-1,2-dihydroquinoline (XIX).—The 6 *N* hydrochloric acid extracts remaining from the above-mentioned attempted *n*-butyraldehyde and 3-pentanone condensation were combined, made alkaline with concentrated ammonia, and the oily basic material separated in the usual manner. Distillation under nitrogen gave 3 ml. of forerun, b.p. 71–100° (0.25 mm.), 13.8 g. of undistillable residue and 117.3 g. of crude amine, b.p. 100–110° (0.25 mm.), n^{25}_{D} 1.5637; redistillation gave 93 g. (40.6% yield based on ethylaniline), b.p. 96–97° (0.2–0.25 mm.), n^{25}_{D} 1.5640, d^{25}_4 0.9593.

Anal. Calcd. for $C_{16}H_{23}N$: C, 83.78; H, 10.11; N, 6.11; M_{D}, 75.28. Found: C, 83.70; H, 10.2; N, 6.0; M_{D}, 77.75.

The picrate separated in long orange needles when recrystallized from 95% ethanol, m.p. 111–115° with decomposition.

Anal. Calcd. for $C_{22}H_{26}N_4O_7$: C, 57.63; H, 5.72. Found: C, 58.03; H, 5.7.

An attempt to condense *n*-butyraldehyde with acetophenone (0.45 mole of each) using ethylanilinomagnesium bromide (0.5 mole) gave recovered acetophenone, 30.4 g. (56% recovery), b.p. 83–91° (14 mm.), 19.6 g. of undistillable residue and 10 g. (20% yield) of the amine XIX, b.p. 100–110° (0.25 mm.), n^{25}_{D} 1.5640. This sample of amine showed 0.035 active hydrogen in a Zerewitinoff determination and 0.1 mole-equivalent additional methylmagnesium iodide reacted. On quantitative hydrogenation at 684 mm. and 23° (95% ethanol solvent, platinum oxide catalyst) a 0.1537-g. sample absorbed 14.4 ml. (S.T.P.) of hydrogen (0.96 mole-equivalent) during 160 minutes, after which time absorption essentially ceased. The molecular weight found (b.p. elevation in benzene) was 220 and 218 in two determinations (calcd. for $C_{16}H_{23}N$, 229). The picrate melted at 111–115° with decomposition, alone and when mixed with the picrate derivative obtained above.

3-Ethyl-2-propylquinoline (XX).—A 19.5-g. (0.085 mole) sample of the above purified amine (XIX) was aromatized by heating at 210–228° with 4.0 g. of palladium-on-charcoal (5%) for two hours, after which time gas evolution almost ceased. The evolving gas was passed through a wet test meter and 1.01 l. (S.T.P.) (0.0451 mole) was obtained (53% yield). The loss in weight which occurred during the heating was 1.49 g. (58% of the theoretical amount assuming the gas to be ethane). After filtering the catalyst, the crude product was distilled giving 3.3 g. of forerun, b.p. 101–130° (0.35 mm.), 11.2 g. of crude amine XX and 1.9 g. of residue. On redistillation, the amine, which darkens rapidly on standing, gave n^{25}_{D} 1.5652, b.p. 178–181° (23 mm.) (lit.[23] b.p. 182–184° (23 mm.)). A 5.8-g. sample of this crude amine was purified by conversion into a picrate (yield 6.8 g., m.p. 166–168°) and 7.4 g. of this picrate decomposed by steam distillation from a dilute sodium hydroxide solution (nitrogen atmosphere). Isolation of the amine from the distillate, followed by distillation, gave 2.5 g. (63% yield from picrate) of colorless product, b.p. 101–108° (0.2 mm.), n^{25}_{D} 1.5774.[23]

Anal. Calcd. for $C_{14}H_{17}N$: C, 84.37; H, 8.60. Found: C, 84.19; H, 8.62.

The picrate melted at 167–168° (161–162° uncor.). When mixed with an authentic sample of the amine picrate,[12] m.p. 167–168°, the m.p. was not depressed (lit. m.p. 161–163° uncor.[12] and 163[13]).

Anal. Calcd. for $C_{20}H_{20}N_4O_7$: C, 56.07; H, 4.70. Found: C, 55.43, 55.51; H, 4.71, 4.65.

Oxidation of Ketols to 1,3-Diketones.—Eight of the ketols listed in Table I were oxidized to the corresponding 1,3-diketones and the results of these experiments are summarized in Table II. A typical oxidation procedure is the following. To 57 g. (0.243 mole) of 5-hydroxy-6-phenyl-2,4,4-trimethyl-3-hexanone (III), suspended in 250 ml. of 4 *N* sulfuric acid, was added 38 g. (0.24 mole) of potassium permanganate, slowly, with stirring, keeping the temperature below 25°. After adding the permanganate the mixture was stirred for two hours and then sufficient sodium bisulfite was added to remove the manganese dioxide. After extracting with ether, the ether extracts were washed twice with *N* sodium hydroxide solution, water, and then dried. Distillation gave 1.7 g. of forerun, b.p. 85–119° (0.7 mm.), 42 g. of crude 1-phenyl-3,3,5-trimethyl-2,4-hexanedione (XIII), b.p. 119–126°, 95%, b.p. 121–125° (0.7 mm.), n^{25}_{D} 1.5056, a tailrun, 3.0 g., b.p. 125–126° (0.65 mm.), n^{25}_{D} 1.5073, possibly containing some unoxidized ketol, and 1.8 g. of residue. The crude diketone and the tailrun (44.6 g. total) were combined and oxidized again by the same procedure using 30 g. of potassium permanganate. Isolating the oxidation product as previously gave 31.7 g. (54% yield) of diketone, b.p. 104–109° (0.25 mm.), n^{25}_{D} 1.5049 (analysis in Table II).

The above procedure involving a repetition of the oxidation gave a more homogeneous product whereas one oxidation generally did not completely oxidize all of the ketol. The unreacted ketol could not be separated efficiently by distillation since the corresponding ketol and diketone often have very close boiling points (compare Tables I and II). This repetition of oxidation was done in the oxidation of ketols III, V, VI and IX. In the other cases the crude diketones were redistilled once or twice through a 25-cm. spiral packed column before analyzing. These latter samples were generally contaminated with a small amount of unoxidized ketol, whereas those obtained by the double oxidation procedure were usually purer and secured in higher yields. However, this was not true in the oxidation of ketol IX; the diketone obtained was impure and benzoic acid (20%) and *n*-caproic acid (8%) were isolated and identified as products of further oxidation.

Saponification of 1,3-Diketones.—In order to establish the structure of the diketones listed in Table II they were hydrolyzed (all except XV) by refluxing with concentrated

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(18) V. Grignard and M. Fluchaire, *Ann. chim.*, [10] **9**, 5 (1928).

(19) The unsaturated ketone obtained here probably contains mainly the β,γ-isomer, 5-ethyl-4-methyl-5-heptene-3-one. G. A. R. Kon and E. Leton (*J. Chem. Soc.*, 2496 (1931)) prepared an authentic sample of this ketone by an alternate synthesis and found b.p. 83–88° (18 mm.), n^{20}_{D} 1.4452, and semicarbazone m. p. 109°. These workers also prepared the corresponding α,β-unsaturated ketone 5-ethyl-4-methyl-4-heptene-3-one and reported b.p. 80° (10 mm.), n^{19}_{D} 1.4545, semicarbazone m.p. 153°. The self condensation of 3-pentanone to form an unsaturated ketone has been reported by other workers (refs. 18, 20, 21 and 22). The m. p. of the semicarbazone derivative has been reported as 108–109° (ref. 21 and 22) and 159° (ref. 22).

(20) J. B. Ekeley and M. S. Carpenter, THIS JOURNAL, **46**, 446 (1924); K. I. Karasew, *J. Gen. Chem.* (*U.S.S.R.*), **7**, 179 (1937) (*C.A.* **31**, 4268 (1937)); W. Wayne and H. Adkins, THIS JOURNAL, **62**, 3401 (1940).

(21) J. Colonge and K. Mostafavi, *Bull. soc. chim. France*, [5] **5**, 1478 (1938).

(22) J. Colonge and D. Joly, *Ann. chim.*, [11] **18**, 286 (1943).

(23) An authentic sample of 3-ethyl-2-propylquinoline prepared for identification purposes according to the procedure of Kharasch, Richlin and Mayo (ref. 12) had b. p. 103–108° (0.2 mm.), n^{25}_{D} 1.5670.

TABLE III

SAPONIFICATION OF 1,3-DIKETONES

Diketone[a]	Moles of sample	NaOH concn., *N*	Reflux time, hr.	Acids produced	Yield,[b] %	Ketones produced	Yield,[c] %	Recovered diketone[d] est. %
XI	0.118	6	15	*n*-Butyric	28	Diisopropyl ketone[e]	34	32
XII	.082	14	48	Isobutyric	25	4-Ethyl-2-methyl-3-octanone[f]	36	16
				2-Ethylhexanoic	6	Diisopropyl ketone	Trace	
XIII	.137	16	9	Phenylacetic	43	Diisopropyl ketone[e]	46	25
				Isobutyric	9	Benzyl isopropyl ketone[g]	6	
XIV	.086	6	15	Benzoic	59	Diisopropyl ketone[e,h]	27	31
XVI	.093	10	17.5	*n*-Heptanoic	54	Diisobutyl ketone[e]	66	3
				Isovaleric	22	2-Methyl-4-decanone[i]	18	
XVII	.0080	6	23	Propionic	Trace	6-Undecanone[j]	54	11
XVIII	.023	11	12.5	Benzoic	68	4-Nonanone[k]	40	26

[a] See Table II for formulas. [b] The acids were identified in the case of the liquids by boiling points, refractive indices, neutral equivalents and the known *p*-phenylphenacyl ester derivatives which were compared with authentic samples (mixed m.p.). The solid acids were identified by m.p., neutral equivalent and by comparison with authentic samples. [c] The ketones were identified in most cases by boiling points, refractive indices and suitable solid derivatives which were compared with authentic samples (mixed m.p.). [d] After distilling the ketones a small neutral residue remained which is believed to be mainly unreacted diketone. In the cases of XIII and XIV the residue was distilled and found to be the diketone; in the other cases the residue was usually too small to be distilled. The estimates given here are calculated by assuming the neutral residue to be entirely unreacted diketone. [e] Identified by the known 2,4-dinitrophenylhydrazone derivative. [f] Numerous attempts to prepare a derivative of this ketone failed. [g] Semicarbazone, m.p. 138–139°. [h] Some of this ketone accidentally lost by volatilization. [i] Identified by the oxalomonophenyldihydrazone derivative (see text). [j] The oxalomonophenyldihydrazone derivative, m.p. 150.5–152.5°, showed no depression in m.p. when mixed with an authentic sample, m.p. 154–154.5°. *Anal.* Calcd. for $C_{19}H_{30}N_4O_2$: C, 65.86; H, 8.73. Found: C, 66.30; H, 9.0. [k] The oxalomonophenyldihydrazone, m.p. 127.5–131.5°, showed no depression in m.p. when mixed with an authentic sample, m.p. 131–131.5°. *Anal.* Calcd. for $C_{17}H_{26}N_4O_2$: C, 64.11; H, 8.23. Found: C, 64.45; H, 8.3.

sodium hydroxide solution for several hours; the acids and ketones produced were then isolated and identified by suitable derivatives. The results of these saponification experiments are summarized in Table III. The following example illustrates the general procedure.

A 23.6-g. (0.093 mole) sample of diketone XVI was refluxed with 100 ml. of 10 *N* sodium hydroxide solution for 17.5 hours. The cooled solution was extracted several times with ether and the combined extracts dried. From the extract was isolated 8.7 g. (66%) of diisobutyl ketone, b.p. 58–68° (15 mm.), n^{25}D 1.4112; the 2,4-dinitrophenylhydrazone, m.p. 92–93.5°, showed no depression in m.p. when mixed with an authentic sample. Also obtained were 1.0 g. of residue and 2.9 g. (18%) of 2-methyl-4-decanone, b.p. 96–101° (14 mm.), n^{25}D 1.4233 (authentic sample, b.p. 105–106° (19 mm.), n^{25}D 1.4238; see preparation below); the oxalomonophenyldihydrazone,[24] m.p. 134.5–136.5°, showed no depression in m.p. when mixed with an authentic sample, m.p. 134.5–136.5°.

The alkaline aqueous layer remaining after extracting with ether was acidified with 6 *N* hydrochloric acid and extracted four times with 100-ml. portions of ether. The combined extracts were dried, concentrated, and the residue distilled. One acid isolated was isovaleric, 2.1 g. (22%), b.p. 91–108° (16 mm.), n^{25}D 1.4055, neut. equiv. 107 (calcd. 102); the *p*-phenylphenacyl ester, m.p. 75–77°, showed no depression in m.p. when mixed with an authentic sample. Also obtained were 0.4 g. of residue and *n*-heptanoic acid, 6.5 g. (54%), b.p. 113–121° (15 mm.), n^{25}D 1.4197, neut. equiv. 131 (calcd. 130); the *p*-phenylphenacyl ester, m.p. 61.5–63.5°, showed no depression in m.p. when mixed with an authentic sample.

4-Ethyl-2-methyl-3-octanol.—This alcohol was prepared by the Grignard reaction in the usual manner from 8.5 g. (0.35 gram atom) of magnesium turnings, 41 g. (0.33 mole) of isopropyl bromide and 38 g. (0.296 mole) of freshly distilled 2-ethylhexanal, b.p. 156–158° (690 mm.). After working up the reaction mixture and distilling the product there was obtained 32.8 g. of crude alcohol, b.p. 90–105° (14–15° mm.); redistillation gave 14.1 g., b.p. 93–99° (14.5 mm.), n^{25}D 1.4367, and 12.5 g., b.p. 99–100.5° (14.5 mm.), n^{25}D 1.4387 (this sample analyzed).

Anal. Calcd. for $C_{11}H_{24}O$: C, 76.67; H, 14.04. Found: C, 76.51; H, 14.29.

4-Ethyl-2-methyl-3-octanone.—The 4-ethyl-2-methyl-3-octanol prepared above, 23.4 g. (0.138 mole), was suspended in 140 ml. of 4 *N* sulfuric acid and treated with 22 g. of potassium permanganate while stirring and keeping the temperature below 25°. After adding the permanganate and stirrring for one and one-third hours, the mixture was treated with sufficient sodium bisulfite to remove the manganese dioxide; the organic material was then extracted with ether. Distillation of the oxidation product gave 13.8 g. (57%) of ketone, b.p. 85–90° (14 mm.); redistillation gave 9.0 g., b.p. 86–88° (14 mm.), n^{25}D 1.4250, of the pure, colorless ketone having a sweet, fruity odor.

Anal. Calcd. for $C_{11}H_{22}O$: C, 77.58; H, 13.02. Found: C, 77.84; H, 13.25.

Many unsuccessful attempts were made to prepare a derivative of this ketone using various carbonyl reagents; generally, only recovered ketone and reagent were obtained.

2-Methyl-4-decanone.—Using the above procedure, 22.8 g. (0.132 mole) of 2-methyl-4-decanol[25] was oxidized to yield 16.6 g. (73%) of the purified ketone, b.p. 104–108° (19 mm.), n^{25}D 1.4236.

Anal. Calcd. for $C_{11}H_{22}O$: C, 77.58; H, 13.02. Found: C, 77.38; H, 13.12.

The oxalomonophenyldihydrazone[24] was prepared by refluxing 0.6 g. of the ketone and 0.5 g. of oxalomonophenyldihydrazide for two hours in 25 ml. of ethanol containing 3 ml. of acetic acid. The clear solution was cooled and diluted with water; the derivative was filtered and recrystallized from benzene, m.p. 134.5–136.5°.

Anal. Calcd. for $C_{19}H_{30}N_4O_2$: C, 65.86; H, 8.73. Found: C, 66.31; H, 8.7.

3-Methyl-1-phenyl-2-butanone (Benzyl Isopropyl Ketone).—To a solution of benzylmagnesium chloride in 50 ml. of ether (prepared from 9 g. (0.37 gram atom) of magnesium turnings and 45.8 g. (0.364 mole) of freshly distilled benzyl chloride) was added 11.6 g. (0.168 mole) of isobutyronitrile during ten minutes (temperature 20–30°, nitrogen atmosphere). After all the nitrile had been added the mixture was refluxed for three hours with stirring and then allowed to stand overnight under nitrogen. After adding 25 ml. of water and 135 ml. of 6 *N* hydrochloric acid, the ether was distilled and the residue refluxed for one and one-fourth hours. The crude ketone was isolated in the usual manner, giving 22 g., b.p. 108–126° (14 mm.); redistillation gave 15.4 g. (56%), b.p. 113–116° (14.5 mm.), n^{25}D 1.5040, of the pale yellow ketone having a sweet, musty odor.

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(24) Oxalomonophenyldihydrazide, introduced as a carbonyl reagent by P. P. T. Sah and H. Wang (*J. Chinese Chem. Soc.*, **14**, 39 (1946); *C.A.*, **43**, 6971 (1949)), has been found by us to form suitable derivatives of many higher aliphatic ketones which generally form solid derivatives with difficulty, or not at all, with other carbonyl reagents.

(25) The 2-methyl-4-decanol was prepared from isobutylmagnesium bromide and heptanal (method of A. D. Petrov, *et al.*, *J. Gen. Chem.* (*U.S.S.R.*), **9**, 2144 (1939); *C.A.* **34**, 4044 (1940)); 31% yield of material, b.p. 113–115° (17 mm.), n^{25}D 1.4304. J. Werner and M. T. Bogert (*J. Org. Chem.*, **3**, 578 (1938)) report b.p. 123–125° (12 mm.), n^{25}D 1.4310, for this compound.

Anal. Calcd. for $C_{11}H_{14}O$: C, 81.44; H, 8.70. Found: C, 81.42; H, 8.70.

The semicarbazone melted at 140.5–141.5° after one recrystallization from dilute ethanol (lit. m.p. 140–141°[26] and 138–139°[27]).

2,4-Dimethyl-1-phenyl-2-pentene-1-one (XXI).—The ketol VIII, 46.1 g. (0.224 mole), was heated in a nitrogen atmosphere with 0.1 g. of iodine at 120–125° for 18 hours; water was evolved. The dehydration product was diluted with ether, extracted three times with 2% sodium bisulfite solution and three times with water, dried and distilled. After removing the ether the residue was distilled under nitrogen giving 21 g. (50%) of crude unsaturated ketone, b.p. 132–147° (14 mm.). After redistilling twice, the pure, colorless ketone had b.p. 79–83° (0.31 mm.), n^{25}D 1.5255.

Anal. Calcd. for $C_{13}H_{16}O$: C, 82.93; H, 8.57. Found: C, 82.84; H, 8.79.

The 2,4-dinitrophenylhydrazone was obtained as small, feathery, orange needles from ethanol, m.p. 191.5–192.5°.

Anal. Calcd. for $C_{19}H_{20}N_4O_4$: C, 61.94; H, 5.47. Found: C, 61.58; H, 5.8.

A 0.1074-g. sample of the ketone was hydrogenated in ethanol at one atmosphere and 25° (platinum oxide catalyst) until 14.1 ml. (S.T.P.), or 0.92 mole-equivalent of hydrogen was absorbed (four hours). Without isolating the hydrogenation product it was converted into its 2,4-dinitrophenylhydrazone, m.p. 117.5–119°; when mixed with an authentic sample of 2,4-dimethyl-1-phenyl-1-pentanone 2,4-dinitrophenylhydrazone, m.p. 118–119°, the m.p. was not depressed.

1-Phenyl-2-propyl-2-butene-1-one (XXII).—The ketol X, 32.3 g. (0.157 mole), was dehydrated using a procedure similar to that above giving 8.2 g. of forerun, b.p. 67–80° (0.2 mm.), n^{25}D 1.5169, 14.3 g. (48%) of crude unsaturated ketone, b.p. 80–99° (0.24 mm.), n^{25}D 1.5260 and 5.6 g., b.p. 99–105° (0.24 mm.), n^{25}D 1.5239, possibly containing some undehydrated ketol. Redistillation of the crude ketone gave 6.5 g., b.p. 84–87° (0.22 mm.); a second redistillation gave b.p. 86–87° (0.27 mm.), n^{25}D 1.5275.

Anal. Calcd. for $C_{13}H_{16}O$: C, 82.93; H, 8.57. Found: C, 82.91; H, 8.80.

A 1.0325-g. sample of the ketone was hydrogenated in ethanol at one atmosphere and 25° (platinum oxide catalyst) for 42 minutes, in which time 145 ml. (S.T.P.) of hydrogen was absorbed (1.2 mole-equivalents). Without isolating the reduction product it was converted into its 2,4-dinitrophenylhydrazone, m.p. 86.5–88.5°; when mixed with an authentic sample of 2-ethyl-1-phenyl-1-pentanone 2,4-dinitrophenylhydrazone, m.p. 87.5–88.5°, the m.p. was not depressed.

The attempted Dehydration of Ketols I and V.—Attempted dehydration of ketol I by heating with iodine gave only diisopropyl ketone (hydantoin, m.p. 208–211°) and *n*-butyraldehyde (2,4-dinitrophenylhydrazone, m.p. 121.5°) in equimolar amounts. The melting points of these derivatives showed no depression when mixed with authentic samples.

Similar results were obtained in the attempted dehydration of ketol V. Acetaldehyde (2,4-dinitrophenylhydrazone, m.p. 148°), diisobutyl ketone (2,4-dinitrophenylhydrazone, m.p. 89–90°) and some unchanged ketol were the only products.

2,4-Dimethyl-1-phenyl-1-pentanone (XXIII).—To 4.5 g. (0.185 gram atom) of magnesium turnings in 25 ml. of ether was added 27.4 g. (0.166 mole) of freshly prepared 2-bromo-4-methylpentane, b.p. 63–66° (72 mm.), n^{25}D 1.4400 (lit.[28] b.p. 61–63° (71 mm.), n^{25}b 1.4400); the solution was refluxed for one hour and cooled. Benzonitrile, 15.4 g. (0.15 mole), in 25 ml. of ether was added during 40 minutes with stirring; a precipitate formed during the addition. The mixture was refluxed for one and one-third hours, cooled, and treated in succession with 50 ml. each of water, 6 *N* hydrochloric acid and concentrated hydrochloric acid. The ether was distilled and the remaining mixture refluxed one and one-half hours, cooled, and extracted with ether. After distilling the ether there was obtained 14.7 g. of crude, recovered, benzonitrile, b.p. 65–88° (23 mm.), n^{20}D 1.4963, 3.2 g. of crude ketone, b.p. 60–86° (0.8 mm.), n^{25}D 1.5071, and 0.5 g. of residue. Redistillation of the ketone gave 2.2 g. (7.8% yield), b.p. 78–79° (0.45 mm.), n^{25}D 1.5052.

Anal. Calcd. for $C_{13}H_{18}O$: C, 82.06; H, 9.54. Found: C, 81.74; H, 9.55.

The 2,4-dinitrophenylhydrazone was obtained as orange needles from ethanol, m.p. 118–119°.

Anal. Calcd. for $C_{19}H_{22}N_4O_4$: C, 61.61; H, 5.99. Found: C, 62.06; H, 6.0.

2-Ethyl-1-phenyl-1-pentanone (XXIV).—To 70 ml. of dry benzene containing 17.5 g. (0.13 mole) of anhydrous aluminum chloride was added 16.5 g. (0.11 mole) of freshly prepared 2-ethylpentanoyl chloride[29] during 20 minutes (temperature 30–50°). The mixture was then heated for ten minutes at 50° and one hour at 75°, cooled, and poured into a mixture of 50 ml. of concentrated hydrochloric acid and 50 g. of ice. The organic layer was separated, diluted with ether, washed with dilute sodium hydroxide solution and water, and dried. After distilling the ether and benzene there was obtained 13 g. (61%) of the ketone, b.p. 82–85.5° (0.5 mm.), n^{25}D 1.5062.

Anal. Calcd. for $C_{13}H_{18}O$: C, 82.06; H, 9.54. Found: C, 81.83; H, 9.69.

The 2,4-dinitrophenylhydrazone crystallized as orange, needle-like prisms from ethanol, m.p. 87.5–88.5°.

Anal. Calcd. for $C_{19}H_{22}N_4O_4$: C, 61.61; H, 5.99. Found: C, 61.98; H, 6.1.

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[26] E. E. Blaise, *Compt. rend.*, **132**, 480 (1901).

[27] G. A. R. Kon and J. P. Thorpe, *J. Chem. Soc.*, **115**, 693 (1919).

[28] H. A. Shonle, J. H. Waldo, A. K. Keltch and H. W. Coles, THIS JOURNAL, **58**, 585 (1936).

[29] 2-Ethylpentanoyl chloride, b.p. 151–154° (690 mm.), was prepared from the corresponding acid and thionyl chloride (81% yield). The 2-ethylpentanoic acid was prepared according to the procedure of H. Kiliani (*Ber.*, **19**, 227 (1886)).