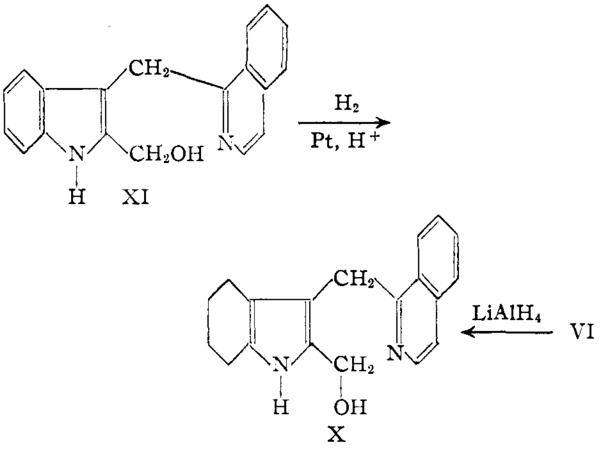
than anticipated and a description of these results will be reserved for a later discussion.

Catalytic Hydrogenation of 1-(2'-Hydroxymethylskatyl)-isoquinoline.—A solution of 500 mg. of 1-(2'-hydroxymethylskatyl)-isoquinoline (XI) in 20 ml. of glacial acetic acid containing 100 mg. of Adams catalyst was subjected to hydrogenation at room temperature and under atmospheric pressure of hydrogen. After two molar equivalents of hydrogen had been absorbed (3 hr.), the catalyst was removed and the solution was made basic with aqueous sodium hydroxide solution. When the resulting precipitate was recrystallized from chloroform, it yielded 400 mg. (79%) of white needles, m.p. 204–205°.

Anal. Calcd. for $C_{19}H_{20}N_2O$: C, 78.05; H, 6.89. Found: C, 78.17; H, 6.86.

It was shown by a mixed melting point determination that this product was identical with the lithium aluminum hydride reduction product of the tetrahydro derivative of 1-(2'-carbethoxyskatyl)-isoquinoline.[2] This product had previously been designated as 1-(2'-hydroxymethyl-3'-indolyl)-methyl-1,2,3,4-tetrahydroisoquinoline but, in view of the earlier discussion in this paper this designation must be incorrect and the compound is now assigned structure X. The two syntheses of this compound are illustrated below. The catalytic reduction product of 1-(2'-carbethoxyskatyl)-isoquinoline, which was previously designated as 1-(2'-carbethoxy-3'-indolyl)-methyl-1,2,3,4-tetrahydroisoquinoline,[2] is now assigned structure VI.



XI

X

ROCHESTER, N. Y.

[CONTRIBUTION FROM THE DEPARTMENT OF ORGANIC CHEMISTRY OF THE UNIVERSITY OF SYDNEY]

β-Acylethylation with Ketonic Mannich Bases. The Synthesis of Some Diketones, Ketonic Sulfides, Nitroketones and Pyridines

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Decomposition of ketonic Mannich bases by controlled heating of their solutions in suitable ketones leads to β-acylethylation of the ketone and formation, primarily, of a 1,5-diketone. Certain of these diketones have been caused to react with hydroxylamine hydrochloride, or, alternatively, with hydrazine followed by hydrogen chloride, to yield pyridines not otherwise readily accessible. Thermal decomposition of ketonic Mannich bases in presence of thiols gives β-acylethyl alkyl (or aryl) sulfides in good yields, as does the interaction in solution of Mannich base methiodides with the alkali salts of thiols. Similarly, thermal decomposition of ketonic Mannich bases in primary or secondary nitroparaffins β-acylethylates them to γ-nitroketones in good yields.

Much of the usefulness of Mannich bases of the type $R{\cdot}CO{\cdot}CH(R'){\cdot}CH_2{\cdot}NR''_2$ in synthesis stems from the fact that they, or their quaternary metho salts, are readily broken down to α,β-unsaturated ketones under alkaline conditions which can further promote the interaction of these products with substances possessing activated hydrogen atoms in reactions of the Michael type. The process can be usefully described as β-acylethylation in analogy with cyanoethylation, and the earliest studies of it[3] have been greatly amplified in recent years.

The methods studied to date for such utilization of ketonic Mannich bases apparently do not include thermal decomposition of the bases in the presence of the reagent to be added, although Snyder and his co-workers[4] have shown that gramine and similar bases can be readily condensed with nitroparaffins or with acetaminomalonic ester by heating them together in presence of a small amount of alkali, dimethylamine or other secondary base being extruded; and Snyder and Brewster[5] have recorded amine exchange reactions of Mannich bases under the influence of heat.

This paper records experiments which show that ketonic Mannich bases break down smoothly when heated in presence of such reagents as reactive ketones, thiols or nitroparaffins, secondary base being extruded and the reagent being added across the olefinic bond of the resulting α,β-unsaturated ketone. Because of the volatility of the extruded secondary base it is best to work with Mannich bases derived from dimethylamine or diethylamine, but almost equally good results can be obtained with Mannich bases derived from amines such as morpholine, when, however, the method of product recovery is less simple.

Heating of a ketonic Mannich base in excess of a suitable ketone containing a keto-methylene system leads to β-acylethylation of the ketone and formation, primarily, of a 1,5-diketone. Thus, as an example, 3-dimethylamino-1-phenyl-1-propanone (A), heated in an excess of cyclohexanone at 160° for 20 minutes gave an almost quantitative yield of 1-(2'-cyclohexanonyl)-3-phenyl-propan-3-one (2-β-benzoylethylcyclohexanone (I)). Further examples are listed in Table I. The formation of 4-(2'-cyclopentanonyl)-butan-2-one (2-β-acetylethylcyclopentanone) from 4-diethylamino-butan-2-one (C) and cyclopentanone, and its failure under the

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[3] *Cf.* S. M. Abdullah, *J. Indian Chem. Soc.*, **12**, 62 (1935); C. Mannich, W. Koch and F. Borkowsky, *Ber.*, **70B**, 355 (1937); E. C. du Feu, F. J. McQuillen and R. Robinson, *J. Chem. Soc.*, 53 (1937).

[4] *Cf.* H. R. Snyder and L. Katz, THIS JOURNAL, **69**, 3140 (1947); E. E. Howe, A. J. Zambito, H. R. Snyder and M. Tishler, *ibid.*, **67**, 38 (1945).

[5] H. R. Snyder and J. H. Brewster, *ibid.*, **70**, 4230 (1948).

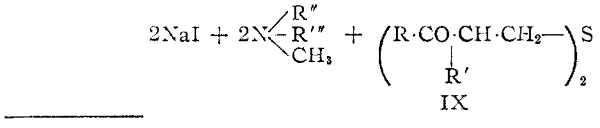
reaction conditions to cyclize to the corresponding indene derivative is noteworthy and to be attributed to the steric factors involved. Attempts to condense C with methyl isobutyl ketone to either piperitone or 3-isobutyl-Δ^2-cyclohexenone failed, the intermediate methyl vinyl ketone polymerizing.

In some experiments with diketones (see Table I) it was observed that the yields were definitely improved by the presence of small amounts of alkali.[4] Also, as was to be expected, the first formed product of reaction lost water and underwent internal cyclization to a cyclohexenone derivative.

Knoevenagel[6] and, later, Stobbe[7] have shown that suitably constituted 1,5-diketones react readily with hydroxylamine hydrochloride in alcoholic solution to yield pyridine derivatives, whilst Wolff and Marburg[8] have described a quite similar synthesis of pyrazine from dihydroxymorpholine (obtained from diacetalylamine) and hydroxylamine hydrochloride. Application was made of this reaction to the diketones I, II, III and IV (see Table I) which were thus readily converted into 2-phenyl-5,6,7,8-tetrahydroquinoline (V), 2-phenyl-5,6-cyclopentenopyridine (VI), 1,2,3,4,5,6,7,8-octahydroacridine (VII) and 2,3-cyclopenteno-5,6,7,8-tetrahydroquinoline (VIII), respectively. The two latter bases have been previously synthesized by v. Braun and his co-workers[9] by catalytic reduction of 1,2,3,4-tetrahydroacridine and 2,3-cyclopentenoquinoline, respectively.

It seemed reasonable also, from the arguments of Robinson and Robinson,[10] to anticipate that the azines from ketones such as I and II should react with hot hydrogen chloride to lose ammonia and be converted to pyridines. On experiment the azine of I yielded V and that of II yielded VI, albeit not in high yields. Pyridine formation could also be effected by heating the azines with ethanolic or aqueous hydrochloric acid.

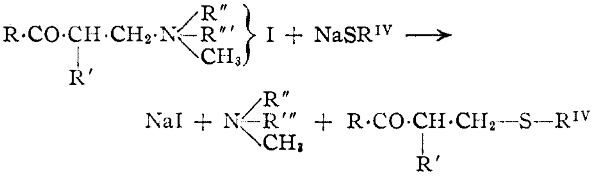
Snyder and Speck[11] have recorded studies on the cleavage of quaternary ammonium salts by sodium hydrogen sulfide and the sodium salts of thiols and have shown that such cleavage is not easy unless the quaternary ammonium salt possesses certain structural features. The quaternary metho salts derived from tertiary ketonic Mannich bases cleave very readily indeed with these reagents. Thus, aqueous solutions of the methiodides of ketonic Mannich bases have been found to react readily with sodium sulfide solution to give bis-(β-acylethyl) sulfides (IX), according to the equation



$$2\mathrm{R{\cdot}CO{\cdot}\underset{R'}{CH}{\cdot}CH_2{\cdot}N}\left\langle\begin{matrix}\mathrm{R''}\\\mathrm{R'''}\\\mathrm{CH_3}\end{matrix}\right\}\mathrm{I} + \mathrm{Na_2S} \longrightarrow 2\mathrm{NaI} + 2\mathrm{N}\left\langle\begin{matrix}\mathrm{R''}\\\mathrm{R'''}\\\mathrm{CH_3}\end{matrix}\right. + \left(\mathrm{R{\cdot}CO{\cdot}\underset{R'}{CH}{\cdot}CH_2}{-}\right)_2\mathrm{S}$$

IX

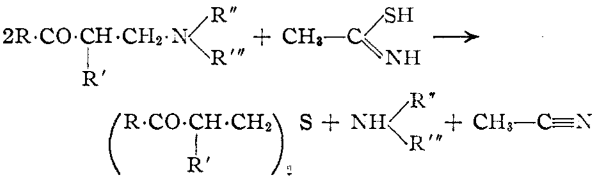
Similarly, such quaternary salts reacted with the alkali derivatives of thiols in aqueous alcoholic solution to give β-acylethyl alkyl (or aryl) sulfides (X), according to the equation



$$\mathrm{R{\cdot}CO{\cdot}\underset{R'}{CH}{\cdot}CH_2{\cdot}N}\left\langle\begin{matrix}\mathrm{R''}\\\mathrm{R'''}\\\mathrm{CH_3}\end{matrix}\right\}\mathrm{I} + \mathrm{NaSR^{IV}} \longrightarrow \mathrm{NaI} + \mathrm{N}\left\langle\begin{matrix}\mathrm{R''}\\\mathrm{R'''}\\\mathrm{CH_3}\end{matrix}\right. + \mathrm{R{\cdot}CO{\cdot}\underset{R'}{CH}{\cdot}CH_2{-}S{-}R^{IV}}$$

X

The results obtained are set out in Table II. It was then found in test experiments that each of these types of products can be very conveniently prepared in high yield by thermal decomposition of a ketonic Mannich base in the presence of a thiol (products X), or in the presence of a thioamide, such as thioacetamide (products IX). This latter reaction is noteworthy. Presumably, the vinyl ketone formed by the decomposition of the Mannich base extracts and adds hydrogen sulfide from the thioamide, which reverts to a nitrile.



$$2\mathrm{R{\cdot}CO{\cdot}\underset{R'}{CH}{\cdot}CH_2{\cdot}N}\left\langle\begin{matrix}\mathrm{R''}\\\mathrm{R'''}\end{matrix}\right. + \mathrm{CH_3{-}C}\left\langle\begin{matrix}\mathrm{SH}\\\mathrm{NH}\end{matrix}\right. \longrightarrow \left(\mathrm{R{\cdot}CO{\cdot}\underset{R'}{CH}{\cdot}CH_2}\right)_2\mathrm{S} + \mathrm{NH}\left\langle\begin{matrix}\mathrm{R''}\\\mathrm{R'''}\end{matrix}\right. + \mathrm{CH_3{-}C{\equiv}N}$$

IX

It has also been found experimentally that non-ketonic Mannich bases such as gramine, or Mannich bases derived from nitroparaffins, readily break down on heating in the presence of thiols, extruding secondary base and forming sulfides in high yields. The nitroalkyl sulfides will be described in a later communication.

A series of γ-nitroketones has been prepared by thermal decomposition of ketonic Mannich bases in primary or secondary nitroparaffins in presence of solid sodium hydroxide. Reichert and Posemann[12] previously reported the preparation of γ-nitroketones by interaction of ketonic Mannich bases with nitromethane in methanolic solution containing sodium methoxide. We have applied the method elaborated by Snyder and Katz[4] for treating gramine with nitroparaffins and later extended by Snyder and Hamlin[13] to the preparation of dinitroparaffins. In our first experiments ketonic Mannich bases derived from volatile secondary bases like dimethylamine were treated with the nitroparaffin in presence of sodium hydroxide to give γ-nitroketones in excellent yields, the extruded secondary base boiling off from the reaction mixture. With certain nitroparaffins, such as nitroethane or β-phenylnitroethane some di-(β-acylethylation) occurred as well as mono-(β-acylethylation) of the nitroparaffin. It was then observed that use of a Mannich base derived from a volatile secondary base offered no advantages other than simplification of the method of product isolation over use of a Mannich base derived from a

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(6) E. Knoevenagel and R. Weissgerber. *Ber.*, **26**, 436 (1893); E. Knoevenagel, *Ann.*, **281**, 33 (1894); **303**, 225 (1898).

(7) H. Stobbe. *Ber.*, **35**, 3978 (1902); H. Stobbe and H. Volland. *ibid.*, **35**, 3973 (1902); H. Stobbe and C. Striegler, *J. prakt. Chem.*, **86**, 241 (1912).

(8) L. Wolff and R. Marburg. *Ann.*, **363**, 215 (1908).

(9) J. v. Braun. A. Petzold and A. Schultheiss. *Ber.*. **56**, 1349 (1923).

(10) G. M. Robinson and R. Robinson. *J. Chem. Soc.*. **113**, 639 (1918).

(11) H. R. Snyder and J. C. Speck. THIS JOURNAL. **61**, 2895 (1939).

(12) B. Reichert and H. Posemann. *Arch. Pharm.*, **275**, 67 (1937).

(13) H. R. Snyder and W. E. Hamlin. THIS JOURNAL. **72**, 5082 (1950).

less volatile secondary base such as morpholine (see Table III).

Certain of these γ-nitroketones were next shown to be accessible by an alternative route. The high yields of 1,5-diketones obtained by treating ketonic Mannich bases with ketones such as cyclohexanone suggested, and experiment confirmed, that heating in cyclohexanone of a Mannich base derived from a nitroparaffin, such as N-(2-nitrobutyl)-dimethylamine, would lead to loss of dimethylamine and formation of the same 2-(γ-nitrobutyl)-cyclohexanone that can be obtained by heating B with 1-nitropropane. The yield in this particular instance was excellent. However, heating of the same Mannich base in the much less reactive acetophenone led to extensive polymerization of the intermediate nitroölefin, and none of the anticipated nitroketone could be isolated, so that the method is not general.

It is worthy of comment that pyrolysis of ketonic Mannich bases in nitromethane was quite unsatisfactory, the reaction mixture invariably becoming very dark and the anticipated products being rarely isolable. When solid sodium hydroxide was used as catalyst it was soon covered by a dark brown tar. The method of Reichert and Posemann would appear to be preferable when working with nitromethane.

Snyder and Katz[4] considered the extensive dialkylation of ethyl nitroacetate by gramine to be due to the low solubilitity of the sodium salt of ethyl nitroacetate in ethanol, the reaction solvent chosen—a conclusion emphasized by the findings of Lyttle and Weisblat.[14] Some comparative experiments reported in Table III on the interaction of the bases A and H with 1-nitropropane and nitroethane would appear to confirm the importance of the effect of solubility of the sodium salt.

Finally, because reductive cyclization of the δ-nitro-α,η-dicarbonyl compounds derived by di-(β-acylethylation) of primary nitroparaffins might well be expected to lead to pyrrolizidines it was thought worthwhile to attempt a second β-acylethylation of a γ-nitroketone with a Mannich base derived from a ketone other than that used in the synthesis of the γ-nitroketone. Using a variation of the method of Reichert and Posemann[12] 3-nitro-6-phenylhexan-6-one was readily condensed with 1-N-morpholino-2-phenylbutan-3-one (G) to give 1,6-diphenyl-4-ethyl-4-nitroöctane-1,7-dione in good yield. It is hoped to report later the development of a general pyrrolizidine synthesis by reductive cyclization of such substances.

Experimental

All melting points recorded are uncorrected. The microanalyses were carried out by Mrs. E. Bielski of this University, whose assistance is gratefully acknowledged.

Mannich Bases.—The bases used have, with one exception, been fully described in the literature. In this work they were often obtained and used as residual oils after recovery with the help of cold alkali and ether from solutions of their pure hydrochlorides. They were: β-dimethylaminopropiophenone (A), 2-dimethylaminomethylcyclohexanone (B), 1-diethylaminobutan-3-one (C), β-N-morpholinopropiophenone (D), 1-N-morpholinobutan-3-one (E), 2-N-morpholinomethylcyclohexanone (F), 1-N-morpholino-2-phenylbutan-3-one (G) and β-diethylaminopropiophenone (H). The base G was first prepared at Sydney by Mr. Ludwig Bauer as follows: Benzyl methyl ketone (6.5 g.), paraformaldehyde (3 g.) and morpholine hydrochloride (7 g.) were added to ethanol (25 ml.) containing a few drops of concentrated hydrochloric acid and the mixture refluxed for 5 hours. A crystalline hydrochloride commenced to separate about 30 minutes after solution of the reactants. This was eventually filtered from the cooled solution, washed with alcohol containing ether and recrystallized from methanol, colorless needles (yield 70%) m.p. 188–189° of **1-N-morpholino-2-phenylbutan-3-one hydrochloride** being thus obtained.

Anal. Calcd. for $C_{14}H_{20}ClNO_2$: C, 62.3; H, 7.5; N, 5.2. Found: C, 62.1; H, 7.5; N, 5.2.

The oily base, **1-N-morpholino-2-phenylbutan-3-one** (G), obtained from this salt with alkali, solidified on cooling and crystallized from petroleum ether in colorless silky needles m.p. 50°.

Anal. Calcd. for $C_{14}H_{19}NO_2$: C, 72.0; H, 8.2; N, 6.0. Found: C, 71.8; H, 8.3; N, 6.1.

The **picrate** formed yellow needles m.p. 134° (from ethanol).

Anal. Calcd. for $C_{20}H_{22}N_4O_9$: N, 12.3. Found: N, 12.0.

Condensation of Mannich Bases with Ketones.—The general procedure was to heat a solution of the Mannich base (1 mole) in the ketone (3 moles) to a suitable temperature for a suitable time during which, if the extruded secondary base were volatile it boiled off. Otherwise, after cooling and addition of ether it was extracted with dilute acid. The excess ketone was then removed by distillation *in vacuo* and the product isolated either by allowing the residue to crystallize or by distillation *in vacuo*. Solid products were usually recrystallized from petroleum ether. Almost always some polymer of the intermediate vinyl ketone was formed and remained at the end of the distillation. In the condensations with diketones two different procedures were used. The former (a) was essentially the same as that just described. In the second (b) the reaction was carried out in the presence of a very small pellet of potassium hydroxide, reaction being then, usually, much more rapid and the reaction product darker in color. However, the yields of pure product were higher. The results are given in Table I.

Conversion of 1,5-Diketones to Pyridines.—Two methods were used. Method (a) was essentially that described by Stobbe and his co-workers.[7] Method (b) consisted in passing dry hydrogen chloride through the molten azine of the diketone at about 235° for five minutes. Dense fumes of ammonium chloride were evolved and the reaction mixture became very dark. It was finally poured into alkali and the base extracted with ether, dried and distilled.

2-Phenyl-5,6,7,8-tetrahydroquinoline (V).—Light-yellow mobile oil, b.p. 214–216° (15 mm.), yield 94% by method (a) and 20% by method (b).

Anal. Calcd. for $C_{15}H_{15}N$: C, 86.0; H, 7.2; N, 6.7. Found: C, 85.9; H, 7.2; N, 6.8.

The **picrate** formed yellow needles (methanol) m.p. 152°.

Anal. Calcd. for $C_{21}H_{18}N_4O_7$: N, 12.8. Found: N, 12.9.

The **methiodide** formed pale yellow needles (acetone–ether), m.p. 161°.

Anal. Calcd. for $C_{16}H_{18}IN$: N, 4.0. Found: N, 4.1.

2-Phenyl-5,6-cyclopentenopyridine (VI) was obtained by method (a) in very pale buff prisms m.p. 80° (yield 80%); and by method (b) as an oil b.p. 200–206° (20 mm.) (yield 16%) which solidified to prisms m.p. 79°.

Anal. Calcd. for $C_{14}H_{13}N$: C, 86.2; H, 6.7; N, 7.2. Found: C, 86.3; H, 6.8; N, 7.3.

The **picrate** formed shiny yellow leaflets (acetone) m.p. 198°.

Anal. Calcd. for $C_{20}H_{16}N_4O_7$: N, 13.2. Found: N, 13.4.

The **methiodide** formed pale yellow needles (acetone–ether) m.p. 162°.

Anal. Calcd. for $C_{15}H_{16}NI$: N, 4.2. Found: N, 4.3.

1,2,3,4,5,6,7,8-Octahydroacridine (VII) was obtained by method (a) as an oil b.p. 191–192° (22 mm.) which solidified. After recrystallization from petroleum ether it was obtained in colorless needles m.p. 71° (yield 95%). v. Braun, *et al.*,[9] give m.p. 69°, and b.p. 175° (17 mm.).

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[14] D. A. Lyttle and D. I. Weisblat, THIS JOURNAL, 69, 2118 (1947).

TABLE I

Mannich base	Ketone	Temp. of reaction, °C.	Time, min.	Product	Formula	Yield, %	M.p. or b.p., °C.	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found
A	Cyclohexanone	160	20	1-(2′-Cyclohexanonyl)-3-phenyl-propan-3-one (I)[a]	$C_{15}H_{18}O_2$	95	53	78.3	78.4	7.9	7.7
D	Cyclohexanone	180–190	60	1-(2′-Cyclohexanonyl)-3-phenyl-propan-3-one (I)[a]		73	53				
A	Cyclopentanone	160	20	1-(2′-Cyclopentanonyl)-3-phenyl-propan-3-one (II)[b]	$C_{14}H_{16}O_2$	95	40	77.8	77.6	7.5	7.4
D	Cyclopentanone	170	120	1-(2′-Cyclopentanonyl)-3-phenyl-propan-3-one (II)[b]		83	40				
A	Acetophenone	200	60	1,5-Diphenyl-1,5-pentandione[c]	$C_{17}H_{16}O_2$	40	65	80.9	80.9	6.4	6.4
A	Desoxybenzoin	210–220	60	1,2,5-Triphenyl-1,5-pentadione[d]	$C_{23}H_{20}O_2$	9	94	84.2	83.9	6.2	6.1
B	Cyclohexanone	190–220	70	2,2′-Dicyclohexanonylmethane (III)[e]	$C_{13}H_{20}O_2$	63	114–118 0.3 mm.	74.9	75.0	9.7	9.5
B	Cyclopentanone	220	40	2-(2′-Cyclohexanonylmethyl)-cyclopentanone. (IV)[f]	$C_{12}H_{18}O_2$	73	180–182 21 mm.	74.3	74.5	9.4	9.6
C	Cyclopentanone	170–180	60	4-(2′-Cyclopentanonyl)-butan-2-one[g]	$C_9H_{14}O_2$	28	144–146 18 mm.	70.1	70.0	9.2	9.3
C	Acetone	160–180	120	3-Methyl-Δ^2-cyclohexenone[h]	$C_7H_{10}O$	16	196–199 760 mm.	76.3	75.8	9.2	9.3
A	Acetylacetone	a. 160	120	2-Acetyl-5-phenyl-Δ^5-cyclohexenone[i]	$C_{14}H_{14}O_2$	36	85	78.5	78.8	6.6	6.5
		b. 160	90	2-Acetyl-5-phenyl-Δ^5-cyclohexenone[i]		50	85				
A	2,5-Hexandione	a. 160	90	2-Acetonyl-5-phenyl-Δ^5-cyclohexenone	$C_{15}H_{16}O_2$	Poor	M 80 B 188–189 1 mm.	78.9	78.5	7.1	7.3
		b. 160	90	2-Acetonyl-5-phenyl-Δ^5-cyclohexenone		22	80				
B	Acetylacetone	a. 200	180	3-Acetyl-2-keto-$\Delta^{1,9}$-octalin	$C_{12}H_{16}O_2$	50	91–92 0.4 mm.	75.0	74.9	8.4	8.6
		b. 180	120	3-Acetyl-2-keto-$\Delta^{1,9}$-octalin		60	91–92 0.4 mm.				
B	2,5-Hexandione	a. 160	90	3-Acetonyl-2-keto-$\Delta^{1,9}$-octalin	$C_{13}H_{18}O_2$	Poor	136–138 0.9 mm.	75.7	75.3	8.8	8.6
		b. 160	90	3-Acetonyl-2-keto-$\Delta^{1,9}$-octalin		29	136–138 0.9 mm.				

[a] The bis-dinitrophenylhydrazone, deep-red platelets (from xylene) m.p. 228°. (Calcd. for $C_{27}H_{26}N_8O_8$: N, 19.0. Found: N, 18.9). The azine, 2-phenyl-5,6-dihydro-6,7-cyclohexano-1,2,4-diazepine, (yield 86% from the diketone (2 g.), hydrazine hydrate (1 g.) and ethanol (20 ml.) containing acetic acid (0.5 g.)) colorless needles m.p. 185°. (Calcd. for $C_{15}H_{18}N_2$: C, 79.6; H, 8.0; N, 12.4. Found: C, 79.2; H, 8.0; N, 12.2). [b] The bis-dinitrophenylhydrazone deep-red plates (from xylene) m.p. 220°. (Calcd. for $C_{26}H_{24}N_8O_8$: N, 19.5. Found: N, 19.3). The azine, 2-phenyl-5,6-dihydro-6,7-cyclopentano-1,2,4-diazepine, very pale-yellow needles (from ethyl acetate) m.p. 196°. (Calcd. for $C_{14}H_{16}N_2$: C, 79.2; H, 7.6; N, 13.2. Found: C, 79.4; H, 7.6; N, 13.2). [c] F. R. Japp and A. C. Michie, *J. Chem. Soc.*, **79,** 1021 (1901), give m.p. 67.5°. [d] C. F. H. Allen and W. E. Baker, THIS JOURNAL, **54,** 741 (1932), give m.p. 95° and m.p. of the mono-dinitrophenylhydrazone as 221°. We found m.p. of the mono-D.N.P., orange needles (from ethyl acetate–ethanol) as 222°. (Calcd. for $C_{29}H_{24}N_4O_5$: N, 11.0. Found: N, 11.0). [e] The bis-semicarbazone, minute colorless prisms (from ethanol) m.p. 217°. (Calcd. for $C_{15}H_{26}N_6O_2$: N, 26.1. Found: N, 25.6). [f] The bis-dinitrophenylhydrazone, orange-red needles (from benzene) m.p. 215–216°. (Calcd. for $C_{24}H_{26}N_8O_8$: N, 20.3. Found: N, 20.0). [g] The bis-semicarbazone, colorless needles m.p. 229°. (Calcd. for $C_{11}H_{20}N_6O_2$: C, 49.3; H, 7.5. Found: C, 49.2; H, 7.6.). [h] The reaction was carried out in an autoclave. A. Blumann and O. Zeitschell, *Ber.*, **46,** 1190 (1913), give b.p. 200–202° (760 mm.). The semicarbazone, colorless needles (from ethanol) had m.p. 202°. C. Harries, *Ber.*, **47,** 790 (1914), gives m.p. 200°. [i] The copper complex, small, brilliant olive-green leaflets (from chloroform–petroleum ether) m.p. 260° (dec.). (Calcd. for $C_{28}H_{26}O_4Cu$: C, 68.6; H, 5.3. Found: C, 68.7; H, 5.7).

Anal. Calcd. for $C_{13}H_{17}N$: C, 83.4; H, 9.2; N, 7.5. Found: C, 83.0; H, 9.3; N, 7.3.

The **picrate** formed yellow needles (ethanol) m.p. 200°. v. Braun, *et al.*, give m.p. 195°.

Anal. Calcd. for $C_{19}H_{20}N_4O_7$: N, 13.5. Found: N, 13.6.

2,3-Cyclopenteno-5,6,7,8-tetrahydroquinoline (VIII) was obtained by method (a) as a pale yellow mobile oil b.p. 160–164° (16 mm.) (yield 74%); v. Braun, *et al.*, give b.p. 160–161° (17 mm.).

Anal. Calcd. for $C_{12}H_{15}N$: C, 83.2; H, 8.7; N, 8.1. Found: C, 82.9; H, 8.7; N, 7.9.

The **picrate** formed yellow needles (water) m.p. 160°; v. Braun, *et al.*, give m.p. 158°.

Anal. Calcd. for $C_{18}H_{18}N_4O_7$: N, 13.9. Found: N, 13.8.

Interaction of Mannich Base Methiodides with Sodium Sulfide.—The general procedure was to reflux a solution of the Mannich base methiodide (2 moles) and sodium sulfide (1.1 moles) in water (1200 ml. for each gram-mole of methiodide) for about three hours. Usually, an upper oily layer formed almost immediately. After cooling the product could be extracted with ether, dried and, after removal of the solvent, either recrystallized from a suitable solvent (usually ethanol) or distilled *in vacuo*.

Interaction of Mannich Base Methiodides with Sodium Salts of Thiols.—The general procedure was to prepare an ethanolic solution of the thiol (1.1 moles) by dissolving the calculated amount of sodium in absolute ethanol (20–30 ml. for each gram of metal) followed by addition of the thiol, and then to add this to a solution of the Mannich base methiodide (1 mole) in water (8,000 ml. for each gram-mole of methiodide) preheated to 45–55°. Usually a turbidity developed at once, followed by separation of an oil which often crystallized within a few hours. Sometimes it was found necessary to allow the reaction mixture to stand at room temperature for several days before product ceased to separate.

Interaction of Mannich Bases with Thiols.—When the Mannich base was derived from dimethylamine or diethylamine the procedure was as follows: A mixture of the Mannich base (1 mole) and the thiol (1 mole) was maintained at a temperature of 130–135° until evolution of volatile base ceased (usually 5–10 minutes). The product remaining on cooling was the almost pure sulfide. Thus, A with benzyl mercaptan gave crystalline 1,5-diphenyl-2-thiapentan-5-one in 87% yield; and with *p*-thiocresol gave 1-phenyl-4-*p*-tolyl-4-thiabutan-1-one in 97% yield. Gramine (1.04 g.) and *p*-thiocresol (0.75 g.) gave **3-indolylmethyl *p*-tolyl sulfide** (yield 85%), colorless leaflets (ethanol) m.p. 107°.

Anal. Calcd. for $C_{16}H_{15}NS$: C, 76.1; H, 5.9; N, 5.5. Found: C, 76.2; H, 6.1; N, 5.6.

Similarly, gramine and benzyl mercaptan gave **3-indolylmethyl benzyl sulfide**, colorless leaflets from ethanol, m.p. 72.5° (yield 85%).

Anal. Calcd. for $C_{16}H_{15}NS$: C, 76.1; H, 5.9; N, 5.5. Found: C, 75.8; H, 6.2; N, 5.7.

TABLE II

Mannich base (as methiodide)	Sulfur compound (as sodium salt)	Product	Formula	M.p. or b.p., °C.	Yield, %	Analyses, % Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found
D	Hydrogen sulfide	1,7-Diphenyl-4-thiaheptan-1,7-dione[a]	$C_{18}H_{18}O_2S$	104	85	72.4	72.1	6.1	6.1
D	Thiophenol	1,4-Diphenyl-1-thiabutan-4-one[b]	$C_{15}H_{14}OS$	75	88	74.3	74.3	5.8	5.8
D	*p*-Thiocresol	1-Phenyl-4-*p*-tolyl-4-thiabutan-1-one[c]	$C_{16}H_{16}OS$	84	84	75.0	74.5	6.3	6.3
D	Benzyl mercaptan	1,5-Diphenyl-2-thiapentan-5-one[d]	$C_{16}H_{16}OS$	39	88	75.0	74.4	6.3	6.3
D	Ethyl thioglycolate	Ethyl ε-phenyl-β-thia-ε-keto caproate[e]	$C_{13}H_{16}O_3S$	37 162–168 0.5 mm.	70	61.9	61.9	6.4	6.4
E	Hydrogen sulfide	4-Thianonan-2,7-dione	$C_8H_{14}O_2S$	130 9 mm.	55	55.1	55.1	8.1	8.2
E	Methyl mercaptan	2-Thiahexan-5-one[f]	$C_6H_{10}OS$	77–78 20 mm.	45	50.8	50.6	8.5	8.3
F	Hydrogen sulfide	Bis-(2-cyclohexanonylmethyl)-sulfide[g]	$C_{14}H_{22}O_2S$	96–98 2 mm.	50	66.1	65.6	8.7	8.6

[a] A sulfur analysis gave the result: Calcd. for $C_{16}H_{18}O_2S$: S, 10.7. Found: S, 10.5. The dinitrophenylhydrazone, scarlet needles from ethyl acetate, m.p. 188°. (Calcd. for $C_{36}H_{26}O_8N_8S$: N, 17.0. Found: N, 16.6). [b] The dinitrophenylhydrazone, scarlet needles from ethanol m.p. 147.5° (Calcd. for $C_{21}H_{18}N_4O_4S$: N, 13.3. Found: N, 12.8). [c] The dinitrophenylhydrazone, scarlet needles from ethyl acetate m.p. 185°. (Calcd. for $C_{22}H_{20}N_4O_4S$: N, 12.8. Found: N, 12.8). [d] The dinitrophenylhydrazone, scarlet needles from methanol, m.p. 127.5° (Calcd. for $C_{22}H_{20}N_4O_4S$: N, 12.8. Found: N, 12.8). [e] The dinitrophenylhydrazone, orange needles from ethanol m.p. 133–134°. (Calcd. for $C_{19}H_{20}N_4O_6S$: N, 13.0. Found: N, 12.8). [f] The dinitrophenylhydrazone, orange prisms from ethanol, m.p. 100.5°. (Calcd. for $C_{11}H_{14}N_4O_4S$: N, 18.8. Found: N, 18.9). The semicarbazone, colorless prisms from chloroform and petroleum ether, m.p. 127–128° (Calcd. for $C_6H_{13}N_3OS$: N, 24.0. Found: N, 24.1). [g] A semicarbazone, colorless prisms from ethanol, m.p. 199°. (Calcd. for $C_{16}H_{28}N_6O_2S$: N, 22.8. Found: N, 22.2).

TABLE III

Procedure	Mannich base	Nitroparaffin	Mol. ratio nitroparaffin/base	Time of reflux (hr.)	Product	M.p. or b.p., °C.	Yield, %	Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen % Calcd.	Nitrogen % Found
I	A	2-Nitropropane	10	6¹/₂	2-Methyl-2-nitro-5-phenylpentan-5-one (XI)	42	82	$C_{12}H_{15}NO_3$	65.2	65.4	6.8	6.9	6.3	6.2
II	D	2-Nitropropane	10	7	XI	42	84							
II	G	2-Nitropropane	10	7¹/₂	2-Methyl-2-nitro-4-phenylhexan-5-one (XII)	41 121–124 0.5 mm.	89	$C_{13}H_{17}NO_3$	66.4	66.7	7.2	7.5	6.0	5.6
II	F	2-Nitropropane	10	7	2-(β-Nitroisobutyl)-cyclohexanone (XIII)	123 2 mm.	81	$C_{10}H_{17}NO_3$	60.3	60.5	8.5	8.7	7.0	7.2
II	C	2-Nitropropane	10	8	2-Methyl-2-nitrohexan-5-one (XIV)	84 1 mm.	85	$C_7H_{13}NO_3$	52.8	53.2	8.2	8.5	8.8	8.4
II	F	1-Nitropropane	10	7¹/₂	2-(β-Nitrobutyl)-cyclohexanone (XV)[a]	116 1.2 mm.	78	$C_{10}H_{17}NO_3$	60.3	60.6	8.5	8.5	7.0	7.3
I	A	1-Nitropropane	10	5¹/₂	3-Nitro-6-phenyl-hexan-6-one (XVI)	36	80	$C_{12}H_{15}NO_3$	65.2	65.4	6.8	6.7	6.3	6.4
III	H	1-Nitropropane	1.4	3	XVI	36	60							
III	D	Nitroethane	1.6	2	4-Methyl-4-nitro-1,7-diphenylheptan-1,7-dione (XVII)	147	30	$C_{20}H_{21}NO_4$	70.8	70.9	6.2	6.0	4.1	4.0
					2-Nitro-5-phenylpentan-5-one (XVIII)	60	48	$C_{11}H_{13}NO_3$	63.8	63.9	6.3	6.6	6.8	6.7
I	A	Nitroethane	10	4	XVII	147	5							
					XVIII	60	72							
II	H	Nitroethane	2	4	XVII	147	50							
					XVIII	60	7							
I	A	β-Phenylnitroethane	3	1¹/₂[b]	1,5-Diphenyl-2-nitropentan-5-one (XIX)	76	68	$C_{17}H_{17}NO_3$	72.1	72.1	6.0	6.0	4.9	4.9
					4-Benzyl-4-nitro-1,7-diphenylheptan-1,7-dione (XX)	198	7	$C_{26}H_{25}NO_4$	75.2	74.9	6.0	6.2	3.4	3.3
I	A	Nitromethane	10	7¹/₂	1-Nitro-4-phenylbutan-4-one (XXI)	66	13[c]	$C_{10}H_{11}NO_3$						
IV	A	Nitromethane	10	5¹/₂	XXI	66	15							

[a] XV was also obtained in 80% yield by heating N-(2-nitrobutyl)-dimethylamine (14.6 g.) and cyclohexanone (30 g.) under nitrogen at 125° until evolution of dimethylamine ceased (1.5 hours). [b] This reaction mixture was not refluxed but heated in a bath maintained at 125°. The same two compounds, XIX and XX, could also be obtained in poorer yields by refluxing a methanolic solution of the methiodide of D (1 mole), β-phenylnitroethane (1.3 mole) and sodium methoxide (1 mole). [c] The crude product largely decomposed on attempted removal of excess nitromethane. The solid isolated was obtained by continued extraction of the tarry material with petroleum ether. Reichert and Posemann give m.p. 66° and m.p. of the semicarbazone 163°. Our semicarbazone had m.p. 163°.

An experiment with a Mannich base derived from a not-so-volatile secondary amine was as follows: β-N-morpholinoethyl phenyl ketone (12.3 g.) and benzyl mercaptan (7 g.) were heated together at 170° for 0.5 hour. After cooling and addition of hydrochloric acid the product was collected and dried with the help of ether. After removal of the solvent 1,5-diphenyl-2-thiapentan-5-one (12.6 g., 92%) was left as a pale yellow solid, which, after recrystallization from petroleum ether, had m.p. 39° (see Table II).

Interaction of β-Dimethylaminopropiophenone with Thioacetamide.—A mixture of A (7.65 g.) and thioacetamide (3.75 g.) was heated at 140–145° for 15 minutes. A vigorous reaction occurred, dimethylamine, hydrogen sulfide and a liquid boiling below 80° being evolved. When reaction ceased the product was cooled and set to a brown solid. Recrystallized from ethanol it had m.p. 104° (yield 62%) and was identical with 1,7-diphenyl-4-thiaheptan-1,7-dione (see Table II).

Interaction of Ketonic Mannich Bases with Nitroparaffins.—Four slightly different procedures (I–IV) were used. Procedure I consisted essentially of refluxing a solution of the Mannich base derived from dimethylamine in excess of the primary or secondary nitroparaffin (which must have been freshly redistilled) in presence of solid sodium hydroxide (1 mole) in an atmosphere of nitrogen. A heavy white precipitate of the sodium salt of the nitroparaffin formed rapidly and dimethylamine was evolved. When this evolution ceased (1.5–7.5 hours) the cooled reaction mixture was acidified with 10% acetic acid and ether-extracted. The extract was washed several times with water, dried, shaken with Norit, filtered and the solvent and excess nitroparaffin distilled off under reduced pressure. The crystalline residue was drained on a porous tile and recrystallized, usually from methanol.

Procedure II, applied to Mannich bases derived from such secondary bases as morpholine, was essentially the same as procedure I except that volatile secondary base was not lost from the reaction mixture and refluxing was maintained for 4–7.5 hours.

Procedure III was almost identical with that described by Reichert and Posemann[12] for the condensation of Mannich bases with nitromethane.

Procedure IV was essentially the same as Procedure I except that sodium hydroxide was omitted from the reaction mixture. The results obtained are set out in Table III.

TABLE IV

SEMICARBAZONES OF NITROKETONES

Ketone	Formula	M.p., °C.	Nitrogen, % Calcd.	Nitrogen, % Found
XI	$C_{13}H_{18}N_4O_3$	136	20.2	19.8
XII	$C_{14}H_{20}N_4O_3$	154.5	19.2	18.8
XIII	$C_{11}H_{20}N_4O_3$	178	21.9	21.8
XIV	$C_8H_{16}N_4O_3$	193	25.9	25.9
XV	$C_{11}H_{20}N_4O_3$	138	21.9	21.6
XVI	$C_{13}H_{18}N_4O_3$	163	20.2	19.9
XIX	$C_{18}H_{20}N_4O_3$	138.5	16.5	16.4

1,6-Diphenyl-4-ethyl-4-nitro-octan-1,7-dione.—Sodium (0.23 g.) was dissolved in anhydrous methanol (5 ml.) and XVI (2.21 g.) in anhydrous methanol (10 ml.) added. A solution of G (2.33 g.) in anhydrous methanol (5 ml.) was then added and the solution refluxed gently for 3 hours. The product (2.5 g., 70%) crystallized on cooling, and after recrystallization from ethanol formed fine white needles, m.p. 163.5°.

Anal. Calcd. for $C_{22}H_{25}NO_4$: C, 71.9; H, 6.8; N, 3.8. Found: C, 72.0; H, 6.9; N, 3.7.

SYDNEY, AUSTRALIA

[CONTRIBUTION FROM THE NATIONAL ADVISORY COMMITTEE FOR AERONAUTICS, LEWIS FLIGHT PROPULSION LABORATORY]

Reaction of Cyclopropyl Chloride with Lithium. Isolation of Dicyclopropyl

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The reaction of cyclopropyl chloride with lithium in ether was investigated. Cyclopropane was the principal product of the reaction; however, 10 to 12% yields of a liquid hydrocarbon product were also obtained. The physical and chemical properties of a hydrocarbon isolated from the liquid product support the opinion that the hydrocarbon is dicyclopropyl. M.p., b.p., $n^{20}D$, d^{20} and the infrared spectrum are presented for the hydrocarbon, and for cyclopropyl chloride, 1,1-dichlorocyclopropane and *trans*-1,2-dichlorocyclopropane. The cyclopropyl halides were prepared by the photochlorination of cyclopropane.

Dicyclopropyl, the smallest of the dicyclic hydrocarbons, was desired for an investigation of the effects of structure on combustion characteristics and other properties pertinent to the research at the Lewis laboratory on aircraft propulsion systems. Several methods are known for the preparation of hydrocarbons which contain one cyclopropyl ring, but a search of the literature when the present work was begun did not reveal any previous attempts to prepare a hydrocarbon which contained two cyclopropyl rings.[1] The reaction of cyclopropyl chloride with lithium was investigated as a possible approach to the synthesis of dicyclopropyl. The properties of a hydrocarbon isolated from the reaction products support the opinion that the hydrocarbon is dicyclopropyl.

Cyclopropane was the principal product of the reaction of cyclopropyl chloride with lithium in ether; however, 10 to 12% yields of a liquid hydrocarbon product, boiling from 70–75°, were also obtained.[2] Unsaturated constituents, traces of which were disclosed by infrared spectra, were removed from the liquid product by extractions with aqueous silver nitrate.[3] The extracted hydrocarbon was then passed through silica gel and, finally, fractionated azeotropically with ethanol through a column at better than 150 theoretical plate efficiency. The physical properties of the purified hydrocarbon, determined by methods previously referenced,[4] are given in Table I.

The composition of the purified hydrocarbon corresponded well to that calculated for C_6H_{10}. Unsaturated structures were ruled out since the hydrocarbon was inert toward both bromine in carbon tetrachloride and potassium permanganate in acetone. The strong absorption in the infrared spectrum (Fig. 1(d)) at 9.82 μ was interpreted to be convincing evidence that the hydrocarbon contained at least one cyclopropyl group, since absorption attributed to the cyclopropyl ring has previously been observed in this region in over 40 hydrocarbon and non-hydrocarbon derivatives of cyclopropane.[5] A comparison of the molecular refractivity of the hydrocarbon with the refractivities of several monoalkylcyclopropanes (Table II) showed the hydrocarbon had twice the exaltation of the structures which contained only one cyclopropyl ring. The method of preparation and these

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(1) Recently, L. I. Smith and E. R. Rogier (THIS JOURNAL, **73**, 3840 (1951)) reported the synthesis of 2-phenylbicyclopropyl. They were unable to prepare the necessary intermediate for the synthesis of dicyclopropyl by the same method.

(2) When methylcyclohexane was used in place of ether, no reaction occurred. When sodium was used in place of lithium in ether, the products were the same, but the yield of liquid product was reduced.

(3) M. Murray and E. Stevenson, THIS JOURNAL, **66**, 812 (1944).

(4) I. A. Goodman and P. H. Wise, *ibid.*, **72**, 3076 (1950).

(5) Unpublished work from this Laboratory and J. M. Derfer, E. E. Pickett and C. B. Boord, *ibid.*, **71**, 2482 (1949).