(uncor.). After several recrystallizations from methanol–ether, an analytical sample was obtained, m.p. 197–198°.

Anal. Calcd. for $C_6H_{14}N_4O \cdot 0.5H_2SO_4$: N, 27.05; S, 7.74. Found: N, 27.09; S, 7.92.

This material produced a melting point depression when mixed with the 1-amidino-O-butylurea sulfate prepared above.

1-Amidino-O-hexylurea Sulfate.—The material obtained by the procedure of Dutta and Ray[1] had a melting point of 132–135°.

1-Amidino-3-hexylurea.—The free base was prepared by the procedure of Curd,[2] m.p. 91–92°. The sulfate was prepared by treatment of a methanolic solution of base with ethereal sulfuric acid until the solution was slightly acidic. The solvent was removed *in vacuo* and the oily residue was dissolved in isopropyl alcohol. The addition of ether precipitated the sulfate, m.p. 128–129° (uncor.). Further recrystallization from isopropyl alcohol–ether raised the melting point to 131–134°.

Anal. Calcd. for $C_8H_{18}N_4O \cdot 0.5H_2SO_4$: C, 40.83; H, 8.14; N, 23.81. Found: C, 41.11; H, 8.09; N, 24.01.

A mixture melting point with the 1-amidino-O-hexylurea sulfate prepared above produced a depression.

1-Amidino-O-ethylurea Sulfate. A.—The compound was prepared by the procedure of Dutta and Ray.[1] As prepared by us it had a melting point of 165–166° which differed from that reported in the literature (137–138°). This experiment was repeated with the same results.

B.—1-Amidino-O-ethylurea hydrochloride was synthesized by the procedure of Kawana,[4] m.p. 162–163° (uncor.), in agreement with the latter workers' melting point. The hydrochloride was converted to the sulfate in the following manner. Amberlite IRA-400 resin (20 g.) was slurried with distilled water, put into a chromatographic column, washed with 2 *N* sulfuric acid until the eluent produced a negative chloride test, and then washed with distilled water to neutrality. 1-Amidino-O-ethylurea hydrochloride (2 g.) was dissolved in 95% ethanol (25 ml.) and passed through the column. Ethanol (100 ml.) was added and the solution was collected and evaporated to yield a white solid which was dissolved in 20 ml. of 95% ethanol. Acetone was added (20 ml.), whereupon a white solid formed, m.p. 166–167°. A mixture melting point with the material obtained by the method of Dutta and Ray[1] showed no depression.

The Rearrangement of 1-Piperidinemethanethiol Esters

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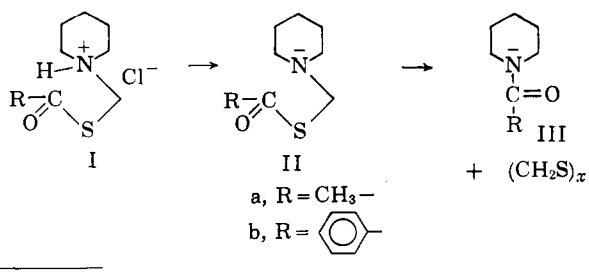
In an attempt to characterize a compound believed to be the hydrochloride salt of 1-piperidinemethanethiol acetate (Ia) it was converted to the free base (IIa). On distillation a clear liquid was obtained which gave an incorrect analysis for the desired product. An investigation of the nuclear magnetic resonance (n.m.r.) and infrared spectra of the distillate indicated the product to be 1-acetylpiperidine (IIIa). This was confirmed by comparison with an authentic sample.



I II III

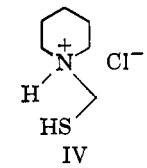
a, R = CH_3–

b, R =

+ $(CH_2S)_x$

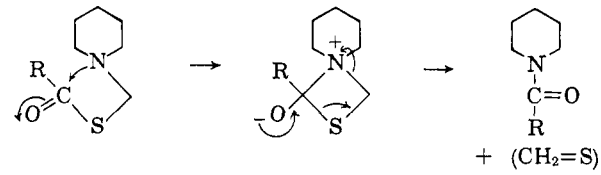
(1) National Institutes of Health Predoctoral Fellow, 1963–1964.

To expand on this study a convenient synthesis for the acetyl and benzoyl esters Ia and Ib from 1-piperidinemethanethiol hydrochloride (IV) was devised. The parent compound, IV, prepared by the method of Binz and Pence,[2] was heated with the corresponding thiolcarboxylic acid to afford the desired compound and hydrogen sulfide.



IV

The rearrangement of the thiol esters was effected by refluxing the free base in benzene. A plausible explanation for this facile rearrangement can be depicted as follows.



+ $(CH_2=S)$

Experimental[3]

1-Piperidinemethanethiol Acetate Hydrochloride (Ia).—To 16.7 g. (0.1 mole) of 1-piperidinemethanethiol hydrochloride (IV) was added 55.0 g. (0.72 mole) of thiolacetic acid and the mixture was heated at steam-bath temperature for 3 hr. The reaction mixture was allowed to cool and then added to 500 ml. of anhydrous ether. The resulting precipitate was collected and washed twice with ether. The white solid was recrystallized from absolute alcohol to give 16.4 g. (79%) of the desired compound: m.p. 169° dec.; $\lambda_{C=O}^{CHCl_3}$ 5.85 μ; n.m.r. 150 (s, $-CH_3$), 269 (s, NCH_2S), 197 (m, NCH_2), and 104 (m, CCH_2) c.p.s. in D_2O.

Anal. Calcd. for $C_8H_{16}ClNOS$: C, 45.82; H, 7.68; N, 6.67; S, 15.29. Found: C, 45.90; H, 7.42; N, 6.78; S, 14.78.

1-Piperidinemethanethiol Benzoate Hydrochloride (Ib).—A suspension of 10.0 g. (0.06 mole) 1-piperidinemethanethiol hydrochloride (IV) and 25.0 g. (0.18 mole) of thiolbenzoic acid in 50 ml. of dichloromethane was heated at steam-bath temperature for 1.5 hr. The dichloromethane was removed and the residue was poured into 500 ml. of anhydrous ether. The resulting precipitate was collected and redissolved in a minimum amount of dichloromethane. This solution was dropped slowly into 250 ml. of anhydrous ether. After repeating this procedure three times, 10.2 g. (63%) of the desired material, a crystalline solid, m.p. 158° dec., was obtained. Decomposition of this material occurred somewhat during the purification procedure with enough impurity being formed to prohibit an accurate elemental analysis. The structure was established by spectral comparison with 1-piperidinemethanethiol acetate hydrochloride (Ia). Ib showed $\lambda_{C=O}^{CHCl_3}$ 5.95 μ; n.m.r. 477 and 484 (d, *ortho* =CH—), 456 (m, *meta* and *para* =CH—), 288 (s, NCH_2S), 190 (m, NCH_2), and 117 (m, CCH_2) c.p.s. in $DCCl_3$.

1-Piperidinemethanethiol Acetate (IIa) and 1-Piperidinemethanethiol Benzoate (IIb).—Aqueous solutions of 1-piperidinemethanethiol acetate hydrochloride (Ia) and 1-piperidinemethanethiol benzoate hydrochloride (Ib) were made basic with saturated sodium bicarbonate solution. These solutions were then extracted with ether and the extracts were dried over anhydrous magnesium sulfate. The ether was removed *in vacuo* without the use of heat; the free bases were examined by n.m.r. and infra-

(2) A. Binz and L. H. Pence, *J. Am. Chem. Soc.*, **61**, 3134 (1939).

(3) Melting points were obtained on a calibrated Kofler micro hot stage and a Thomas–Hoover Unimelt and are corrected. Infrared data were recorded on Beckman IR5 and IR8 spectrophotometers. Nuclear magnetic resonance data were recorded on a Varian Associates Model A-60 spectrophotometer using TMS as the internal standard. Microanalyses were conducted by Drs. G. Weiler and F. B. Strauss, Oxford, England.

red. IIa showed $\lambda_{C=O}^{CHCl_3}$ 5.95 μ; n.m.r. 140 (s, $-CH_3$), 271 (s, NCH_2S), 144 (m, NCH_2), and 89 (m, CCH_2) c.p.s. in CCl_4; IIb showed $\lambda_{C=O}^{CHCl_3}$ 6.00 μ; n.m.r. 479 and 486 (d, *ortho* =CH—), 449 (m, *meta* and *para* =CH—), 287 (s, NCH_2S), 150 (m, NCH_2), and 87 (m, CCH_2) c.p.s. in CCl_4.

Rearrangement of 1-Piperidinemethanethiol Acetate (IIa) to 1-Acetylpiperidine (IIIa).—A solution of 7.6 g. (0.044 mole) of 1-piperidinemethanethiol acetate (IIa) in 25 ml. of benzene was prepared. The solution was heated for 12 hr. The residue on distillation afforded 2.18 g. (60%) of 1-acetylpiperidine, b.p. 56–60° at 1.0 mm. (lit.[4] b.p. 226–227° at 760 mm.). The infrared and n.m.r. spectra of this substance were identical with those of an authentic sample: $\lambda_{C=O}^{CHCl_3}$ 6.14 μ; n.m.r. 117 (s, $-CH_3$), 205 (m, NCH_2), and 96 (m, CCH_2) c.p.s. in CCl_4.

Rearrangement of 1-Piperidinemethanethiol Benzoate (IIb) to 1-Benzoylpiperidine (IIIb).—The same procedure was used in the rearrangement of IIa. A solution of 8.2 g. (0.034 mole) of 1-piperidinemethanethiol benzoate (IIb) afforded 3.30 g. (50%) of 1-benzoylpiperidine, b.p. 118–120° at 1.0 mm., m.p. 46–47° (lit.[4] b.p. 320–321° at 760 mm., m.p. 48°). The mixture melting point, infrared, and n.m.r. spectra of this substance were identical with those of an authentic sample: $\lambda_{C=O}^{CHCl_3}$ 6.18 μ; n.m.r. 439 (s, all =CH—), 206 (m, NCH_2), and 94 (m, CCH_2) c.p.s. in CCl_4.

Polymeric Thioformaldehyde.—The undistillable residue obtained in the rearrangement of IIa and IIb was recrystallized from $CHCl_3$. The yield was 0.98 g. (48%) of a mixture of polymeric forms of thioformaldehyde, m.p. 136–145°, in the rearrangement of IIa and 0.71 g. (45%) in the rearrangement of IIb [lit.[5] m.p. 175–176° for $(CH_2S)_x$, m.p. 216° for $(CH_2S)_3$]. No attempt was made to isolate trithiane from the mixture or to characterize the other thioformaldehyde polymers.

Acknowledgment.—The authors gratefully acknowledge the support of this project by the National Institutes of Health Grants 1-F1-GM 14, 467-01A2, and RG-9254.

(4) "Dictionary of Organic Compounds," I. M. Heilbron, *et. al.*, Ed., Oxford University Press, New York, N. Y., 1953.
(5) A. Wohl, *Ber.*, **19**, 2344 (1886).

The Chemistry of Carbanions. VII. The Stereochemistry of Addition of Various Methylmagnesium Reagents[1]

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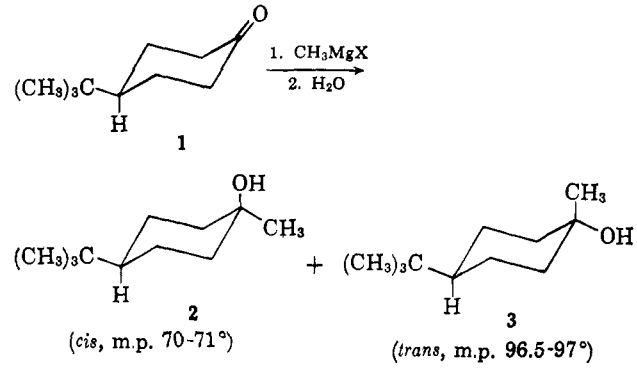
Earlier studies[2,3] of additions of organomagnesium compounds to ketones had demonstrated that dialkylmagnesium compounds are more reactive than alkylmagnesium halides (Grignard reagents). Either organometallic reactant, when in excess, produces the same proportion of addition product to by-products resulting from enolization or reduction. However, the organometallic reagent, corresponding stoichiometrically to an alkylmagnesium alkoxide, obtained from reaction of 1 mole of a dialkylmagnesium with either 1 mole of a ketone or 1 mole of a tertiary alcohol produced much greater proportions of by-products from enolization and reduction on reaction with simple ketones.[3] This latter result was observed only when the alkylmagnesium alkoxide reagent was free from magnesium halide. One interpretation of these results is that all of the reactions in the presence of magnesium halide as well as reactions employing an excess of a dialkylmagnesium each involve the same organomagnesium species, perhaps a dialkylmagnesium, as the actual reacting species, whereas reactions with halide-free alkylmagnesium alkoxides involve a different reacting species which may be either an alkylmagnesium alkoxide or some more complex structure. To examine this hypothesis further we have examined the n.m.r. spectra of various organomagnesium reagents, a study to be reported elsewhere, and have studied the stereochemical course of additions of various methylmagnesium derivatives to a ketone to learn if differences could be detected.

This latter study, reported here, utilized the reaction of various methylmagnesium derivatives with 4-*t*-butylcyclohexanone (**1**) to form the *cis*- (**2**) and *trans*-carbinols (**3**).[4] In this reaction we wished to take advantage of the seemingly valid generalization[5] that use of a more hindered cyclohexanone derivative or use of a more hindered organometallic reagent can be expected to increase the proportion of the cyclohexanol isomer with an axial hydroxyl function and an equatorial alkyl group (corresponding to **2**). From the proportions of isomers **2** and **3** formed we might hope to learn whether the reacting species derived from various methylmagnesium reagents were different. The results of this study are summarized in Table I which lists the average values obtained from two or more determinations. All reaction mixtures obtained from organomagnesium reagents in the presence of magnesium bromide or with excess dimethylmagnesium yielded predominantly a mixture of alcohols **2** and **3** with little enolization (as measured by the amount of ketone **1** recovered). The products of these reactions contained 55–65% of the axial alcohol **2**. From reaction mixtures containing the halide-free methylmagnesium salt of 3-methyl-3-pentanol, a large amount



(1) This research has been supported by research grants from the National Institutes of Health (R. G. 8761) and the National Science Foundation (G-25214).
(2) (a) J. G. Aston and S. A. Bernhard, *Nature*, **165**, 485 (1950); (b) D. O. Cowan and H. S. Mosher, *J. Org. Chem.*, **27**, 1 (1962); **28**, 204 (1963); (c) M. Anteunis, *ibid.*, **26**, 4214 (1961); **27**, 596 (1962); M. Anteunis and R. D'Hollander, *Tetrahedron Letters*, **No. 26**, 1275 (1962); (d) N. M. Bikales and E. I. Becker, *Can. J. Chem.*, **41**, 1329 (1963); (e) A. Kirrmann, M. Vallino, and J. F. Fauvarque, *Bull. soc. chim. France*, 1408 (1963).
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(4) (a) B. Cross and G. H. Whitham, *J. Chem. Soc.*, 3892 (1960); (b) C. H. DePuy and R. W. King, *J. Am. Chem. Soc.*, **83**, 2743 (1961); (c) W. J. Houlihan, *J. Org. Chem.*, **27**, 3860 (1962); (d) H. Favre and D. Gravel, *Can. J. Chem.*, **39**, 1548 (1961).
(5) (a) G. Just and R. Nagarajan, *Experientia*, **18**, 402 (1962); (b) G. F. Hennion and F. X. O'Shea [*J. Am. Chem. Soc.*, **80**, 614 (1958)] found that addition of ethylmagnesium bromide to **1** gave product containing 73% of the product with an axial hydroxyl function (corresponding to **2**), whereas use of methylmagnesium bromide produced a mixture containing 55–60% of the corresponding isomer **2** (ref. 4 and this study).