ments (see Experimental). The mass spectral fragmentation pattern of III is interesting and indicates a number of rearrangement peaks, which may warrant a more detailed examination of the electron impact behavior of such trithiones. The molecular ion peak at *m/e* 342 was quite small (2% intensity relative to the base peak), while the base peak at mass 81 apparently corresponds to $C_6H_9^+$. The next highest peak occurs at *m/e* 114 ($C_6H_{10}S^+$), while other sulfur-containing peaks may be those at *m/e* 146 ($C_6H_{10}S_2^+$) and 228 ($C_{12}H_{20}S_2^+$). The appropriate sulfur isotope peaks at *m/e* 344, 116, 148, and 230 were also observed.

In conclusion it may be stated that while the reaction of hydrogen sulfide with morpholinoenamines may lead to interesting sulfur-containing products, it does not represent a feasible method to monomeric thiones as claimed by Nomura and Takeuchi.[5]

EXPERIMENTAL[9]

Reaction of 1-morpholinocyclohexene with hydrogen sulfide. A solution of 5.5 g. of cyclohexanone, 11 g. of morpholine, and 50 mg. of *p*-toluenesulfonic acid in 150 cc. of benzene was heated under reflux overnight in a Soxhlet extraction apparatus, the thimble of which contained 10 g. of Linde No. 4 molecular sieves, care being taken to exclude all atmospheric moisture. Distillation afforded 7.2 g. of the enamine I,[6] b.p. 143–145°/20 mm., as a colorless liquid, which exhibited no infrared carbonyl absorption but did show a strong band at 1630 cm.$^{-1}$

Anal. Calcd. for $C_{10}H_{17}NO$: C, 71.81; H, 10.25; N, 8.38. Found: C, 71.22; H, 10.05; N, 8.00.

The freshly prepared enamine (6.5 g.) was dissolved in 100 cc. of dry dimethylformamide and hydrogen sulfide (directly from tank) was passed through the ice cooled solution for a period of 6 hr. Pentane (160 cc.) was added to the yellow solution followed (with cooling) by 50 cc. of 6*N* hydrochloric acid. The cold, pink organic layer was washed with water, dried, and distilled to afford 5.2 g. of a pink colored liquid, b.p. 70–72°/13 mm., whose color faded over a period of a few hours. The substance had a powerful and extremely unpleasant odor; its absorption spectrum, determined immediately after distillation, exhibited $\lambda_{max}^{isooctane}$ 510 mμ, ε 0.8; based on the extinction of a pure steroid thione,[3] this *1,1-dithiocyclohexane* (II) specimen could not have contained more than 5% of thione. The infrared spectrum did not contain any carbonyl bands, but only strong SH absorption at 2520 cm.$^{-1}$, while integration of the NMR spectrum confirmed the presence of 12 protons, of which 2 were involved in the SH signal at 147 c.p.s. relative to tetramethylsilane.

Anal. Calcd. for $C_6H_{12}S_2$: C, 48.64; H, 8.16; S, 43.20. Found; C, 49.14; H, 7.88; S, 41.93.

Pyrolysis of 4.0 g. of II by distillation through a heated Pyrex tube (320°) provided 3.6 g. of dicyclohexyl disulfide,[7] b.p. 115°/1 mm., which lacked SH absorption in the infrared.

Anal. Calcd. for $C_{12}H_{22}S_2$: C, 62.58; H, 9.63. Found: C, 62.32; H, 9.76.

When the hydrogen sulfide reaction was repeated as described above except that a 1:1 mixture of dimethylformamide and anhydrous ether was employed as solvent, distillation yielded 76% of a pale yellow liquid, b.p. 125°/0.1 mm., melting at 95–99° after crystallization from methanol which represents the *trimer* III.[10] The infrared spectrum of the substance exhibited no carbonyl, SH, or double bond bands, the ultraviolet and visible spectra indicated the total absence of thione absorption and the NMR spectrum contained no signals attributable to a proton attached to sulfur.

Anal. Calcd. for $C_{18}H_{30}S_3$: C, 63.13; H, 8.83; mol. wt., 342. Found: C, 63.63; H, 9.09; mol. wt., 342 (mass spectrum[8]).

1,1-Dithiocyclopentane. Cyclopentanone was transformed in 87% yield into 1-morpholinocyclopentene[11] (b.p. 126°/25 mm.; *Anal.* Calcd. for $C_9H_{15}NO$: C, 70.55; 9.87; N, 9.14. Found: C, 70.23; H, 9.70; N, 9.30), and then treated with hydrogen sulfide gas in dimethylformamide solution exactly as described above for I. Distillation provided 69% of *1,1-dithiocyclopentane* as a pinkish liquid, b.p. 70–72°/10 mm., whose absorption maximum (isooctane solution) at 495 mμ (ε 0.9) indicated the presence of less than 5% of thione; the infrared spectrum exhibited the expected strong SH band at 2500 cm.$^{-1}$

Anal. Calcd. for $C_5H_{10}S_2$: C, 44.77; H, 7.52. Found: C, 45.65; H, 7.74.

Reaction of 3-morpholino-Δ²-cholestene (IV) *with hydrogen sulfide.* Cholestan-3-one (745 mg.) was transformed into the enamine IV by the above described procedure; yield, 698 mg., m.p. 119–124° (after recrystallization from ether-methanol), $[\alpha]_D$ +43° (*c*, 1.0 in chloroform). The infrared spectrum confirmed the absence of a carbonyl band.

Anal. Calcd. for $C_{31}H_{53}NO$: C 81.69; H, 11.72. Found: C, 81.30; H, 1.48.

Hydrogen sulfide gas was passed for 3 hr. at 0° through a solution of 472 mg. of IV in 200 cc. of 1:1-dimethylformamide–anhydrous ether. Evaporation of the solvent provided 416 mg. of colorless crystals, which showed no absorption whatsoever above 300 mμ. One recrystallization from methanol-chloroform afforded the analytical sample of the trimer V, m.p. 153–155°, $[\alpha]_D$ +21 (*c*, 1.0 in chloroform), which did not exhibit any carbonyl, SH, or double bond absorption in the infrared, nor did the NMR spectrum contain any signal in the 147 c.p.s. region (see II). The substance was recovered unchanged after shaking for 6 hr. at room temperature in chloroform solution with 6*N* hydrochloric acid.

Anal. Calcd. for $C_{81}H_{138}S_3$: C, 80.54; H, 11.52; S, 7.95. Found: C, 80.30; H, 11.52; S, 7.85.

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(9) Boiling points are uncorrected. We are indebted to Dr. Lois J. Durham for the NMR spectra, measured at 60 mc., and to Mr. Erich Meier for the microanalyses.

(10) See E. Fromm, *Ber.*, **60**, 2090 (1961).

(11) S. Hünig and W. Lendle, *Ber.*, **93**, 909 (1960).

Alkylation of Amines by Esters and Lithium Aluminum Hydride. II

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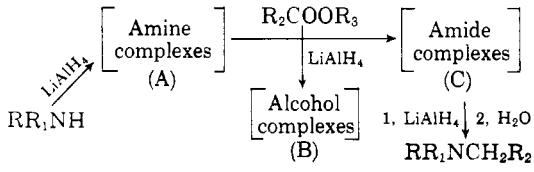
The *one-step* alkylation of amines by esters and lithium aluminum hydride has been reported by Segre *et al.*,[1] Testa *et al.*,[2] and by this laboratory.[3]

(1) (a) A. Segre, R. Viterbo, and G. Parisi, *Ann. chim. (Rome)*, **47**, 1177 (1957); (b) A. Segre and R. Viterbo, *Experientia*, **14**, 54 (1958).

(2) E. Testa, L. Fontanella, L. Mariani, and G. F. Cristiani, *Ann.*, **633**, 56 (1960).

(3) W. B. Wright, Jr., *J. Org. Chem.* **25**, 1033 (1960).



Additional experiments have now been run which indicate that this procedure is unsatisfactory for the preparation of secondary amines from primary amines, but is often suitable for the preparation of tertiary amines from secondary amines. This method is operable at relatively low temperatures and may, therefore, find application in the preparation of tertiary amines from sensitive compounds. The preparation and isolation of an amide, often required as an intermediate in the preparation of amines by lithium aluminum hydride reduction, is avoided. This method should also be considered in reactions where quaternary salts are to be avoided, or in place of reductive procedures where such groups as halogen would be hydrogenized.

The alkylation of secondary amines by esters and lithium aluminum hydride appears to be a general reaction for the preparation of tertiary amines. However, yields vary from poor to excellent depending upon the nature of the reagents and the reaction conditions used. Low yields were obtained when arylalkylamines were alkylated.[3] On the other hand, high yields were often obtained when dialkylamines were alkylated (Table I), especially if the reagents were such that side reactions like ester condensation could not occur. Ethyl benzoate and ethyl acetate were effective alkylating agents as evidenced by the preparation of 1-benzylpiperidine and 1-ethylpiperidine in yields of 80–85%, and 1-benzyl-4-methylpiperazine and 1-benzyl-4-phenylpiperazine in yields of about 60%. Yields were less satisfactory when ethyl butyrate was used as a reagent for the introduction of the butyl group. Yields of 1-phenethylpiperidine and 1-phenethylpyrrolidine were less than 20%, due to concomitant ester condensation of the ethyl phenylacetate. Also of interest are the reactions of piperidine with ethyl 3-piperidinopropionate to form trimethylenebispiperidine in 23% yield, and with propiolactone to form 3-piperidinopropanol in 48% yield.

We were unable to alkylate primary amines by this procedure. All attempts to prepare secondary amines by the reaction of phenethylamine, cyclohexylamine, or aniline with lithium aluminum hydride and ethyl acetate or ethyl benzoate failed. However, we did isolate low yields of amides from those reactions in which the lithium aluminum hydride used was less than that required to both liberate the active hydrogen from the amine and reduce the ester to the alcohol. The possibility was considered that the amides were obtained instead of the secondary alkylamines because insufficient lithium aluminum hydride was present, but when a larger ratio of lithium aluminum hydride was used, neither the amide nor the secondary amine was isolated.

Efforts to prepare amides in high yield by using only 0.25–0.50 mole of lithium aluminum hydride per mole of primary amine and a large excess of ester resulted in yields of only 28–42%. Similarly, when piperidne was allowed to react with 0.25 mole of lithium aluminum hydride and an excess of ethyl benzoate and ethyl acetate, 1-benzoylpiperidine and 1-acetylpiperidine were obtained in yields of 15–20%.

The mechanism for the alkylation of secondary amines by esters and lithium aluminum hydride has been discussed.[3] The fact that primary amines are not easily alkylated, but under the conditions just described are converted to amides, suggests the following explanation. When the amine and lithium aluminum hydride are mixed, hydrogen is liberated and lithium aluminum amine complexes (A) are formed. As the ester is added to the mixture, it is rapidly reduced by unchanged lithium aluminum hydride to alcohols, also present as lithium aluminum complexes (B). If ester is still present after all of the lithium aluminum hydride is used up in forming A and B, a *slower* reaction occurs in which the ester is amidated by A to form a lithium aluminum complex of an amide (C). This third step becomes important only if excess ester is present. Secondary amines are not formed as there is no lithium aluminum hydride available for reduction of C. Addition of water then liberates the amide, alcohols, and recovered amine.

As evidence for the above series of reactions, amides were isolated from every reaction of primary amines with esters and lithium aluminum hydride, in which there was less lithium aluminum hydride than that required to form amine complexes and completely reduced the ester. On the other hand, when excess lithium aluminum hydride was used, neither amide nor secondary amine was observed.

It appears that the amidation step (C) is much more rapid with secondary amine complexes than with primary amine complexes, and occurs while lithium aluminum hydride is still present. This reaction is apparently faster than the lithium aluminum hydride reduction of the ester. Reduction of the amide complex occurs and an alkylated product results.

Higuchi *et al.*[4] state that amine complexes are generally very soluble in tetrahydrofuran or ether solvents when one hydrogen is liberated, but insoluble in these solvents when the second hydrogen is replaced. This difference in solubility may be an important factor in the determination of the course of this reaction. We observed this difference in solubility in some of our reactions. However, the product from the

(4) T. Higuchi, J. Concha, and R. Kuramoto, *Anal. Chem.*, **24**, 685 (1952).

TABLE I

REACTIONS OF SECONDARY AMINES WITH ESTERS AND LITHIUM ALUMINUM HYDRIDE

Reagents				Molar Ratios[a]		Yield,	B.P./		Picrate		Carbon		Hydrogen		Nitrogen	
Ester	Amine	Product	Method	L/A	E/A	%	Mm.	n_D^{25}	M.P.	Formula[c]	Calcd.	Found	Calcd.	Found	Calcd.	Found
Ethyl benzoate	Piperidine	1-Benzylpiperidine	A[d]	1.5	3.0	85	120–124/14[e]	1.525	183–184[f]	$C_{18}H_{20}N_4O_7$	53.5	53.4	5.0	5.3	13.9	14.0
Ethyl benzoate	Piperidine	1-Benzoylpiperidine	B[g]	0.25	1.2	15	170–175/14[h]			$C_{12}H_{15}NO$	76.2	76.1	8.0	8.7	7.4	7.4
Ethyl benzoate	1-Methylpiperazine	1-Benzyl-4-methylpiperazine	A	2.5	3.0	60	128–132/12[i]	1.525	265 dec.[j]	$C_{24}H_{24}N_8O_{14}$	44.4	44.0	3.7	3.6	17.3	17.3
Ethyl benzoate	1-Phenylpiperazine	1-Benzyl-4-phenylpiperazine	A	2.5	3.0	63	160–170/1[k]		185–187[l]	$C_{29}H_{26}N_8O_{14}$	49.0	48.7	3.7	3.8	15.8	15.8
Ethyl acetate	Piperidine	1-Ethylpiperidine	A	2.0	3.0	80	126–130[l]	1.442	170–172[m]	$C_{13}H_{18}N_4O_7$	45.6	45.8	5.3	5.5	16.4	16.4
Ethyl acetate	Piperidine	1-Acetylpiperidine	B[g]	0.25	1.2	20	103–105/14[n]			$C_7H_{13}NO$[n]	66.1	66.6	10.3	10.6	11.0	10.2
Ethyl butyrate	Piperidine	1-Butylpiperidine	A[d]	1.5	3.0	55	170–174[o]	1.445	133–134[o]	$C_{15}H_{22}N_4O_7$	48.6	48.7	6.0	6.2	15.1	14.8
Ethyl butyrate	1-Phenylpiperazine	1-Butyl-4-phenylpiperazine	A	2.5	3.0	6[p]	166–172/12[q]	1.542	150–152[j]	$C_{26}H_{28}N_8O_{14}$	46.2	46.6	4.2	4.5	16.6	16.9
Ethyl phenylacetate	Pyrrolidine	1-Phenethylpyrrolidine	A	2.5	2.5	17	118–124/11[r]	1.523	140–142[s]	$C_{18}H_{40}N_4O_7$	53.5	53.3	5.0	5.3	13.9	13.8
Ethyl phenylacetate	Piperidine	1-Phenethylpiperidine	B[d]	1.5	3.0	<20[t]	134–138/15[u]	1.527	150–151[v]	$C_{19}H_{22}N_4O_7$	54.5	54.5	5.3	5.6	13.4	13.2
Propiolactone	Piperidine	3-Piperidinopropanol	A	2.0	2.0	48	102–105/12[w]	1.475	66–67[x]	$C_{14}H_{20}N_4O_8$	45.2	45.1	5.4	5.6	15.0	14.7
Ethyl 3-piperidinopropionate	Piperidine	1,1-Trimethylenebispiperidine	B	2.0	2.0	23	136–140/11[y]	1.484	225–227[l,z]	$C_{25}H_{32}N_8O_{14}$	44.9	44.8	4.8	4.8	16.8	16.4

[a] L/A = lithium aluminum hydride/amine; E/A = ester/amine. [b] Melting points are uncorrected. [c] Formulas and analyses are for the picrate if reported. [d] One hour at reflux temperature. [e] H. T. Clarke, *J. Chem. Soc.*, 1788 (1912) reports b.p. 119°/13 mm. Ref. 1a reports m.p. 170°. [f] Three hours at reflux temperature. [g] H. Staudinger and H. Schneider, *Ber.*, 56, 699 (1923) report b.p. 180°/15 mm. [i] M. Borovička *et al.*, *Chem. listy* 49, 231 (1955) report b.p. 88°/0.6 mm. [j] Dipicrate. [k] Solidified on cooling. V. Prelog and Z. Blažek, *Collection Czechoslov. Chem. Communs.* 6, 549 (1934) report m.p. 59°. [l] H. T. Clarke, *J. Chem. Soc.*, 1788 (1912) reports b.p. 129°. [m] Ref. 1a reports m.p. 167°. [n] H. Staudinger and H. Schneider, *Ber.*, 56, 699 (1923) report b.p. 125°/30 mm. Although analysis was poor, the infrared spectrum appeared to be satisfactory. [o] J. von Braun, *Ber.*, 40, 3914 (1907) reports b.p. 175–176° for the base and m.p. 132° for the picrate. [p] Purification by distillation was difficult. Actual yield was extimated to be 20%. [q] K. Fujii *et al.*, *J. Pharm. Soc. Japan*, 74, 1052 (1954) report b.p. 150°/5 mm. [r] B. Wojcik and H. Adkins, *J. Am. Chem. Soc.*, 56, 2419 (1934), report b.p. 113–115°/9 mm. [s] J. von Braun and R. S. Cahn, *Ann.*; 436, 262 (1924) report m.p. 139–140°. [t] Impure. IR spectrum contained bands which appeared to be due to amide and alcohol groups. Identified as picrate. [u] C. Mannich and H. Davidsen, *Ber.*, 69, 2106 (1936), report b.p. 138–139°/14 mm. [v] A. Pollard and R. Robinson, *J. Chem. Soc.*, 2770 (1927) report m.p. 144–145°. [w] J. G. M. Dunlop, *J. Chem. Soc*, 1998 (1912) reports b.p. 100°/10 mm. [x] J. von Braun *et al.*, *Ber.*, 55, 1666 (1922) report m.p. 63–64°. [y] A. P. Terent'ev and E. A. Terent'eva, *J. Gen. Chem.*, 12, 415 (1942) report 141–142°/10 mm. [z] H. Hörlein and R. Kneisel, *Ber.*, 39, 1429 (1906) report m.p. 215–220°.

TABLE II

REACTIONS OF PRIMARY AMINES WITH ESTERS AND LITHIUM ALUMINUM HYDRIDE

Reagents				Molar Ratios[b]		Hours at	Yield of Amide,	
Ester	Amine	Amide Isolated[a]	Method	L/A	E/A	Reflux	%	M.P.[c]
Ethyl benzoate	Aniline	Benzanilide	C	0.25	1.2	3	42	164–166[d]
Ethyl benzoate	Aniline	Benzanilide	C	0.25	1.2	3	37	164–166
Ethyl benzoate	Aniline	Benzanilide	A	1.5	3.0	18	17	164–165
Ethyl benzoate	Aniline	[e]	A	2.5	3.0	18	[e]	
Ethyl benzoate	Cyclohexylamine	Cyclohexylbenzamide	B	1.5	3.0	3	[f]	148–149[f]
Ethyl benzoate	Phenethylamine	[g]	A	3.0	3.0	18	[g]	
Ethyl acetate	Aniline	[h]	A	1.5	3.0	1	[h]	
Ethyl acetate	Cyclohexylamine	Cyclohexylacetamide	C	0.25	1.2	3	35	106–108[i]
Ethyl acetate	Cyclohexylamine	Cyclohexylacetamide	C	0.50	1.2	3	28	104–105
Ethyl acetate	Cydlohexylamine	Cyclohexylacetamide	A	1.5	3.0	18	37	108–109
Ethyl acetate	Cyclohexylamine	[g]	A	2.5	3.0	18	[g]	
Ethyl acetate	Phenethylamine	[g]	A	3.0	3.0	18	[g]	

[a] Alcohols and primary amines were also present in the reaction mixture. [b] L/A = lithium aluminum hydride/amine; E/A = ester/amine. [c] Uncorrected. Microanalyses were satisfactory. [d] A. F. Holleman *et. al.*, *Ber.*, **44**, 704 (1911) report m.p. 164°. [e] Infrared spectrum of product from ether extract of acid solution lacked a carbonyl band. Ether extract from alkaline solution did not contain amide or secondary amine. [f] Yield not determined. O. Wallach, *Ann.*, **343**, 40 (1905), reports m.p. 149°. [g] Ether extract from acid solution was not examined. Ether extract from alkaline solution did not contain amide or secondary amine. [h] Infrared spectrum of product contained a strong amide band. The reaction product was not purified. [i] A. Skita and H. Rolfes, *Ber.*, **53**, 1242 (1920), report m.p. 109°.

reaction of cyclohexylamine with 0.5 mole of lithium aluminum hydride was soluble in tetrahydrofuran; and yet we were unable to isolate alkylated products when such a solution was treated with esters. It appears, therefore, that some other factor, perhaps steric effects resulting from the polymeric structure of the primary amine/lithium aluminum hydride complexes, is more important in determining the course of this reaction.

EXPERIMENTAL

The picrates were prepared by adding an excess of ethanolic picric acid to a solution of the base in ethanol. The mixture was warmed on the steam bath for a few minutes and allowed to cool to room temperature. The picrate was filtered, washed with ethanol, dried in an oven at 65°, and submitted for analysis without further purification.

The amines were treated with the esters and lithium aluminum hydride by procedures essentially as described below.

Reactions of secondary amines with esters and lithium aluminum hydride (*Table I*). *Method A.* A solution of 0.1 mole of the amine in tetrahydrofuran was added dropwise to a solution of 0.2 mole of the lithium aluminum hydride in 250 ml. of tetrahydrofuran. Nitrogen gas was passed over the mixture during this addition. The reaction mixture was stirred for 15–30 min. and then heated to reflux temperature. A solution of the ester in about 2 parts of tetrahydrofuran was added dropwise over a period of about 1 hr. The reaction mixture was heated under reflux for 18 hr. and cooled. Eight milliliters of water, 24 ml. of 15% sodium hydroxide, and 24 ml. of water were added successively, and the solid was filtered off and washed with tetrahydrofuran. The mother liquor was treated with 20 ml. of concentrated hydrochloric acid and concentrated to remove the solvent. The residue was diluted with water and extracted with ether to remove nonbasic products. The aqueous layer was made alkaline and the basic products were extracted into ether and distilled.

Method B. The reaction was run as described above, except that hydrochloric acid was not added and the extractions were omitted.

Method C. A solution of 0.025–0.05 mole of lithium aluminum hydride in 50–100 ml. of tetrahydroduran was added dropwise to a solution of 0.1 mole of the amine in 50 ml. of tetrahydrofuran. A solution of 0.12 mole of the ester in 40 ml. of tetrahydrofuran was added and the mixture was heated under reflux for 3 hr. The reaction mixture was treated with water and 15% sodium hydroxide, filtered, and the mother liquor was concentrated to remove the solvent. The residue was triturated with ether or ethyl acetate, and filtered. If crystals did not form, the product was distilled.

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Reactive Methylene Compounds. III. Attempted Syntheses of Cinnolines

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During the course of investigations on reactive methylene compounds,[2,3] the synthesis of cinnolines (II) by heating methyl 2,3-dioxobutyrate α-phenylhydrazones (I. R = substituted phenyl; R′ = CH_3) with sulfuric acid or anhydrous aluminum chloride was attempted. However, under the various conditions tried, only deesterification took place and the various acids thus obtained (I. R = substituted phenyl; R′ = H) are reported in Table I. The behavior is similar with ethyl

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(2) H. G. Garg and S. S. Joshi, *J. Org. Chem.*, **26**, 946 (1961).

(3) H. G. Garg, *J. Org. Chem.*, **26**, 948 (1961).