A sensitive helical quartz spring was used to weigh a crystal of pure stearic acid of about 40 micrograms with an accuracy of 0.05 microgram. The water in a Teflon-coated film balance was heated to 71°—slightly above the melting point of stearic acid.[4] The crystal was placed on the surface between two barriers; it disappeared in a few seconds. The system was allowed to cool to room temperature, and the pressure–area isotherm was determined. In replicate experiments, reproducibility was excellent.

A typical isotherm is shown in the figure. In position and shape, it is almost identical to those obtained with *n*-hexane solvent; it differs slightly from those obtained with benzene, and only at pressures below 15 dynes. Extrapolation of the upper portion to zero pressure gives an area per molecule of 20.2 Å.^{2}, which agrees well with the values 20.0 to 20.5 obtained with benzene, *n*-hexane, and chloroform solvents.[3,5] Collapse occurs at slightly higher pressures and is less abrupt.

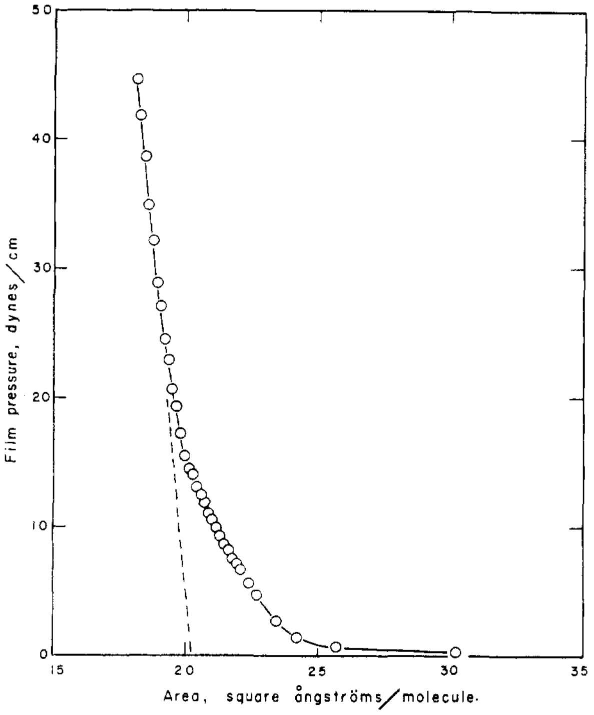

Fig. 1.—Pressure-area isotherm for stearic acid spread without solvent.

Examination of detailed plots of several such isotherms reveals that they consist of many straight-line segments, each extending through several data points. At lower pressures, the segments are short and numerous; they differ from experiment to experiment but give smiliar smoothed curves. At higher pressures, they are longer and often occur in isotherms obtained with solvents. Rapid expansion–compression reversibility has been observed along the segments and the downward extensions of them. Elastic deformation of islands or island clusters may produce such segments; changes in slope may correspond to sudden rearrangements in the monolayer when a limit of elasticity is exceeded. Such observations are not consistent with classical phase changes.[6,7]

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[4] Small crystals spread slowly at room temperature but the time required for complete spreading was prohibitive. See N. K. Adam, "The Physics and Chemistry of Surfaces," 3rd edition, Oxford University Press, London, 1941, p. 102.

[5] H. E. Reis, Jr., and H. D. Cook, *J. Colloid Sci.*, **9**, 535 (1954).

[6] N. K. Adam, "The Physics and Chemistry of Surfaces," 3rd edition, Oxford University Press, London, 1941, p. 39.

[7] W. D. Harkins, "The Physical Chemistry of Surface Films," Reinhold Publ. Corp., New York, N. Y., 1952, p. 106.

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RECEIVED OCTOBER 29, 1958

LITHIUM DIETHOXYALUMINOHYDRIDE AS A SELECTIVE REDUCING AGENT—THE REDUCTION OF DIMETHYLAMIDES TO ALDEHYDES

Sir:

The introduction of alkoxy substituents into lithium aluminum hydride provides a means of moderating the reducing capacity of this powerful reagent. In this way, lithium tri-*t*-butoxyaluminohydride proved to be a mild reducing agent[1] which made possible the convenient reduction of acid chlorides to aldehydes.[2] The yields of 40 to 60% realized in the case of certain aliphatic and alicyclic acid chlorides led us to examine alternative routes which would permit the synthesis of such aldehydes in higher yields by the selective reduction of carboxylic acid derivatives.

The reduction of the N-acylcarbazoles by lithium aluminum hydride has been utilized as a convenient route to the unsaturated aldehydes, $C_5H_6(CH{=}CH)_nCHO$ ($n = 2$, 4 and 6),[3] and Weygand has demonstrated that the related reduction of the N-methylanilides is applicable to a wide range of aldehyde preparations.[4] Consequently, we undertook an examination of the reduction of tertiary amides by various alkoxyaluminohydrides.

We have observed that the addition of lithium diethoxyaluminohydride (10% excess, in ether solution) to two molar equivalents of the acyldimethylamides in ether solution at 0° results in the synthesis of aldehydes in yields of 75–90% after hydrolysis. The procedure appears to be equally satisfactory, both for aliphatic and alicyclic derivatives and for aromatic. The scope of the reaction is indicated by the data in Table I.

The reagent may be synthesized conveniently *in situ* by addition of either two moles of ethanol or one mole of ethyl acetate to one mole of lithium aluminum hydride in ether solution. The synthesis of cyclohexanecarboxaldehyde given below is typical.

A solution of 20.6 g. (0.234 mole) of ethyl acetate in 250 ml. of anhydrous ether was added over a period of 2 hours to 200 ml. of a 1.17 *M* solution of lithium aluminum hydride (0.234 mole) in ether, cooled in an ice-bath. The reagent solution thus prepared was added over a period of 30 min. to a well-stirred solution of 60.6 g. (0.390 mole) of N,N-dimethylcyclohexanecarboxamide in 250 ml.

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[1] H. C. Brown and R. F. McFarlin, THIS JOURNAL, **78**, 252 (1956); **80**, 5372 (1958).

[2] H. C. Brown and B. C. Subba Rao, *ibid.*, **80**, 5377 (1958).

[3] G. Wittig and P. Hornberger, *Ann.*, **577**, 11 (1952).

[4] F. Weygand, *et al.*, *Angew. Chem.*, **65**, 525 (1953).

TABLE I

YIELDS OF ALDEHYDE IN THE REDUCTION OF ACYL DIMETHYLAMIDES BY LITHIUM DIETHOXYALUMINOHYDRIDE

Acid	Yield of aldehyde, % Analysis with 2,4-dinitrophenylhydrazine	By isolation
n-Butyric	90	
n-Hexanoic	80	67
Lauric	90	
Isobutyric	89	
Pivalic	75	63
Cyclohexanecarboxylic	85	71
Cyclopropanecarboxylic	78	
α-Naphthoic	81	
o-Chlorobenzoic	80	78
o-Methoxybenzoic	84	
Nicotinic	89	
10-Undecenoic	87	
Ethylthioacetic	69	

of ether (0°). After 30 min. at 0°, the reaction mixture was refluxed gently for another 30 min., and hydrolyzed at 0° with 2 *N* sulfuric acid. The ether layer and extracts were separated, dried and distilled. The aldehyde, b.p. 76.5–77.5° at 48 mm., $n^{20}D$ 1.4495, was isolated in a yield of 30.6 g.-71%.

This new aldehyde synthesis should provide a convenient alternative route for proceeding from carboxylic acids to the corresponding aldehydes.

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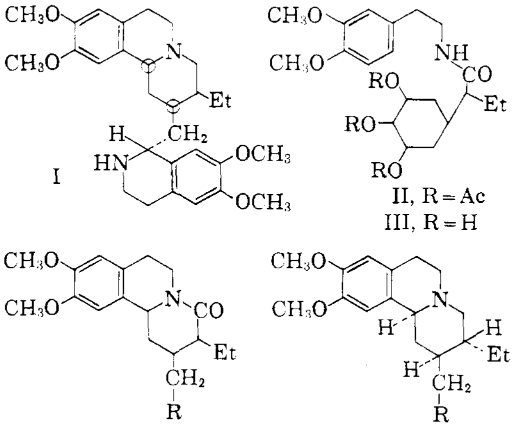
RECEIVED DECEMBER 4, 1958

THE SYNTHESIS OF EMETINE FROM HEXAHYDROGALLIC ACID

Sir:

Recent studies[1] on the stereochemistry of emetine (I) and reports[2] of the total synthesis of this important ipecac alkaloid have been of widespread interest. By employing a derivative of hexahydrogallic acid as the source of a β-substituted glutaric dialdehyde intermediate,[3] we have found a fundamentally new route to emetine.

High pressure reduction of gallic acid with 5% rhodium-on-alumina furnished hexahydrogallic acid of m.p. 198–199° in yields of 45 to 50%.[4] Following acetylation[4] and conversion to the corresponding diazoketone derived from 1-diazopropane, this acid was homologated by the Arndt–Eistert procedure in the presence of homoveratrylamine to the amide II. Selective hydrolysis of II provided the free triol III, m.p. 197–198°,[5] in 25% over-all yield from the acetylated acid. Cleavage of III with periodic acid and cyclization of the product with warm phosphoric acid gave, as a mixture of isomers, the aldehyde lactam IV [infrared ($CHCl_3$), 5.80 and 6.17 μ].[6] This, by oxidation with silver oxide, was converted, in 15–20% yield from III, to the lactam acid Va, m.p. 190–191° (acetone-soluble). Also formed, in comparable or lower yields, were two isomeric lactam acids Vb, m.p. 194–196°, and Vc, m.p. 221–223° (both acetone-insoluble).



I

II, R = Ac
III, R = H

IV, R = CHO
V, R = CO_2H

VI, R = CO_2Et or CO_2Me
VII, R = CH_2OH
VIII, R = CH_3

Reduction of the lactam function in Va by sodium in alcohol led, after esterification with ethanol, to the known[1,2] amino ester VI (R = CO_2Et), m.p. 65–66°,[2a] whose conversion to emetine already has been described[2a,c] and confirmed[7] (with R = CO_2Me). Hydride reduction of the methyl ester, m.p. 53–54°, of Va yielded the amino alcohol VII, which proved, on the basis of indistinguishable IR spectra and undepressed perchlorate mixed m.p. 178–181°, to be identical with that prepared from authentic[2a,7] samples of VI, but which differed from preparations derived from Vb and Vc. In addition, Va was converted, by hydride reduction, O-tosylation, and further reduction, to the previously synthesized[1d,8] *trans*-diethyltricyclic base VIII (hydrochloride m.p. and mixed m.p. 247–248°; identical infrared spectra).[1d,7] Evidence for the emetine stereochemistry of VIII has already been presented.[1a,d,7,8]

Other synthetic applications of hexahydrogallic acid are under investigation.

Acknowledgments.—We are greatly indebted to Drs. A. R. Battersby and E. E. van Tamelen for comparison samples and spectra; to the Eli Lilly Company for homoveratrylamine; to the University of Kansas for a grant from the General Re-

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[1] (a) A. R. Battersby, *Chemistry & Industry*, 1324 (1958); (b) A. Brossi, A. Cohen, J. M. Osbond, Pl. A. Plattner, O. Schnider and J. C. Wickens, *ibid.*, 491 (1958); (c) A. R. Battersby, R. Binks, D. Davidson, G. C. Davidson and T. P. Edwards, *ibid.*, 982 (1957); (d) E. E. van Tamelen, P. E. Aldrich and J. B. Hester, Jr., THIS JOURNAL, **79**, 4817 (1957).

[2] (a) A. R. Battersby and J. C. Turner, *Chemistry & Industry*, 1324 (1958); (b) M. Barash and J. M. Osbond, *ibid.*, 490 (1958); (c) R. P. Ebstigneeva, R. S. Livshits, L. I. Zakharkin, M. S. Baĭnova and N. A. Preobrazhenskiĭ, *Doklady Akad. Nauk, S.S.S.R.*, **75**, No. 4, 539 (1950) [*C. A.*, **45**, 7577 (1951)] and later papers.

[3] Such synthetic potentialities were apparently first recognized by H. O. L. Fischer and G. Dangschat [*Helv. Chim. Acta*, **17**, 1200 (1934)] in connection with quinic and shikimic acids.

[4] For previous synthesis, *cf.* W. Mayer, P. Bachmann and F. Kraus, *Ber.*, **88**, 316 (1955).

[5] Correct analytical and spectral data were obtained for this and all other intermediates whose melting points are recorded.

[6] *Cf.* a similar reaction sequence in the recently announced total synthesis of yohimbine [E. E. van Tamelen, M. Shamma, A. W. Burgstahler, J. Wolinsky, R. Tamm and P. E. Aldrich, THIS JOURNAL, **80**, 5006 (1958)]. For a closely related cyclodehydration to form the erythrinane and erysotrine skeletons, *cf.* B. Belleau, *ibid.*, **75**, 5765 (1953); *Chemistry & Industry*, 410 (1956).

[7] E. E. van Tamelen and J. B. Hester, Jr., THIS JOURNAL, **81**, 507 (1959).

[8] A. R. Battersby and S. Cox, *Chemistry & Industry*, 983 (1957).