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., $n^{20}\mathrm{D}$ 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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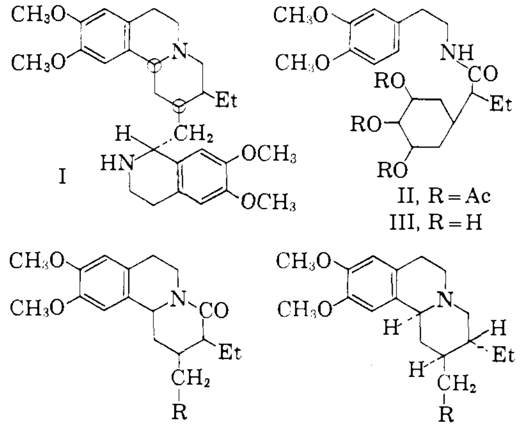
RECEIVED DECEMBER 4, 1958

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).

search Fund; and to the National Institutes of Health for a summer research appointment.

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RECEIVED NOVEMBER 19, 1958

GRIGNARD SYNTHESIS OF ALKYL DECABORANES

Sir:

Inorganic Grignard reagents derived from decaborane, and the condensation reaction to prepare benzyldecaborane recently have been reported.[1] We subsequently found that these reagents could not be used readily to prepare a series of alkyl decaboranes by the normal Grignard condensation reaction, using *n*-alkyl chlorides, bromides and iodides. Seeking a general method for preparing alkyl decaboranes, other types of condensing agents were tried with $B_{10}H_{13}MgX$. Success with a tri-alkyl oxonium salt, R_3OBF_4,[2] led us to believe that alkyl fluorides might be used as condensing agents. Although alkyl fluorides have not been used in Grignard condensation reactions[3] (presumably because of the strong carbon–fluorine bond in *n*-alkyl fluorides), we found that $B_{10}H_{13}MgX$ could be condensed successfully with a series of *n*-alkyl fluorides, and an alicyclic fluoride. The substituted decaboranes prepared by this principle are shown in Table I.

TABLE I

Substituted decaborane	Yield, %	Elemental analyses, %					
		Theoretical			Found		
		C	H	B	C	H	B
Butyl[a]	25	26.9	12.4	60.1	25.6	12.5	59.7
Amyl[a]	40	31.3	12.5	56.3	31.2	12.7	58.1
Hexyl[a]	24	35.0	12.6	52.4	35.1	12.8	53.2
Cyclohexyl[b]	6	35.3	11.8	52.9	33.8	11.8	51.9
Heptyl[a]	23	38.2	12.7	49.0	37.5	12.7	51.1
Octyl[a]	16	41.0	12.8	46.1	40.9	12.6	44.9

[a] Colorless liquid. [b] White solid, m.p. 90–91°.

Since this reaction appeared to be of general interest to organic chemistry, we tested it with a simple organic Grignard reagent that could not be alkylated with the usual *n*-alkyl halides. Accordingly, after ethylmagnesium bromide failed to react with *n*-butyl bromide, the former was treated with *n*-butyl fluoride. This resulted in a substantial yield of *n*-hexane (11%) and 3-methylpentane (7%); the latter were identified by their mass spectra.

Experimental.—$B_{10}H_{13}MgBr$ was prepared by the reaction of equivalent quantities of decaborane and CH_3MgBr, using 5 to 6 g. of decaborane. The ether solvent was then distilled and a two-fold excess of alkyl fluoride was added. The resulting solution was stirred for 48–64 hours under nitrogen, at ambient temperature; in some cases an ice-bath was necessary initially. After the prolonged standing the highly volatile components were distilled and the residues were extracted with dried petroleum ether. These extracts were fractionally vacuum distilled. The substituted decaboranes were characterized by elemental composition and cryoscopic molecular weight.

The *n*-alkyl fluorides were prepared by[4] adding mercuric fluoride slowly to an alkyl bromide or iodide, at 40–50°. The product was then vacuum distilled and redistilled at atmospheric pressure.

Acknowledgment.—The authors are indebted to Marshall Wheeler for technical assistance, Phyllis Wheeler for analyses, and James V. Lowe, Jr., for the preparation of the alkyl fluorides. The encouragement of Drs. Sol Skolnik and F. A. H. Rice is gratefully acknowledged.

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(1) B. Siegel, J. Mack, J. Lowe and J. Gallaghan, THIS JOURNAL, **80**, 4523 (1958).

(2) H. Meerwein, *et al.*, *J. prakt. Chem.*, **154**, 83 (1939).

(3) The only report on this subject was a recent Russian article in which, in the specialized instance of several tertiary fluorides, greater yields of condensation were obtained than was the case with tertiary chlorides: A. D. Petrov, *et al.*, *Chem. Abstracts*, **50**, 16057 (1956).

(4) A. L. Henne and T. Midgley, THIS JOURNAL, **58**, 884 (1936).

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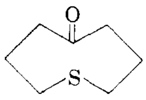
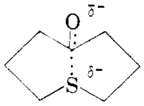
RECEIVED OCTOBER 11, 1958

TRANSANNULAR SULFUR-CARBONYL INTERACTION

Sir:

We have now obtained evidence of transannular sulfur–carbonyl interaction across an eight-membered ring in the model compound 1-thiacyclooctan-5-one (I). Prediction of the occurrence of


I



Ia

such interaction was made earlier,[1] as methods were being developed for the detection of nitrogen–carbonyl interaction in cyclic aminoketones and aminoacyloins of medium ring size.[2]

Compound I was obtained (45% crude yield) by the Dieckmann cyclization of diethyl γ,γ'-thiabis-butyrate[3] using potassium *t*-butoxide in xylene under high dilution conditions, with high speed stirring under nitrogen,[4] then hydrolysis and decarboxylation, and was purified by recrystallization from ether–pentane and sublimation, colorless needles, m.p. 53.2–54.2° (*Anal.* Calcd. for $C_7H_{12}OS$: C, 58.29; H, 8.39. Found: C, 58.21; H, 8.36).[5] A by-product, when the addition rate of the sulfide diester was relatively rapid (25 hours),[6] was the sixteen-membered ring compound, 1,9-dithiacyclohexadecane-5,13-dione, colorless needles, m.p. 65–66°, $\nu_{\max}^{\mathrm{CCl_4}}$ 1715 cm.$^{-1}$ (*Anal.* Found: C, 58.64; H, 8.25; mol. wt., 252 (calcd. 288)).

Indication of the contribution of $S–C_{CO}$ "interacted" forms (Ia) of 1-thiacycloöctan-5-one was found in the infrared carbonyl maximum (shoulder) at 1684

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(1) N. J. Leonard, R. C. Fox and M. Ōki, THIS JOURNAL, **76**, 5708 (1954).

(2) For the most recent articles in the series on transannular nitrogen-carbonyl interaction, see: (a) N. J. Leonard, J. A. Adamcik, C. Djerassi and O. Halpern, *ibid.*, **80**, 4858 (1958); (b) N. J. Leonard, D. F. Morrow and M. T. Rogers, *ibid.*, **79**, 5476 (1957).

(3) Made in this laboratory in 1954 by T. Hashizume, private communication.

(4) N. J. Leonard and R. C. Sentz, *ibid.*, **74**, 1704 (1952).

(5) This product was identical with a sample of the same material kindly forwarded to us by Dr. Charles G. Overberger of the Polytechnic Institute of Brooklyn and described in the accompanying Communication by C. G. Overberger and A. Lusi; see also: A. Lusi, Master's Thesis, Polytechnic Institute of Brooklyn, 1959.

(6) N. J. Leonard, M. Ōki and S. Chiavarelli, *ibid.*, **77**, 6234 (1955).