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

DEPARTMENT OF CHEMISTRY
UNIVERSITY OF KANSAS ALBERT W. BURGSTAHLER
LAWRENCE, KANSAS ZOE J. BITHOS

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 C	H	B	Found 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.

(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).

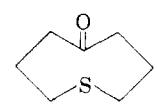
U. S. NAVAL PROPELLANT PLANT JOHN GALLAGHAN
INDIAN HEAD, MD. BERNARD SIEGEL

RECEIVED OCTOBER 11, 1958

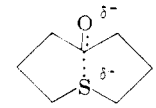
TRANSANNULAR SULFUR-CARBONYL INTERACTION

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°, $\nu_{max}^{CCl_4}$ 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

(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).

cm.$^{-1}$, accompanying the strong maximum at 1703 cm.$^{-1}$ (0.01 M soln. in CCl_4)[7] corresponding to "non-interacted" conformations of I. By contrast, under the same conditions, tetrahydro-4H-1-thiapyran-4-one (II)[8] and 1-thiacycloheptan-4-one (III)[9] exhibited single maxima at 1716 and 1711 cm.$^{-1}$, respectively. The dipole moment of the eight-membered ring compound (I), 3.81 D in benzene, was higher than that of the seven-membered ring compound (III) (3.04 D; 1.73 D for II).[2b] It is important to note that S–C_{CO} interaction occurs to a lesser extent than N–C_{CO} transannular interaction in the electronic *ground state* by comparison (infrared especially) of 1-thiacycloöctan-5-one with 1-methyl-1-azacycloöctan-5-one.[7]

Finally, the ultraviolet absorption maxima of I in cyclohexane, at 226 mμ (ϵ 2445) and ~232 mμ (ϵ 2150), are associated with *excitation* of the interacting S–C_{CO} system (λ^{III}_{max} 223 mμ (ϵ 695), λ^{II}_{max} 233 mμ (ϵ 507).[10]

(7) N. J. Leonard, M. Ōki, J. Brader and H. Boaz, THIS JOURNAL, **77**, 623 (1955).

(8) E. A. Fehnel and M. Carmack, *ibid.*, **70**, 1813 (1948).

(9) C. G. Overberger and A. Katchman, *ibid.*, **78**, 1965 (1956).

(10) E. Fehnel and M. Carmack (*ibid.*, **71**, 84 (1949)) have suggested earlier that the difference between the ultraviolet spectrum of tetrahydro-4H-1-thiapyran-4-one (II) and those of its acyclic analogs is attributable to direct interaction between the 1,4-atoms in the excited state. (See also V. Georgian, *Chemistry and Industry*, 1480 (1957).) If this is correct, the four- to five-fold increase in intensity for the eight membered ring over the six-membered ring may be regarded as manifestation of the greater contribution of transannular interaction in the medium-ring compound.

(11) Sinclair Refining Co. Fellow in Organic Chemistry, 1957–1958. Work done under the sponsorship of the Sinclair Research Laboratories, Inc.

THE NOYES CHEMICAL LABORATORY NELSON J. LEONARD
UNIVERSITY OF ILLINOIS THEODORE L. BROWN
URBANA, ILLINOIS TERRY W. MILLIGAN[11]

RECEIVED DECEMBER 4, 1958

ON THE MECHANISM OF OXIDATIVE DECARBOXYLATION OF PYRUVATE

Sir:

Extracts of *Escherichia coli* contain an enzyme system which catalyzes an oxidative decarboxylation of pyruvate represented by reaction 1.[1,2,3]

$$\text{Pyruvate} + \text{DPN}^{+}[4] + \text{CoA} \xrightarrow[(RS_2)]{(TPP)} \text{acetyl CoA} + CO_2 + \text{DPNH} + H^{+} \quad (1)$$

We have obtained highly purified preparations (250-fold purification) of this system from extracts of the Crookes strain. It is apparently an enzyme complex,[5] and sediments in the ultracentrifuge (1 to 2 hr. at 144,000 × g) as a dark yellow, fluorescent pellet. The complex contains a flavin which has been tentatively identified as FAD. Release of the flavin by precipitation of the enzyme complex with ammonium sulfate at pH 3.6 resulted in a decrease in the enzymatic activities: dihydrolipoic dehydrogenase, DPN reduction (reaction 1), pyruvate dismutation, and reduction of free lipoic acid (reaction 2).[3,6] These activities were restored by

$$CH_3COCO_2H + \text{LipS}_2 + HPO_4^{=} \xrightarrow[(CoA)]{(TPP,RS_2)} CH_3COOPO_3^{=} + \text{Lip(SH)}_2 + CO_2 \quad (2)$$

addition of FAD, but not of FMN (Table I). The dihydrolipoic transacetylase activity of the preparation was not affected by removal of flavin.

TABLE I

REACTIVATION OF SPLIT PYRUVATE DEHYDROGENATION SYSTEM WITH FAD

Assay system	Before splitting	Specific activities[a] After splitting: Without FAD	With FAD[g]	With FMN[g]
Lipoic DeH[b]	870	214	544	228
Dismutation[c]	870	214	486	144
Reaction 1[d]	156	20	62	20
Reaction 2[e]	90	32	64	32
Lip. transac.[f]	112	100	110	100

[a] Expressed as μmoles/hr./mg. protein based on assays described previously. [b] Ref. 7, pH 7. [c] Ref. 3. [d] Ref. 8. [e] Ref. 6, pH 7, 5 μmoles DL-lipoamide employed. [f] Ref. 8. [g] Aliquots of split complex incubated 10 min. at 30° with FAD or FMN before assay. Final concentration of added flavin in assays was 10^{-5} to 10^{-6} M.

These data indicate that FAD is an essential component of the enzyme complex, presumably associated with dihydrolipoic dehydrogenase. The data are consistent with the reaction sequence[2,3] shown for oxidative decarboxylation of pyruvate by the enzyme complex.

$$CH_3COCO_2H + \text{TPP} \rightleftharpoons [CH_3CHO\text{–TPP}] + CO_2 \quad (3)$$

$$[CH_3CHO\text{–TPP}] + \begin{matrix}S\\|\\S\end{matrix}\!\!>\!R \rightleftharpoons \begin{matrix}HS\\CH_3COS\end{matrix}\!\!>\!R + \text{TPP} \quad (4)$$

$$\text{CoA–SH} + \begin{matrix}HS\\CH_3COS\end{matrix}\!\!>\!R \rightleftharpoons CH_3COS\text{–CoA} + \begin{matrix}HS\\HS\end{matrix}\!\!>\!R \quad (5)$$

$$\begin{matrix}HS\\HS\end{matrix}\!\!>\!R + \text{FAD} \rightleftharpoons \begin{matrix}S\\|\\S\end{matrix}\!\!>\!R + \text{FADH}_2 \quad (6)$$

R = $-CH_2CH_2\underset{|}{C}H(CH_2)_4CO$-enzyme

The reduced flavoprotein produced in reaction 6 apparently can interact with DPN (*cf.* reaction 1) and free lipoic acid (*cf.* reaction 2).

(1) S. Korkes, *et al.*, *J. Biol. Chem.*, **193**, 721 (1951).

(2) I. C. Gunsalus, in "The Mechanism of Enzyme Action," The Johns Hopkins Press, Baltimore, Md., 1954, p. 545.

(3) L. J. Reed, *et al.*, *J. Biol. Chem.*, **232**, 123, 143 (1958).

(4) Abbreviations: DPN, diphosphopyridine nucleotide; CoA, coenzyme A; TPP, thiamine pyrophosphate; FAD, flavin adenine dinucleotide; LipS_2, free lipoic acid; Lip(SH)_2, free dihydrolipoic acid; RS_2, protein-bound lipoic acid.

(5) R. S. Schweet, *et al.*, *J. Biol. Chem.*, **196**, 563 (1952); D. R. Sanadi, *et al.*, *ibid.*, **197**, 851 (1952).

(6) I. C. Gunsalus, *Federation Proc.*, **13**, 715 (1954).

(7) L. P. Hager and I. C. Gunsalus, THIS JOURNAL, **75**, 5767 (1953).

(8) L. P. Hager, Thesis, University of Illinois, 1953.

(9) During this investigation Dr. V. Massey, *Biochim. et biophys. acta*, **30**, 205 (1958) communicated to us his significant finding (ref. 9) that highly purified diaphorase exhibited strong dihydrolipoic dehydrogenase activity.

CLAYTON FOUNDATION BIOCHEMICAL
INSTITUTE AND DEPARTMENT OF CHEMISTRY
UNIVERSITY OF TEXAS MASAHIKO KOIKE
AUSTIN, TEXAS LESTER J. REED

RECEIVED NOVEMBER 25, 1958

CHELATION AS A DRIVING FORCE IN SYNTHESIS. A NEW ROUTE TO α-NITRO ACIDS AND α-AMINO ACIDS

Sir:

Dibasic α-nitro acids (I) are converted in weakly basic media to acid salts which rapidly decarbox-