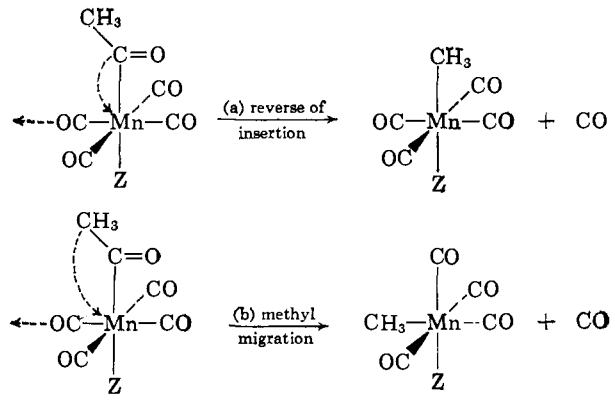

Fig. 1.—Decarbonylation of *trans*-$CH_3COMn(CO)_4Z$: (a) by reverse of insertion, (b) by methyl migration.

is by methyl migration (see Fig. 1, Z = $P(Ph)_3$). This would require that the rate of disappearance of the acetyl band in *trans*-$CH_3COMn(CO)_4P(Ph)_3$ be equal to the rate of change of the arrangement of terminal C–O stretching frequencies from that for *trans*-$CH_3COMn(CO)_4P(Ph)_3$ to that for *cis*-$CH_3Mn(CO)_4P(Ph)_3$. Since previous work[1] on the related reaction shown in eq. 1 had shown that in *n*-hexane the formation of intermediates, which could complicate kinetics and make a decision on a mechanism more difficult, was avoided, *n*-hexane was used as the solvent for the present work.

The reactions were followed by thermostating solutions of *trans*-$CH_3COMn(CO)_4P(Ph)_3$ in dry *n*-hexane under nitrogen. Samples were withdrawn at intervals and their spectra recorded in 1-mm. cells on a Beckman IR9 spectrophotometer. Solution concentrations were 0.6×10^{-2} *M* for following changes in terminal C–O stretching frequencies, and 1.5×10^{-2} *M* for following the disappearance of the acetyl C–O band.

The change from the terminal C–O frequencies of *trans*-$CH_3COMn(CO)_4P(Ph)_3$ to the arrangement for *cis*-$CH_3Mn(CO)_4P(Ph)_3$, as calculated from the rate of appearance of the bands in the product at 2055 and 1983 $cm.^{-1}$, was a first-order process with a rate constant of $3.83\ (\pm 0.05) \times 10^{-5}$ $sec.^{-1}$. The disappearance of the acetyl band of *trans*-$CH_3COMn(CO)_4P(Ph)_3$ was also a first-order process with a rate constant of $3.71\ (\pm 0.08) \times 10^{-5}$ $sec.^{-1}$.

The agreement between these two figures is good evidence for the direct conversion of *trans*-$CH_3COMn(CO)_4P(Ph)_3$ to *cis*-$CH_3Mn(CO)_4P(Ph)_3$ by methyl migration (see Fig. 1, Z = $P(Ph)_3$).

It is possible to devise more complicated mechanisms, involving two or more steps, one of which is rate controlling and the others very rapid, which are compatible with our kinetic results. However, we regard methyl migration as the simplest and by far the most likely mechanism for this reaction. This is believed to be the first real evidence for such a migration in these systems.[4]

We have also shown that a solution of *cis*-$CH_3Mn(CO)_4P(Ph)_3$ in tetrahydrofuran is reconverted, by storing under CO, to *trans*-$CH_3COMn(CO)_4P(Ph)_3$.

(4) Similar results have since been obtained by us in tetrahydrofuran solution, the rate constant obtained by either method being $2.70\ (\pm 0.07) \times 10^{-5}$ $sec.^{-1}$. Our results in this solvent show that the sample of $CH_3COMn(CO)_4P(Ph)_3$, whose isolation was referred to in an earier publication,[1] was in fact a mixture of *cis*-$CH_3Mn(CO)_4P(Ph)_3$ and *trans*-$CH_3COMn(CO)_4P(Ph)_3$ in which the former compound predominated. There is no evidence for the existence of *cis*-$CH_3COMn(CO)_4P(Ph)_3$.

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New Lincomycin-Related Antibiotics

Sir:

Chemical studies[1] have elucidated the structure of lincomycin[2–6] (Ia). We now report the isolation and the structure of four new lincomycin-related antibiotics designated U-21,699, U-11,921, U-11,973, and U-20,943. Antibiotic U-21,699 normally occurs in lincomycin fermentations, while the production of U-11,921, U-11,973, and U-20,943 is induced by addition of DL-ethionine, methyl α-thiolincosaminide (IIa), and ethyl α-thiolincosaminide (IIb), respectively, to fermentation media of *S. lincolnensis*. The antibiotics were recovered by adsorption on carbon followed by elution with aqueous acetone and crystallization as hydrochloride salts.

Antibiotic U-21,699 (Ib) hydrochloride, $C_{17}H_{32}N_2O_6S \cdot HCl \cdot 0.5H_2O$,[7] $[\alpha]^{25}D$ +147°, contains one $-NCH_3$, one $-SCH_3$, two $C-CH_3$, and one basic function, pK_a' 7.68. Infrared absorptions (3400, 1690, and 1590 $cm.^{-1}$) indicated OH, NH, and amide functions. The n.m.r.[8,9] spectrum of Ib is very similar to that of Ia, except that it shows eight hydrogens in the 30–90-c.p.s. region, while the spectrum of Ia shows ten hydrogens in the same area. Both display the doublet at 67 and 75 c.p.s. (3H) assigned to the CH_3-CHO grouping present in methyl α-thiolincosaminide (IIa) and a triplet at 45, 52, and 59 c.p.s. (3H) assigned to the CH_3CH_2- of the side chain on the hygric acid nucleus (IIIa). This triplet, along with two hydrogens in the $-CH_2-$ region, is indicative of an ethyl group replacing the propyl group of lincomycin. Thus, Ib represents the structure of U-21,699. This conclusion was substantiated by hydrazinolysis of U-21,699 affording authentic methyl α-thiolincosaminide (IIa), and the hydrazide of a new amino acid which was hydrolyzed to the crystalline hydrochloride $C_8H_{15}NO_2 \cdot HCl$ (IIIb). Infrared spectra and the positive rotational shift at lower pH suggested an α-L-amino acid.

The n.m.r. spectra of IIIa and IIIb differ only in the area from 40 to 120 c.p.s. in that IIIa has a triplet

(1) H. Hoeksema, B. Bannister, R. D. Birkenmeyer, F. A. MacKellar, F. Kagan, B. J. Magerlein, W. Schroeder, G. Slomp, and R. R. Herr, *J. Am. Chem. Soc.*, **86**, 4423 (1964).

(2) Lincocin is the trademark of The Upjohn Company for lincomycin hydrochloride.

(3) D. J. Mason, A. Dietz, and C. DeBoer, *Antimicrobial Agents Chemotherapy*, 554 (1962).

(4) R. R. Herr and M. E. Bergy, *ibid.*, 560 (1962).

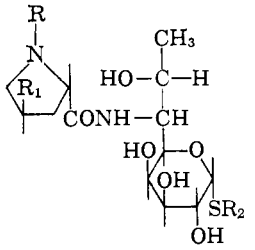
(5) L. J. Hanka, D. J. Mason, M. R. Burch, and R. W. Treick, *ibid.*, 565 (1962).

(6) C. N. Lewis, H. W. Clapp, and J. E. Grady, *ibid.*, 570 (1962).

(7) Analytical values for all the compounds described in this paper were consistent with the indicated formulas.

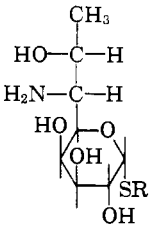
(8) Spectra were calibrated in c.p.s. units at 60 Mc., downfield from internal sodium 2,2-dimethyl-2-silapentane-5-sulfonate. Spectra were observed with a Varian A-60 spectrometer on solutions (*ca.* 0.4 ml., *ca.* 0.25 *M*) of the compounds in deuterium oxide.

(9) The helpful discussions with Messrs. F. A. MacKellar and J. F. Zieserl are gratefully acknowledged.

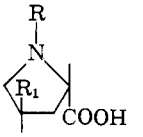


Ia, R = CH_3; R_1 = $CH_2CH_2CH_3$; R_2 = CH_3
b, R = CH_3; R_1 = CH_2CH_3; R_2 = CH_3
c, R = CH_3; R_1 = $CH_2CH_2CH_3$; R_2 = CH_2CH_3
d, R = H; R_1 = $CH_2CH_2CH_3$; R_2 = CH_3
e, R = H; R_1 = $CH_2CH_2CH_3$; R_2 = CH_2CH_3

(3H) and a broad peak (4H) assigned to the propyl side chain where IIIb has a triplet (3H) and a broad peak (2H) attributable to an ethyl side chain. The similarity of IIIa and IIIb in specific rotation (−46.8° and −46°, respectively) and n.m.r. spectra is suggestive of identical stereochemistry.[1]



IIa, R = CH_3
b, R = CH_2CH_3



IIIa, R = CH_3; R_1 = $CH_2CH_2CH_3$
b, R = CH_3; R_1 = CH_2CH_3
c, R = H; R_1 = $CH_2CH_2CH_3$

Crystalline U-11,921 hydrochloride (Ic), $C_{19}H_{36}N_2O_6S \cdot HCl \cdot H_2O$, $[\alpha]^{25}D$ +143°, contains one basic function, pK_a' 7.73, one NCH_3, and three -C-CH_3 groups. The n.m.r. spectra of Ic and Ia differ in that the sharp singlet at 125 c.p.s. (3H) attributable to the -SCH_3 group present in Ia is missing in the spectrum of Ic. Instead, it shows a quadruplet at 147, 155, 162, and 170 c.p.s. and a triplet at 65, 75, and 85 c.p.s., assigned to an -SCH_2CH_3 group; *i.e.*, the structure of U-11,921 is represented by Ic. In addition, hydrazinolysis of Ic, followed by acid hydrolysis, afforded crystalline 4-*n*-propyl-L-hygric acid (IIIa). The remaining fragment was isolated as crystalline colorless base, $C_{10}H_{21}NO_5S$ (IIb), m.p. 191–195° dec., $[\alpha]^{25}D$ +258° (*c* 0.7, water), pK_a' 7.17, equiv. wt. 271 (calcd. 267). The n.m.r. spectrum of IIb, called ethyl α-thiolincosaminide, differs from that of IIa in that the sharp singlet (3H), due to the -SCH_3 group present in IIa, has been replaced by a quadruplet at 150, 157, 164, and 171 c.p.s. and a triplet at 71, 78, and 85 c.p.s. which have been assigned to an -SCH_2CH_3 group. Thus, IIb has structure identical with that of IIa except for the substitution of the -SCH_3 group of IIa by an -SCH_2CH_3 in IIb.

Crystalline U-11,973 hydrochloride (Id), $C_{17}H_{32}N_2O_6S \cdot HCl \cdot H_2O$, $[\alpha]^{25}D$ +149° (*c* 0.9, water), contains one -SCH_3, two C-CH_3, and one basic function, pK_a' 7.58, equiv. wt. 445 (calcd. 446.5). Infrared absorptions at 1687 and 1596 cm.$^{-1}$ indicated an amide linkage. Due to the limited solubility of Id in desirable solvents, the n.m.r. spectrum had limited usefulness, but did indicate close similarity to the other lincomycin-related antibiotics, with the striking exception of the absence of the signal attributed to the -NCH_3 group. Methylation of Id with methyl iodide afforded lincomycin (Ia), identified by paper and thin layer chromatography, specific rotation, and infrared and n.m.r. spectra. Thus, the structure of U-11,973 is Id, N-demethyllincomycin.

Crystalline U-20,943 hydrochloride (Ie), $C_{18}H_{34}N_2O_6S \cdot HCl \cdot H_2O$, $[\alpha]^{25}D$ +153°, pK_a' 8.00, contains two C-CH_3, but no -SCH_3 or -NCH_3. That Ie could be the structure for U-20,943 was suspected because of its manner of preparation. This was proven by reacting U-20,943 with CH_3I and isolating U-11,921 (Ic), identified as such by paper and thin layer chromatography, rotation, and infrared and n.m.r. spectra.

Antibiotics U-11,973 and U-20,943 have been used as starting materials for a series of N-substituted analogs. This work will be the subject of a future communication.

We gratefully acknowledge the analytical and spectral work of Drs. W. A. Struck and G. Slomp and associates.

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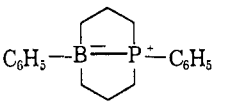
RECEIVED OCTOBER 3, 1964

Synthesis of a Novel Heterobicycloalkane Containing Boron and Phosphorus

Sir:

A recent review on heterocyclic organic boron compounds[1] has shown the absence of information on such compounds containing both boron and phosphorus. We would like to report the synthesis of such a compound, 1,5-diphenyl-1-bora-5-phosphabicyclo[3.3.0]octane (I). The compound, stable in the atmosphere,



I

was prepared in 28% yield by refluxing a dilute toluene solution containing equimolar quantities of triethylamine–phenylborane and diallylphenylphosphine. The triethylamine–phenylborane was synthesized by the method of Hawthorne[2] and the diallylphenylphosphine by the method of Jones, *et al.*[3] The product was isolated by distilling the reaction mixture into crude fractions and crystallizing the product from acetone at low temperatures. Recrystallization yielded a white solid, m.p. 75.5–76.5°.

Anal. Calcd. for $C_{18}H_{22}BP$: C, 77.16; H, 7.92; B, 3.86; P, 11.05; mol. wt., 280. Found: C, 77.08; H, 7.71; B, 4.02; P, 10.90; mol. wt., 287 (vapor pressure osmometer).

The infrared spectrum of the product showed no boron–hydrogen or olefinic bonds in accord with the assigned structure which results from intramolecular

(1) P. M. Maitlis, *Chem. Rev.*, **62**, 224 (1962).
(2) M. F. Hawthorne, *J. Am. Chem. Soc.*, **80**, 4291 (1958).
(3) W. J. Jones, W. C. Davies, S. T. Bowden, C. Edwards, V. E. Davis, and L. H. Thomas, *J. Chem. Soc.*, 1446 (1947).