considerably more positive potentials, also have been studied. Again, plots of $\tau^{1/2}$ *vs.* concentration show the expected linearity for a chronopotentiometric reaction which is proceeding independent of any previous electrode process. Oxidation reactions with potentials as high as +1.0 v. appear possible with the mercury chloride electrode.

The electrode can also be operated in a more conventional polarographic sense. The halide film is formed by application of an anodic potential for a short period of time. The compound to be oxidized is then introduced and the voltage scanned in an increasing anodic direction using a Leeds and Northrup Electrochemograph. With DPP and ferrocyanide, typical quiet pool polarograms[2] are obtained whose peak heights are proportional to concentration. Investigations are in progress to evaluate the effect of stirring and changing scan rate on peak currents as well as application of the technique to the hanging drop electrode.

A detailed report of this work will be published shortly.

(2) C. A. Streuli and W. D. Cooke, *Anal. Chem.*, **25**, 1691 (1953).

DEPARTMENT OF CHEMISTRY
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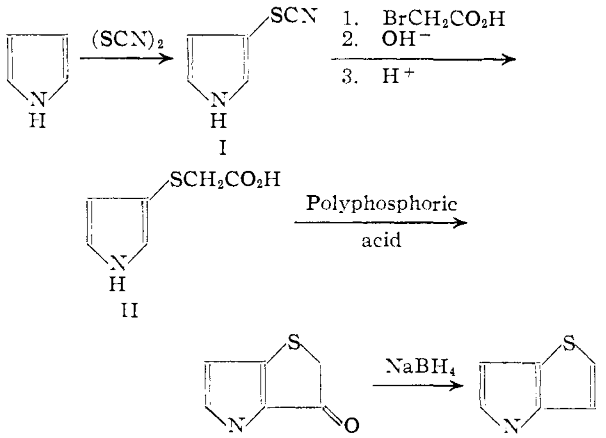
RECEIVED MAY 20, 1957

A PRACTICAL SYNTHESIS OF THIENO[3,2-*b*]PYRROLE

Sir:

We have synthesized thieno[3,2-*b*]pyrrole (IV) from pyrrole in four steps. The new synthesis makes this isostere of indole readily available for conversion to various derivatives of biological interest.



From analogous electrophilic substitutions and resonance theory,[1] thiocyanation of pyrrole was expected to occur preferentially at the 2-position. However, recent molecular orbital calculations[2] indicate that the orientation of substitution in the pyrrole nucleus cannot be predicted unambiguously; π-electron localization energy favors 2-substitution but π-electron densities favor 3-substitution. When the reaction was carried out by rapidly mixing cold (−75°) methanolic solutions of pyrrole and thiocyanogen (prepared at −60° from potassium thiocyanate and bromine), the product collected after pouring the reaction mixture onto ice and salt, and amounting to 50% yield after recrystallization from methylene chloride–methylcyclohexane, was 3-thiocyanopyrrole (I), m.p. 40–44°. *Anal.* Calcd. for $C_5H_4N_2S$: C, 48.36; H, 3.25; N, 22.55. Found: C, 48.72; H, 3.15; N, 22.80.

Treatment of a cold methanolic solution of I and bromoacetic acid with an excess of potassium hydroxide in aqueous methanol furnished in 90% yield (3-pyrrolylthio)-acetic acid (II), characterized as the ammonium salt which crystallized when anhydrous ammonia was introduced into a methylene chloride solution of the acid. The salt melted at 127–133° (dec.). *Anal.* Calcd. for $C_6H_{10}N_2O_2S$: C, 41.35; H, 5.78; N, 16.08. Found: C, 41.59; H, 5.73; N, 15.77. Addition of a dilute methylene chloride solution of II over 1 hr. to vigorously stirred polyphosphoric acid at 125°, followed by dilution of the mixture with water, extraction with ethyl acetate and sublimation of the product, yielded 36% of 2H,3H-thieno[3,2-*b*]-pyrrol-3-one (III), m.p. 183–188.5°. The analytical sample, m.p. 187–190°, was prepared by a series of recrystallizations and resublimations. *Anal.* Calcd. for C_6H_5NOS: C, 51.78; H, 3.62; N, 10.07. Found: C, 52.04; H, 3.82; N, 10.14. The infrared spectrum of III (Nujol) contained strong bands at 1635 (C=O) and 3150 cm.$^{-1}$ (NH). The structure of III was proved by desulfurization with Raney nickel catalyst to 2-acetylpyrrole, shown to be identical with an authentic sample[3] by infrared spectra (chloroform), m.p. and mixture m.p. Treatment of III with sodium borohydride in methanol yielded 62% of sublimed thieno[3,2-*b*]-pyrrole (IV), m.p., after further purification, 25–28°. *Anal.* Calcd. for C_6H_5NS: C, 58.50; H, 4.09; N, 11.38. Found: C, 58.60; H, 4.27; N, 11.32. The infrared spectrum of IV (smear) was identical with that[4] of a less pure sample prepared[5] unequivocally from thiophene, except for bands due to a carboxylic acid present as an impurity in the latter sample.

(1) R. C. Elderfield, "Heterocyclic Compounds," Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1950, pp. 300–301.

(2) R. D. Brown, *Australian J. Chem.*, **8**, 100 (1955).

(3) (a) B. Oddo, *Ber.*, **43**, 1012 (1911); (b) structure proof of 2-acetylpyrrole, G. Ciamician and P. Silber, *ibid.*, **20**, 2594 (1887).

(4) J. F. Zack, Ph.D. Thesis, University of Illinois, 1956.

(5) H. R. Snyder, L. A. Carpino, J. F. Zack and J. F. Mills, THIS JOURNAL, **79**, 2556 (1957).

(6) National Science Foundation Predoctoral Fellow, 1954–1957.

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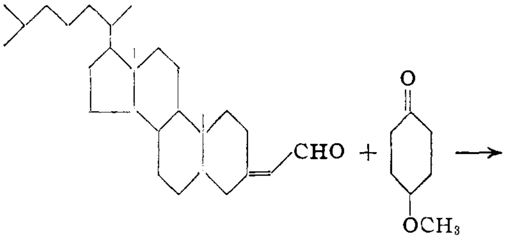
RECEIVED MAY 6, 1957

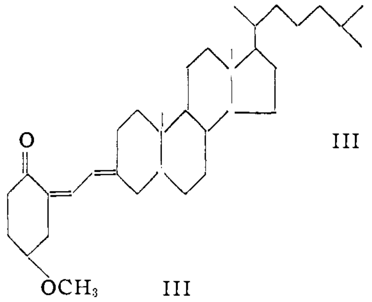
STUDIES IN THE SYNTHESIS OF THE ANTIRACHITIC VITAMINS. IV. THE SYNTHESIS OF A BIOLOGICALLY ACTIVE VITAMIN D HOMOLOG

Sir:

We wish to report the synthesis of 1-cholestanylidene-2-(5′-methoxy-2′-methylene-1′-cyclohexylidene)-ethane (V), a homolog of vitamin D, which is biologically active. Following the scheme outlined in previous publication,[1] 7.54 g. of 2-cholestanylideneethan-1-al (I) [m.p. 114–115°. *Anal.* Calcd. for $C_{29}H_{48}O$: C, 84.39; H, 11.72. Found: C, 84.00; H, 11.82; ε (244.5 mμ), 30,250 (ethanol); $[\alpha]^{25}D$ −9.38° (chloroform)] was condensed in the dark with 4.7 g. of 4-methoxycyclohexanone (II) in a liter of *t*-butanol containing 4 g. of sodium hydroxide and 10 cc. of water. The mixture was stirred under nitrogen in the dark for 24 hr. A yellowish-brown amorphous product (7.4 g.) was isolated from this reaction and chromatographed in the dark using alumina (Act. III) from which was obtained two fractions: one the 2,1'-*trans*-dienone (10%), m.p. 221–224° (dec.). *Anal.* Calcd. for $C_{36}H_{58}O_2$: C, 82.70; H, 11.18. Found: C, 82.73; H, 11.33; ε (309 mμ), 30,600 (ethanol); infrared α,β-conjugated >C=O band at 1674 cm.$^{-1}$; $[\alpha]^{25}D$, +86.8° (chloroform). Semicarbazone, m.p. 220–222°. *Anal.* Calcd. for $C_{37}H_{62}N_3O_2$: C, 76.50; H, 10.76; N, 7.23. Found: C, 76.72; H, 10.95; N, 6.94. The other fraction was the 2,1'-*cis*-dienone (12%), m.p. 186°. *Anal.* Calcd. for $C_{36}H_{58}O_2$: C, 82.70; H, 11.18; $|^{=}$, 2.00. Found: C, 82.71; H, 11.07; $|^{=}$, 1.85 (Pd.); ε (307 mμ), 12,200 (ether); infrared α,β-conjugated >C=O band at 1675 cm.$^{-1}$; $[\alpha]^{25}D$, +40.3° (chloroform).

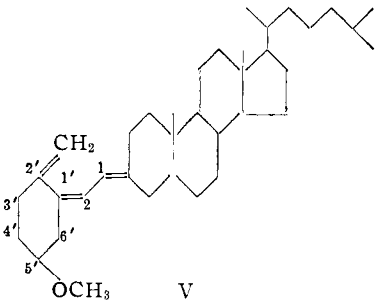


I II



III

III + $Ph_3P^{+}—CH_2^{-}$ →
IV



V

Reaction of the 2,1'-*cis*-dienone (III) with triphenylphosphinemethylene (IV) in a pressure bottle gave an amorphous solid (23%), m.p. 193° (dec.); ε (265 mμ), 20,200 (ether). This was further purified by chromatography in a nitrogen atmosphere and in the dark giving again an amorphous product which had the following analyses.[2] *Anal.* Calcd. for $C_{37}H_{60}O$: C, 85.34; H, 11.61. Found: C, 84.22; 11.55; $[\alpha]^{25}D$, −10.6°; ε (267 mμ), 31,300 (ether); principal infrared bands[3] for $=CH_2$: 3100R, 1641W, 892S cm.$^{-1}$. Principal infrared bands for $=CH_2$ of vitamin D_3: 3100R, 1645M, 892M cm^{-1}.

An exploratory biological test of this homolog was carried out by Professor Robert S. Harris of the Nutritional Biochemical Laboratories of M.I.T. and he reports that the group of rachitic rats which was fed this homolog showed nearly the same degree of healing as the group which was fed vitamin D_2 at approximately the same concentration. These preliminary results do make it possible to estimate exactly the potency of the 2,1'-*cis*-homolog (V) but indicate quite definitely that its activity may approach that of vitamin D_2.

The 2,1'-*trans*-homolog was also synthesized from the 2,1'-*trans*-dienone and had an ε (272 mμ), 34,700 (ether). The *trans*-homolog also was found to be biologically active but very much less so than the *cis*-homolog. Details of this work will be published elsewhere.

Acknowledgment.—The authors are indebted to Dr. Nagy and his associates for all the analyses, to Dr. Nelson and Miss Cassie for the infrared spectra, to Prof. Robert S. Harris for the biological results and to Research Corporation–Milas–M.I.T. Fund for financial support of this investigation.

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[1] N. A. Milas, L. C. Chiang, C. P. Priesing, A. A. Hyatt and J. Peters, THIS JOURNAL, **77**, 4180 (1955).

[2] This substance is highly sensitive to air oxidation and in spite of extensive precautions the carbon was always low.

[3] R = shoulder, W = weak, S = strong, M = medium.

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RECEIVED JUNE 6, 1957

A NEW SYNTHESIS OF THE CHROMIUM HEXACARBONYL

Sir:

We wish to report a new synthesis of chromium hexacarbonyl starting from easily available chromium compounds which appear to have been converted now for the first time, into the hexacarbonyl.

At present the only well described method for this synthesis is the "Grignard method" discovered by Job and Cassal[1] and substantially improved by Owen and co-workers.[2] Recently Fischer and Hafner[3] synthesized the carbonyl starting from chromium bis-cyclopentadienyl (no yield reported). Both these valuable methods suffer from some disadvantages such as the unsatisfactory over-all yields,[4] or the requirement of a rather

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[1] A. Job and A. Cassal, *Compt. rend.*, **183**, 392 (1926).

[2] B. B. Owen, J. English, Jr., H. G. Cassidy and C. Vanderbilt Dundon, THIS JOURNAL, **69**, 1723 (1947).

[3] E. O. Fischer and W. Hafner, *Z. Naturf.*, **10b**, 140 (1955).

[4] W. H. Cumming, J. A. Horn and P. O. Ritchie, *J. Appl. Chem.*, **2**, 624 (1952).