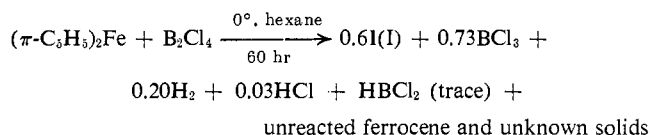


band assigned to N→B at 715 cm⁻¹ in addition to bands assignable to B-Cl and the ferrocenyl group.

The most abundant volatile products from the preparative reaction were BCl₃ and H₂; traces of HCl and HBCl₂ were also observed. A representative reaction may now be written as



No unreacted B₂Cl₄ was detected; the fate of all of the boron is unknown at the present time. The presence of HCl may be accounted for by our observation that BCl₃ and ferrocene react slowly in hexane at 0° to produce observable amounts of HCl and I. The evolution of hydrogen in the course of the reaction is noteworthy.¹⁰ Hydrogen is known to react very rapidly with B₂Cl₄ to produce dichloroborane which then disproportionates to BCl₃ and B₂H₆.¹¹ While we observed a trace of dichloroborane, no diborane was detected. Furthermore, in view of the rapidity of the H₂-B₂Cl₄ reaction, it is surprising that the evolved hydrogen is not removed by reaction with any B₂Cl₄ which has not yet reacted with ferrocene. A possible explanation for this apparent anomaly is that B₂Cl₄ does indeed form a π complex with ferrocene as the first step in the reaction; in this condition B₂Cl₄ may not react with hydrogen. The stabilization of B₂Cl₄ by π-donor molecules has previously been noted,¹² but it is not known whether the tetrahalide is thereby rendered stable to reaction with hydrogen. The probable sources of the volatile products, as they relate to the mechanism of the ferrocene-diboron tetrachloride reaction, are currently under investigation.

Several groups of workers have shown that there is a direct correlation between the oxidation potentials of substituted ferrocenes and the electron-withdrawing properties of the substituents.¹³ In order to obtain information concerning the extent of electron withdrawal by the -BCl₂·N(CH₃)₃ group, cyclic voltammetry studies were initiated. A reversible, one-electron oxidation of II in acetonitrile occurred at an E_{1/2} of 0.45 V vs. sce; this is characteristic of the oxidation of a ferrocene to a ferricenium complex. Since we found ferrocene to have an oxidation potential (E_{1/2}) of 0.42 V, it is evident that the -BCl₂·N(CH₃)₃ group has little or no effect on the oxidation potential. Of most interest in this brief study was the observation of two, partially reversible, one-electron reduction waves at E_{1/2} = -0.24 and -0.93 V for compound II. Ferrocene itself is not reduced at cathodic potentials of down to -2.0 V vs. sce. Thus, we tentatively suggest that the substituent is the site of the reduction, but this awaits experimental proof.

(10) The hydrogen observed in these experiments apparently arises from the B₂Cl₄-ferrocene reaction and not from the hydrolysis of B-B bonds. Every precaution was taken to ensure the absence of water; furthermore, hydrogen was evolved in all 14 reactions attempted.

(11) R. J. Brotherton in "Progress in Boron Chemistry," Vol. 1, H. Steinberg and A. L. McCloskey, Ed., The Macmillan Co., New York, N. Y., 1964, p 42.

(12) J. Feeney, A. K. Holliday, and F. J. Marsden, *J. Chem. Soc.*, 356 (1961).

(13) D. W. Hall and C. D. Russell, *J. Amer. Chem. Soc.*, 89, 2316 (1967).

Only one previous study of the reactions of diboron tetrachloride with aromatic systems has been reported; naphthalene gave rise to an addition product, whereas a substitution reaction occurred with benzene to give phenyldichloroborane.¹⁴ It might be noted that the rate of reaction of B₂Cl₄ with ferrocene is apparently greater than with benzene; a 60% yield of ferrocenyldichloroborane was obtained in 60 hr, while 36 days was required to produce approximately the same yield of phenyldichloroborane.

Ferrocenylboronic acid and organoferrocenylboronic acids are the only boron derivatives of ferrocene previously reported in the literature.^{15,16} Since a dihaloboryl group possesses a more versatile chemistry than a dihydroxyboryl group, the synthesis of ferrocenyldichloroborane opens the possibility of more extensive investigations into the properties of borane groups attached to a metallocene.

Acknowledgments. We wish to thank Dr. M. Dale Hawley and Mr. James Lawless for the cyclic voltammetry data, and Professor Riley Schaeffer for helpful discussions. We also wish to thank the Research Corporation for partial support of this research.

(14) W. B. Fox and T. Wartik, *ibid.*, 83, 498 (1961).

(15) G. Marr, R. E. Moore, and B. W. Rockett, *J. Chem. Soc., C*, 24 (1968), and references therein.

(16) We thank a referee for pointing out that H. Rosenberg and F. Hedberg reported on a number of boron derivatives of ferrocene at the Third International Symposium on Organometallic Chemistry, Munich, Germany, Aug 1967.

(17) National Science Foundation Trainee, 1965-1968.

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Studies on the Synthesis of Dimeric Vinca Alkaloids¹

Sir:

The dimeric Vinca alkaloids have stimulated considerable interest from both a chemical and a biological standpoint.² Our continued interests in this area³ necessitated an investigation directed at the development of a reaction which would have potential application for syntheses of the dimeric systems.

In a previous communication⁴ we reported the conversion of 4β-dihydrocleavamine (I, R = R' = H; R'' = CH₂CH₃) into its ester derivative I (R = CO-OCH₃; R' = H; R'' = CH₂CH₃) via a sequence which required, as its key step, the reaction of cyanide ion with the chloroindolenine II (R = R' = H; R'' = CH₂CH₃) to provide an 18-cyanodihydrocleavamine. We now report our results which illustrate that such chloroindolenine intermediates are also important for the synthesis of dimeric compounds.

All of the dimeric alkaloids in this family contain a carbomethoxy group at C_{18'} (see, for example, IV,

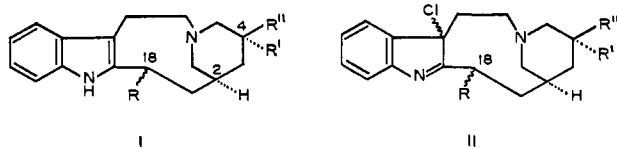
(1) Presented by J. P. Kutney at a Symposium on the Chemistry of Natural Products, University of West Indies, Kingston, Jamaica, Jan 2-5, 1968.

(2) For a recent review of the chemistry and biological properties in this family, see "Proceedings of the First Symposium of the European Cancer Chemotherapy Group," Excerpta Medica Foundation, New York, N. Y., 1966.

(3) J. P. Kutney, K. K. Chan, A. Failli, J. M. Fromson, C. Gletsos, and V. R. Nelson, *J. Am. Chem. Soc.*, 90, 3891 (1968).

(4) J. P. Kutney, W. J. Cretney, P. Le Quesne, B. McKague, and E. Piers, *ibid.*, 88, 4756 (1966).

$R'' = \text{COOCH}_3$), and for this reason its introduction during any dimerization process would be an important step in subsequent syntheses of these substances. For this purpose, the previously unknown chloroindolenine of carbomethoxy-4 β -dihydrocleavamine (II, $R = \text{COOCH}_3$; $R' = \text{H}$; $R'' = \text{CH}_2\text{CH}_3$), obtained as an amorphous solid by the method previously reported,^{4,5} was allowed to react with vindoline (III, $R = \text{OCH}_3$; $R' = \text{CH}_3\text{CO}$) in refluxing anhydrous methanol containing 1.5% hydrogen chloride. The resulting product from this reaction was dimer IV ($R = \text{OCH}_3$;



$R' = \text{CH}_3\text{CO}$; $R'' = \text{COOCH}_3$) isolated as an amorphous powder, in 45% yield. High-resolution mass spectrometry⁶ established the formula, $\text{C}_{46}\text{H}_{58}\text{O}_8\text{N}_4$ (found: mol wt, 794.419; calcd: mol wt, 794.425), while spectral and chemical evidence conclusively established structure IV for this compound. The uv spectrum [$\lambda_{\text{max}}^{\text{MeOH}}$ $m\mu$ (log ϵ) 265 (4.22), 287 (4.19), 296 (4.17), 310 (sh, 3.97)] was in excellent agreement with expectation,⁷ while the nmr spectrum⁸ was so instructive in this and the other series mentioned later that it virtually proved the structure on its own merits. In all instances, the spectrum was a summation of the signals characteristic of the individual monomeric units. Thus, for the above dimer, the following nmr signals were observed: 2.55–3.15 (4 H, aromatic, cleavamine portion), 3.05 (1 H, singlet, C_{14}H , vindoline portion), 4.04 (1 H, singlet, C_{17}H , vindoline portion), 6.27 (3 H, singlet, COOCH_3 at C_{18} '), 9.09 (3 H, triplet, CH_2CH_3 , cleavamine portion), 9.34 (3 H, triplet, CH_2CH_3 , vindoline portion). Chemical evidence in support of IV became available when mild cleavage of this dimer (1.5 *N* methanolic HCl, Sn, SnCl_2) afforded the starting monomers, carbomethoxy-4 β -dihydrocleavamine and vindoline.

The generality of the dimerization reaction was further demonstrated when other novel dimeric systems necessary for biological evaluation as possible antitumor agents were synthesized. The above chloroindolenine, when allowed to react with deacetylvindoline hydrazide⁹ (III, $R = \text{NHNH}_2$; $R' = \text{H}$), provided the desired C_{18} '-carbomethoxy dimer IV ($R = \text{NHNH}_2$; $R' = \text{H}$; $R'' = \text{COOCH}_3$), $\text{C}_{43}\text{H}_{56}\text{N}_6\text{O}_6$ (found: mol wt, 752.427; calcd: mol wt, 752.426), as an amorphous powder in 25% yield. This substance exhibited the following spectral properties: $\lambda_{\text{max}}^{\text{MeOH}}$ $m\mu$ (log ϵ) 264 (4.11), 290 (4.06), 296 (4.05), 313 (sh, 3.87); nmr signals: 2.48–3.10 (4 H, aromatic, cleavamine portion), 3.06 (1 H, singlet, C_{14}H , vindoline portion), 4.07 (1 H, singlet, C_{17}H , vindoline portion), 6.30 (3 H, singlet,

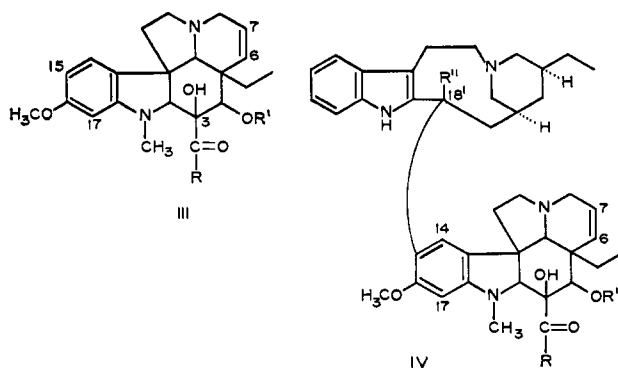
(5) Complete characterization of this intermediate will be reported in our detailed paper.

(6) High-resolution mass measurements were performed on an AEI MS9 mass spectrometer. In all instances, mass measurements were made at several masses to confirm these results.

(7) N. Neuss, "Physical Data of Indole and Dihydroindole Alkaloids," Lilly Research Laboratories, Indianapolis 6, Ind., 1960.

(8) All nmr spectra were determined on a Varian HA-100 spectrometer. The values are given in τ units.

(9) N. Neuss, M. Gorman, W. Hargrove, N. J., Cone, K. Biemann, G. Büchi, and R. E. Manning, *J. Am. Chem. Soc.*, **86**, 1440 (1964).



COOCH_3 at C_{18} '), 9.08 (3 H, triplet, CH_2CH_3 , cleavamine portion), 9.20 (3 H, triplet, CH_2CH_3 , vindoline portion). Cleavage of this molecule under the above-mentioned conditions provided carbomethoxy-4 β -dihydrocleavamine and deacetylvindoline hydrazide, identified by comparison with authentic samples.

In a similar fashion, the dimer IV (6,7-dihydro; $R = \text{OCH}_3$; $R' = \text{CH}_3\text{CO}$; $R'' = \text{COOCH}_3$), $\text{C}_{46}\text{H}_{60}\text{O}_8\text{N}_4$ (found: mol wt, 796.441; calcd: mol wt, 796.441), from the reaction of the chloroindolenine and dihydrovindoline (III, 6,7-dihydro; $R = \text{OCH}_3$; $R' = \text{CH}_3\text{CO}$) was obtained as an amorphous solid in 42% yield. The spectral properties of this compound were similar to those presented above for the other dimers, while mild cleavage into the starting monomers again provided indisputable evidence for the assigned structure.

Using methods analogous to those applied to the C_{18} '-carbomethoxy dimers as discussed above, we also prepared dimer IV ($R = \text{NHNH}_2$; $R' = R'' = \text{H}$) in 77% yield and dimer IV ($R = \text{OCH}_3$; $R' = \text{CH}_3\text{CO}$; $R'' = \text{H}$) in 68% yield utilizing the chloroindolenine II ($R = R' = \text{H}$; $R'' = \text{CH}_2\text{CH}_3$). The former compound has been recently reported in an independent investigation by the Lilly group.¹⁰

The above dimerization provides the first synthesis of dimeric systems bearing the desired ester function at C_{18} ' known to be present in the Vinca alkaloids. It is hoped that this reaction will find application in the laboratory synthesis of the natural dimers.

Acknowledgment. Financial aid from the National Cancer Institute of Canada, National Research Council of Canada, and Medical Research Council of Canada is gratefully acknowledged.

(10) N. Neuss, M. Gorman, N. J. Cone, and L. L. Huckstep, *Tetrahedron Letters*, 783 (1968).

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Reactions of Aromatic Radical Anions. II. A Moderate-Temperature Reaction of Sodium Naphthalene and Molecular Hydrogen

Sir:

Whereas present schemes for the preparation of sodium hydride employ the high-temperature reaction of sodium metal and hydrogen,^{1,2} we wish to report

(1) G. W. Mattson and T. P. Whaley, *Inorg. Syn.*, **5**, 10 (1957).

(2) The absorption of hydrogen by sodium is reported to begin at about 200°: D. T. Hurd, "An Introduction to the Chemistry of Hydrides," John Wiley and Sons, New York, N. Y., 1952, p 31.