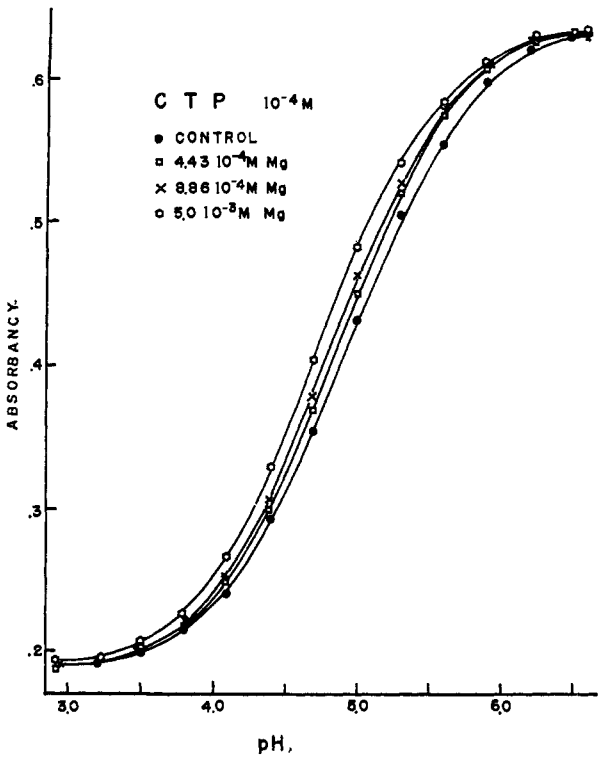



Fig. 2.—Spectrophotometric titration of $NH_2$-group in CTP in 0.05 $M$ $(CH_3)_4NCl$ at 245 mμ.

Over-all values of $K_m(M^{-1})$ obtained not spectrally but with an titrimeter (and therefore sensitive to proton displacement from the whole molecule not just the ring) are[11]: ITP, $1.2 \times 10^4$; ATP, $8 \times 10^3$; IDP $5.7 \times 10^3$; ADP, $2.2 \times 10^3$ $M^{-1}$. These are in the range reported by others.[8,12–15] Variation among previous reports probably was due to concentration effects. For instance, the values of Smith and Alberty[8] who used rather high concentrations, are lower than those of others[12–14] who used lower concentrations. Except Burton's results[16] there is an inverse correlation between concentrations of nucleotide and $Mg^{++}$ and apparent $K_m$.

TABLE I

AFFINITY CONSTANTS FOR $Mg^{++}$ OF PURINE AND PYRIMIDINE RING IN 0.05 $M$ $(CH_3)_4NCl$

| Mg. concn. $M \times 10^3$ | Apparent affinity constant $\times 10^{-3}$ $M^{-1}$ ITP $10^{-4}$ $M$ | ATP $10^{-4}$ $M$ | CTP $10^{-4}$ $M$ | IDP $10^{-4}$ $M$ | ADP $10^{-4}$ $M$ | CDP $10^{-4}$ $M$ |
|---|---|---|---|---|---|---|
| 0.044 | 15.6 | | | | | |
| 0.115 | 6.9 | | | | | |
| 0.44 | 2.0 | | | 1.3 | | |
| 0.88 | | | 0.30 | 1.05 | | |
| 1.0 | 1.4 | 0.42 | .18 | 0.42 | | |
| 2.5 | | .15 | | | | |
| 5.0 | 0.26 | .17 | .09 | .24 | | 0.030 |
| 10.0 | | .09 | .048 | .063 | 0.026 | .026 |
| 5.0 | 12.2[a] | | | | | |
| 8.8 | 0.15[a] | | | | | |
| 50.0 | .22[a] | | | | | |

[a] These values are for $10^{-3}$ $M$ ITP concentration.

Comparing spectrally-obtained (ring) affinity constants with titrimeter-obtained (over-all) affinity constants we found ratios of the order of 1:100 with ITP and 1:50 with ATP. From these ratios can be estimated the fraction of nucleotide in "curled" and "linear" forms. Ring $K_m$ (ITP) > Ring $K_m$ (ATP), but at neutral $p$H due to the great difference in ring ionization constants of the two nucleotides, the fraction of ATP binding $Mg^{++}$ will be about 100 times greater than the corresponding fraction for ITP. This may be particularly important for the model[5] of myosin NTPase which assumes interaction between the 6-position in the purine ring and $Mg^{++}$ or $Ca^{++}$ and myosin.

We gratefully acknowledge the counsel of Professor S. Watanabe. This work was supported by U.S.P.H.S. Grants H-3598 and 2G-174, and by an American Heart Association Career Investigatorship to Manuel F. Morales.

(11) The concentration of nucleotides was $10^{-4}$ $M$ and of $MgCl_2$ $10^{-4}$ $M$; solvent was 0.05 $M$ tetramethylammonium chloride.

(12) L. B. Nanninga, *J. Phys. Chem.*, **61**, 1144 (1957).

(13) A. E. Martell and G. Schwarzenbach, *Helv. chim. acta*, **39**, 653 (1956).

(14) E. Walaas, *Acta chem. scand.*, **12**, 528 (1958).

(15) K. Burton, *Biochem. J.*, **71**, 388 (1959).

(16) At neutral $p$H, $[N_0] = 10^{-4}$ $M$, $[M_0] = 10^{-4}$ $M$, the approximate fraction of metal-ring complex can be calculated as: $K_m[M]/\{(1 + K_m[M] + K_h[H]\}$ substituting the values: $K_m$, $0.42 \times 10^3$, $1.4 \times 10^3$ $M^{-1}$; $K_h$, $10^{4.5}$, $10^{9.5}$ $M^{-1}$ for ATP and ITP, respectively, and $[H] = 10^{-7}$, $[M] = 10^{-4}$ $M$, we get the fraction for ATP, 0.30; for ITP, 0.003.

CARDIOVASCULAR RESEARCH INSTITUTE KEN HOTTA
UNIVERSITY OF CALIFORNIA MEDICAL CENTER J. BRAHMS
SAN FRANCISCO 22, CALIFORNIA MANUEL MORALES

RECEIVED DECEMBER 19, 1960

## THE STEREOCHEMISTRY OF RIMUENE

*Sir:*

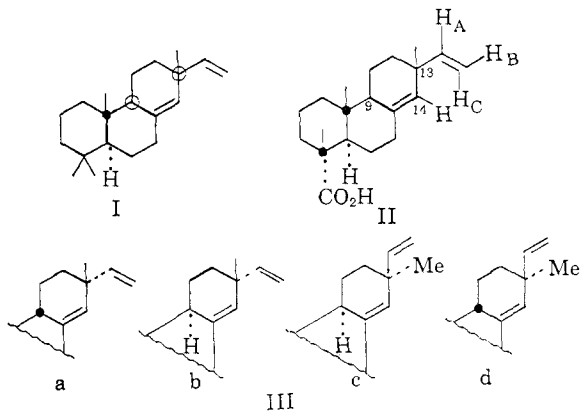
Rimuene has attracted attention in recent years in view of its possible central position in the biosynthesis of tetracarbocyclic diterpenic substances.[1] While physical and chemical evidence has pointed to I as its structure,[2] no rigorous stereochemical assignment of its asymmetric centers C-9 and 13 has been made. Contrastingly, the structurally related isopimaric, sandaracopimaric and pimaric acids (II) have been shown to possess configurations IIIa, b and c, respectively.[3] The nonidentity of the hydrocarbons derived from these acids with rimuene[4] suggests that rimuene may

(1) (a) E. Wenkert, *Chemistry & Industry*, 282 (1955); (b) L. H. Briggs, B. F. Cain, B. R. Davis and J. K. Wilmhurst, *Tetrahedron Letters*, No. 8, 13 (1959).

(2) (a) L. H. Briggs, B. F. Cain and J. K. Wilmhurst, *Chemistry & Industry*, 599 (1958) and references contained therein; (b) L. H. Briggs, B. F. Cain and R. C. Cambie, *Tetrahedron Letters*, No. 8, 17 (1959).

(3) (a) E. Wenkert and J. W. Chamberlin, *J. Am. Chem. Soc.*, **81**, 688 (1959); (b) O. E. Edwards and R. Howe, *Can. J. Chem.*, **37**, 760 (1959); (c) B. Green, A. Harris and W. B. Whalley, *J. Chem. Soc.*, 4715 (1958); (d) O. E. Edwards, A. Nicholson and M. N. Roger, *Can. J. Chem.*, **38**, 663 (1960); (e) A. K. Bose, *Chemistry & Industry*, 1104 (1960).

(4) The conversions of pimaric and isopimaric acids to their hydrocarbons have been accomplished in These Laboratories (unpublished experiments by B. G. Jackson and J. W. Chamberlin) and in the laboratories of Professors L. H. Briggs (Auckland, New Zealand) (private communication) and R. E. Ireland (Michigan) (*cf.* R. E. Ireland and P. W. Schiess in Abstracts of Papers of the International Symposium on the Chemistry of Natural Products, Australia, August 15–25, 1960, p. 57). The Michigan workers also transformed Edwards' sandaracopimaric acid[3d] into a hydrocarbon and carried out a total synthesis of racemic pimaradiene of the pimaric and sandaraco-




possess the yet unencountered configuration IIId. The study confirms this stereochemistry.

Inspection of the n.m.r. spectra of the methyl esters of the three acids and of rimuene (see Fig. 1) in the olefinic and tertiary allylic hydrogen regions reveals a pattern which permits classification of the natural products into two sets of two substances each.[5,6] Methyl sandaracopimarate (IIIb) and methyl pimarate (IIIc), 9$\alpha$ compounds, exhibit their tertiary allylic proton resonance at 7.8 $\tau$ (see Table I) while methyl isopimarate (IIIa) and rimuene have theirs shifted upfield and there masked by the secondary allylic proton peaks. Rimuene's 9$\beta$ configuration is supported further by the resonance behavior of the hydrogen on the nuclear double bond C(14)-H. While methyl sandaracopimarate (IIIb) and methyl pimarate (IIIc) show a single peak in the 4.8 $\tau$ region, both methyl isopimarate (IIIa) and rimuene reveal theirs at somewhat lower field in form of a doublet and an unresolved triplet or quadruplet, respectively (see Fig. 1 and Table I).

In the vinyl proton part of the spectrum (the vinyl group being considered an ABC system) the two $\alpha$-vinyl compounds, methyl isopimarate (IIIa) and methyl sandaracopimarate (IIIb), exhibit twelve lines with a quartet in the A region, while methyl pimarate (IIIc) and rimuene show fourteen lines with a sextet in the A region (see Fig. 1).[7]

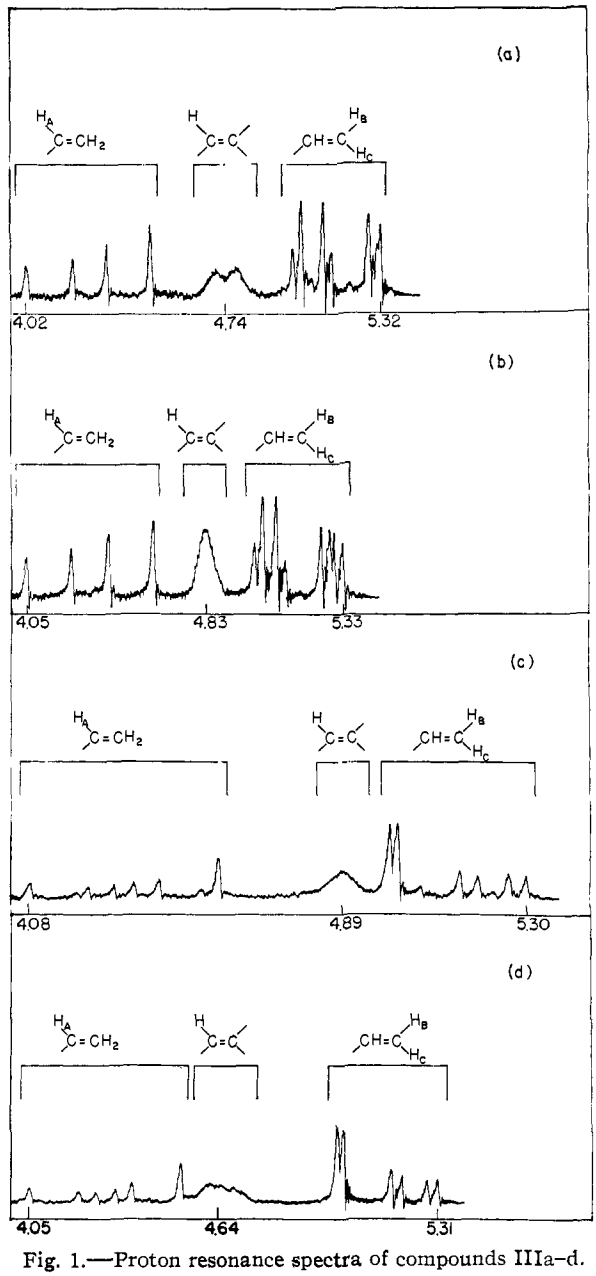



Fig. 1.—Proton resonance spectra of compounds IIIa–d.

All four substances have chemical shifts and spin-coupling constants characteristic of vinyl hydrogens (see Table I).[8] Thus the n.m.r. spectra indicate a 13$\beta$ vinyl function in rimuene.

TABLE I

CHEMICAL SHIFTS (IN $\tau$) AND SPIN-COUPLING CONSTANTS (IN C.P.S.) FOR COMPOUNDS IIIa-d

| | H(9) | H(14) | H(A) | H(B) | H(C) | $J_{AB}$ | $J_{AC}$ | $J_{BC}$ |
|---|---|---|---|---|---|---|---|---|
| IIIa | | 4.74 | 4.24 | 5.22 | 5.18 | 9.5 | 17.0 | 1.4 |
| IIIb | 7.80 | 4.83 | 4.28 | 5.32 | 5.16 | 10.5 | 17.4 | 1.7 |
| IIIc | 7.78 | 4.89 | 4.31 | 5.10 | 5.15 | 10.1 | 17.1 | 1.9 |
| IIId | | 4.64 | 4.28 | 5.10 | 5.21 | 9.0 | 15.5 | 1.4 |

pimaradiene. The identity of the infrared spectra of these products with those of the hydrocarbons derived from the acids rigorously excludes the Edwards sandaracopimaric acid stereochemistry (IIIb) for rimuene. This work is of utmost significance in view of the claim by V. Galík, J. Kuthan and F. Petrů [*Chemistry & Industry*, 722 (1960)] to have converted their sandaracopimaric acid into rimuene.

(5) The spectra were obtained with *ca.* 25% deuteriochloroform solutions on a Varian Model HR60 spectrometer at 60 mc./sec. with tetramethylsilane acting as internal standard [*cf.* G. V. D. Tiers, *J. Phys. Chem.*, **62**, 1151 (1958)]. Position of the major peaks was determined by the audiofrequency side band technique, that of minor peaks by linear interpolation.

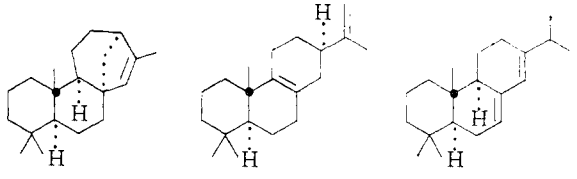
(6) The n.m.r. spectra of methyl pimarate and methyl isopimarate, reported recently by J. C. W. Chien [*J. Am. Chem. Soc.*, **82**, 4762 (1960)], confirmed the known dissimilarity of their C-9,13 stereochemistry. His assignment of the tertiary allylic proton peaks proved important in our work.

(7) While the former spectra represent two examples of the well-known degenerated ABX system, the latter are quite unusual. A recent study by T. Schaefer and W. G. Schneider [*Can. J. Chem.*, **38**, 2066 (1960)] on specific solvent effects on the proton resonance spectrum of vinyl bromide has shown a dramatic change of the spectra with increasing concentrations of benzene from one like those of IIIa and b to one like those of IIIc and rimuene. Since this change is attributed to an increase of electronic screening of the vinyl hydrogens by benzene with an increase of solvent, an attractive, albeit not yet compelling, explanation of our results must lie in the possible difference of intramolecular shielding of the diterpenic vinyl hydrogens by the nuclear double bond.

(8) *Cf.* (a) J. A. Pople, W. G. Schneider and H. J. Bernstein, "High Resolution Nuclear Magnetic Resonance," McGraw-Hill Book Co., Inc., New York, N. Y., 1959, and (b) L. M. Jackman, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press, Ltd., London, England, 1959.

Further support for rimuene's C-13 configuration (IIId) came from an inspection of the optical rotatory dispersion curves of rimuene and the three resin acids (IIIa,b,c), while isopimaric (IIIa) and sandaracopimaric (IIIb) acids have plain negative curves, pimaric acid (IIIc) and rimuene have plain positive curves.[3d,e] Since C-13, the asymmetric center surrounded by both chromophores in all four compounds, would be expected to be the major contributor to the sign and shape of these curves, the o.r.d. data confirm a pimaric-type C-13 stereochemistry for rimuene.

The consequent formulation IIId for rimuene precludes the latter's reported acid-catalyzed conversion[2b] to isophyllocladene (IV)[9] by a mechanism analogous to the suggested[1] and recently proved[10] path of biosynthesis of tetracarbocyclic diterpenes. Instead, nuclear double bond and 13-methyl migrations could be expected to lead to a mixture of abietadienes from which both isophyllocladene (IV) (via diene V) and the reported[2b] second product VI can emerge.[11]



IV V VI

NOTE ADDED IN PROOF.—Through the courtesy of Professor Petrü the m.m.p. of his and Edwards' samples of sandaracopimaric acid was measured and their infrared and n.m.r. spectra compared. The former was undepressed and the latter identical.

(9) *Cf.* P. K. Grant and R. Hodges, *Tetrahedron*, **8**, 261 (1960); R. F. Church, R. E. Ireland and J. A. Marshall, *Tetrahedron Letters*, No. **17**, 1 (1960); R. B. Turner and P. E. Shaw, *ibid.*, No. **18**, 24 (1960).

(10) A. J. Birch, R. W. Richards, H. Smith, A. Harris and W. B. Whalley, *Tetrahedron*, **7**, 241 (1959).

(11) Only the generous aid by Professor L. H. Briggs and by Dr. P. K. Grant (Wellington, New Zealand) in furnishing samples of rimuene, by Dr. O. E. Edwards (Ottawa, Canada) and Dr. R. V. Lawrence (Olustee, Florida) in supplying samples of sandaracopimaric acid and the other resin acids, respectively, and by Dr. W. A. Struck (Upjohn) in carrying out the o.r.d. measurements made our work possible.

(12) Public Health Service Predoctoral Research Fellow, 1960–1961.

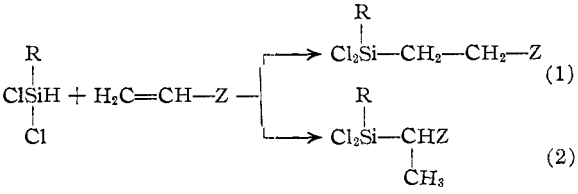
DEPARTMENT OF CHEMISTRY
IOWA STATE UNIVERSITY ERNEST WENKERT
AMES, IOWA PETER BEAK[12]

RECEIVED DECEMBER 27, 1960

## SILICON HYDRIDE–OLEFIN ADDITIONS

*Sir:*

We wish to report a new catalyst system which is unique in its effect on the addition of silicon hydrides to olefins containing double bonds conjugated with strongly electronegative groups. This addition reaction has been reported to occur, using a variety of catalysts, to give either an *alpha*- or a *beta*-adduct (reaction (2) or (1), respectively) or a mixture thereof.



The course of the reaction is determined by the nature of the electronegative group, Z, the presence of organic substituents on the olefinic carbon atoms, the type of group, R, attached to the silicon atom, and the kind of catalyst.

An unusual example of this reaction exists when Z is a nitrile group, *i.e.*, with acrylonitrile, and when R is a methyl group, as in methyldichlorosilane, in that the *beta* addition (reaction 1) is effected poorly, if at all. Many catalysts for this reaction have been investigated, including tertiary amines,[1,2,3] platinum-on-carbon,[4,5] and amides.[6] The best reported results[2] are those obtained with a pyridine catalyst in acetonitrile solvent at 160–170°, whereupon less than a 10% yield of β-cyanoethylmethyldichlorosilane was isolated. Using a platinum catalyst[4] a 26% yield of the *alpha*-adduct was obtained after 26 hr. at 75°. In contrast, trichlorosilane adds to acrylonitrile[7,8,9] to give relatively good yields of either α- or β-cyanoethyltrichlorosilane.

The catalyst system which we have found facilitates the preparation of β-cyanoethylmethyldichlorosilane in yields greater than 75%. Three components are involved in this catalyst: tri-*n*-butylamine, N,N,N′,N′-tetramethylethylenediamine, and copper(I) chloride. Low yields of *beta*-adduct result if the tributylamine is omitted and larger amounts of the diamine are substituted.

In a typical synthesis, a mixture of 23 ml. (0.22 mole) of methyldichlorosilane, 10 ml. (0.15 mole) of acrylonitrile, 1.0 ml. (0.007 mole) of N,N,N′,N′-tetramethylethylenediamine, 4.0 ml. (0.017 mole) of tri-*n*-butylamine, and 2.0 g. (0.02 mole) of copper (I) chloride was heated under reflux for 40 hours. During this time the temperature of the refluxing reaction mixture rose from 51° to over 126°. The darkly colored liquid was vacuum distilled to give 20 g. (79% of theoretical) of product, b.p. 83–85° (8 mm.) (lit.[2] for β-cyanoethylmethyldichlorosilane, b.p. 111–113° (40 mm.)). Infrared analysis is consistent with the structure of the *beta*-adduct and indicates the absence of the *alpha*-adduct (lit.[4] b.p. 60–62° (4 mm.)).

As an indication of the scope of this three-component catalyst we have examined the reaction of other silicon hydrides and other olefins and find the present catalyst beneficial for the synthesis of many other *beta*-adducts. Of immediate interest is the addition of trichlorosilane to acrylonitrile reported[1] to give a 56% yield of β-cyanoethyltrichlorosilane after 24 hr. reflux using 5 mole % of tri-*n*-butylamine as a catalyst. When an equimolar amount of trichlorosilane was used in place of methyldichlorosilane, in the experiment described above using the three catalyst components, the

(1) M. Prober, French Patent 1,118,500 (1956).

(2) A. D. Petrov and V. M. Vdovin, *Izvest. Akad. Nauk S.S.S.R., Otdel. Khim. Nauk.* 1490 (1957).

(3) K. Shiina and M. Kumada, "Memoirs of the Faculty of Engineering, Osaka City University," Japan, Vol. 1, Dec. 1959.

(4) L. Goodman, R. M. Silverstein and A. Benitez, *J. Am. Chem. Soc.*, **79**, 3073 (1957).

(5) F. P. MacKay, Ph.D. Thesis, Pennsylvania State University, June, 1956.

(6) J. C. Saam and J. L. Speier, *J. Org. Chem.*, **24**, 427 (1959).

(7) S. Nozakura and S. Konotsune, *Bull. Chem. Soc. Japan.*, **29**, 322, 326 (1956).

(8) L. H. Sommer, F. P. MacKay, O. W. Steward and P. G. Campbell, *J. Am. Chem. Soc.*, **79**, 2764 (1957).

(9) R. A. Pike, J. E. McMahon, V. B. Jex, W. T. Black and D. L. Bailey, *J. Org. Chem.*, **24**, 1939 (1959).