out in about 7% over-all yield based on [2.2]paracyclophane, with the yield in the primary dichloroformylation reaction being only 15%.[6c] The previous preparation[8] of [3.3]paracyclophane required a difficult ten-step synthesis involving a particularly unfavorable acyloin reaction occurring in only about 1% yield (over-all yield was 0.1%). Consequently, the ring expansion route represents a distinct improvement.

Acknowledgment. The authors wish to acknowledge helpful discussions with Professors M. A. Battiste and D. J. Cram.

E. Hedaya, L. M. Kyle
Union Carbide Research Institute
Tarrytown, New York
Received May 25, 1966

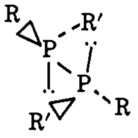
The Inversion of Diphosphines

Sir:

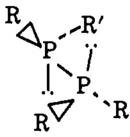
The configurational instability of asymmetric tertiary amines has thus far prevented their resolution into optical antipodes, although inversion about nitrogen has been studied by nmr spectroscopy.[1] In the absence of ring constraints or ponderous substitution, inversion is generally too rapid to permit kinetic analysis even by this method. The recently reported isolation of optically active phosphines[2] might imply that inversion about phosphorus, on the other hand, is too slow for detection by nmr spectroscopy. We wish to report that the resonances of diphosphines exhibit reversible, temperature-dependent properties that are the kinetic result of phosphorus inversion. p_π–d_π bonding between the phosphorus atoms in diphosphines[3] apparently decreases the configurational stability with respect to that of monophosphines.[2]

Unsymmetrical diphosphines (I) may exist in two diastereomeric forms, the *meso* (II) and the *dl* (III), which should produce separate and distinct resonances.

RR′P-PRR′
Ia, R = CH_3; R′ = C_6H_5
Ib, R = CH_3; R′ = p-$CH_3C_6H_4$



II



III

Indeed, the ^{31}P spectrum of Ia is reported by Maier to consist of two peaks.[4] We have found that the aromatic region of the proton spectrum[5] of Ia also consists of two distinct multiplets below 130°. The *meso* form (II) may be converted to the *dl* form (III) (and *vice versa*) by a single inversion about phosphorus.[6] If this process becomes fast with respect to the nmr time scale, the effective loss of diastereomeric identity would cause the peaks to coalesce. Between 130 and 180°, the phenyl peaks broaden and coalesce into a single resonance with a line width comparable to that of the resonances at slow exchange. The aromatic methyl group of Ib also gives a doublet resonance that collapses to a sharp singlet at elevated temperatures. The slow-exchange spectra may be reproduced by lowering the temperature. The spectral properties at high temperatures are therefore consistent with rapid and reversible inversion about phosphorus.

Since the ring protons of each diastereomer are not magnetically equivalent, the aromatic resonances of Ia are highly structured. In order to develop an unambiguous kinetic analysis, we have synthesized 1,2-dimethyl-1,2-bis(2,4,6-trideuteriophenyl)diphosphine (Ia-d_3).[7] The unsplit but broad resonances of the *meta* protons have been kinetically analyzed at various temperatures by the Gutowsky–Holm–Borčić method.[8] The equilibrium constant at 32° (1.35) corresponds to a free-energy difference between diastereomers of 180 cal/mole.[9] From an Arrhenius plot of the kinetic data (Table I), the activation energy for inversion was calculated to be 26.0 ± 2 kcal/mole.

Table I. Kinetic Data for the Interconversion of Diastereomeric Diphosphines

T, °C	τ_A, sec[a]	τ_B, sec[a]	$W_{1/2}$, hertz[b]
125	...	...	3.7
140	0.4	0.3	...
146	0.25	0.19	...
149	0.195	0.15	...
153	0.163	0.125	...
160	0.091	0.070	...
162	0.071	0.055	...
168	0.058	0.045	...
200	...	...	4.5

[a] Mean lifetime. [b] Line width at half-height.

Several alternative explanations have been considered. (1) Since the distance between the two peaks of Ia-d_3

---

(1) A. T. Bottini and J. D. Roberts, *J. Am. Chem. Soc.*, **78**, 5126 (1956); A. Loewenstein, J. F. Neumer, and J. D. Roberts, *ibid.*, **82**, 3599 (1960); A. T. Bottini, R. L. VanEtten, and A. J. Davidson, *ibid.*, **87**, 755 (1965); D. L. Griffith and J. D. Roberts, *ibid.*, **87**, 4089 (1965); W. N. Speckamp, U. K. Pandit, and H. O. Husiman, *Tetrahedron Letters*, **No. 44**, 3279 (1964); V. F. Bystrov, R. G. Kostyanovskii, O. A. Panshin, A. U. Stepanyanta, and O. A. Iuzhakova, *Opt. Spectry. (USSR)*, **19**, 122 (1965).

(2) L. Horner, H. Winkler, A. Rapp, A. Mentrup, H. Hoffman, and P. Beck, *Tetrahedron Letters*, **No. 5**, 161 (1961); L. Horner and H. Winkler, *ibid.*, **No. 9**, 461 (1964); D. P. Young, W. E. McEwen, D. C. Velez, J. W. Johnson, and C. A. VanderWerf, *ibid.*, **No. 7**, 359 (1964); I. G. M. Campbell and J. K. Way, *J. Chem. Soc.*, 5034 (1960).

(3) For a review of the chemistry and properties of diphosphines, see A. H. Cowley, *Chem. Rev.*, **65**, 617 (1965).

(4) L. Maier, *Ber.*, **94**, 3043 (1961); L. Maier, *J. Inorg. Nucl. Chem.*, **24**, 275 (1962).

(5) Methyldibromophosphine sulfide and the phenyl Grignard reagent were converted to *dl*- and *meso*-1,2-dimethyl-1,2-diphenyldiphosphine disulfide according to the method of Maier.[4] Either isomer gave the same *dl*-/*meso*-diphosphine mixture upon reduction. The methyl resonances of Ia were masked by the solvent, tri-*n*-butylphosphine sulfide. All spectra were taken with a temperature-adaptable Varian A-60 spectrometer. Accurate temperatures were obtained by measurement of the distance between the resonances of ethylene glycol.

(6) The simultaneous inversion of both phosphorus atoms with a planar, alkene-like transition state would introduce statistical factors that only influence the preexponential portion of the rate expression. The essentials of the following discussion would not be altered.

(7) Deuterium was introduced into the *ortho* and *para* positions of aniline hydrochloride by treatment with deuterium oxide at 100°. The free amine was then converted by way of the Sandmeyer reaction to bromobenzene-2,4,6-d_3, which was used in Maier's diphosphine synthesis.[4,5]

(8) J. B. Lambert, W. L. Oliver, and J. D. Roberts, *J. Am. Chem. Soc.*, **87**, 5085 (1965).

(9) An equilibrium constant different from unity eliminates the possibility that the distinct resonances are due to *meta* protons that are nonequivalent by hindered rotation about the P–C bond. This conclusion is confirmed by the coalescence of the aromatic methyl resonances of Ib (*vide supra*).

was found to be linearly proportional to the strength of the magnetic field (6.4 hertz at 60 Mhertz; 10.7 hertz at 100 Mhertz),[10] the splitting of the aromatic resonances cannot be due to spin-spin interactions. (2) Although a dissociation–recombination mechanism would also bring about interconversion of the diastereomers, the resulting phosphine radicals should have caused significant broadening of the spectral lines. Diphosphines are known to cleave by thermal means.[11] In the present situation, however, a dissociation would have to be followed by rapid, intramolecular recombination, since the spectral changes are reversible. Such a process, if exceedingly rapid, would be practically indistinguishable by nmr methods from inversion. This mechanism is not favored because line broadening was not appreciable (Table I) and irreversible radical reactions were not apparent. (3) Of the six rotational isomers that may be written for each diphosphine diastereomer, three do not contain eclipsed interactions.[8] Of these, either *gauche* conformation would be of much higher energy than the *trans* form (II, III), which minimizes not only the nonbonded interactions between substituents, but also the lone pair–lone pair repulsions.[12] Our conclusions require either that diphosphines are frozen into the *trans* conformation or that there is free rotation about the phosphorus–phosphorus bond. The equivalence of all the protons in P_2H_4 is consistent with this model.[3,13] Furthermore, the ^{31}P spectra of numerous diphosphines of the type R_2P-PR_2 or $R_2P-PR'_2$, for which rotamers, but not diastereomers, can exist, have never been reported to exhibit multiple resonances, except from chemically distinct species.[4,14] Coalescence of the phenyl resonances at elevated temperatures is therefore best explained in terms of phosphorus inversion, rather than equilibration of rotamers. Studies with related polyphosphine systems are continuing.

---

(10) We are grateful to Professor M. R. Willcott of the University of Houston for measuring the 100-Mhertz spectra.

(11) R. S. Davidson, R. A. Sheldon, and S. Trippett, *J. Chem. Soc.* (*Org.*), 722 (1966).

(12) C. A. Coulson, "Valence," Oxford University Press, New York, N. Y., 1961, pp 178–179.

(13) R. M. Lynden-Bell, *Trans. Faraday Soc.*, **57**, 888 (1961).

(14) K. Moedritzer, L. Maier, and L. C. D. Groenweghe, *J. Chem. Eng. Data*, 7, 307 (1962); E. Fluck and K. Issleib, *Ber.*, **98**, 2674 (1965).

(15) National Science Foundation Undergraduate Research Participant, 1965–1966.

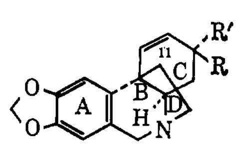
Joseph B. Lambert, David C. Mueller[15]
Department of Chemistry, Northwestern University
Evanston, Illinois 60201

Received May 20, 1966

A Total Synthesis of (±)-Crinine

Sir:

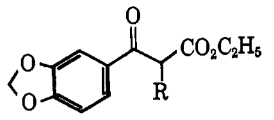
Crinine (I)[1a] and epicrinine (II)[1b] are representatives of one of the more widely occurring groups of Amaryllidaceae alkaloids,[2] the 5,10b-ethanophenanthridines.



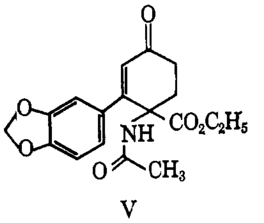
I, R = H; R' = OH
II, R = OH; R' = H

While several communications have appeared in the past few years concerning the synthesis of various 5,10b-ethanophenanthridine alkaloids,[3] no total syntheses have been reported. We now wish to report the first total synthesis of (±)-crinine (I) and (±)-epicrinine (II) and to describe a versatile pathway with potential for the elaboration of structurally similar alkaloids.

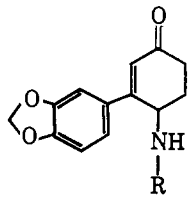
Ethyl piperonylacetate (III)[4] was nitrosated (sodium nitrite–acetic acid) and then reduced and acetylated (zinc–acetic acid–acetic anhydride) to ethyl N-acetylpiperonylglycinate (IV) (mp 122–123°).[5] Condensation of IV with methyl vinyl ketone (Triton B-benzene) followed by cyclization of the Michael adduct (1,4-diazabicyclo[2.2.2]octane, piperidine, acetic acid, and xylene)[6] gave the α,β-unsaturated ketone V (mp 176–178°). Saponification and decarboxylation of V led to VIa (mp 197–199°) in 59% over-all yield based on III.



III, R = H
IV, R = $NHCOCH_3$



V



VIa, R = $COCH_3$
b, R = H
c, R = $COCH_2CO_2CH_3$

Reduction of VIa with sodium borohydride gave a nearly quantitative yield of a mixture of epimeric alcohols VII (mp 166–170°). Refluxing the mixture VII in benzene or toluene with 1,1-dimethoxy-1-dimethylaminoethane[7] gave the diamides VIIIa and b[8] (45% after chromatography),[9] accompanied by a 50% yield of the diene IX[10] (mp 137–138°; $\lambda\lambda_{\max}^{\text{ethanol}}$ mμ

---

(1) (a) W. C. Wildman, *J. Am. Chem. Soc.*, **80**, 2567 (1958); (b) R. E. Lyle, E. A. Kielar, J. R. Crowder, and W. C. Wildman, *ibid.*, **82**, 2620 (1960).

(2) For a review, see W. C. Wildman in "The Alkaloids," Vol. VI, R. H. F. Manske, Ed., Academic Press Inc., New York N. Y., 1965, p 290; K. W. Bentley, "The Alkaloids," Vol. VII, Interscience Publishers, Inc., New York, N. Y., 1965, p 54.

(3) H. W. Whitlock, Jr., and G. L. Smith, *Tetrahedron Letters*, 1389 (1965); J. B. Hendrickson, C. Foote, and N. Yoshimura, *Chem. Commun.*, 165 (1965).

(4) T. Kametani and H. Iida, *J. Pharm. Soc. Japan*, 73, 681 (1953).

(5) Satisfactory analytical data have been obtained for all new compounds reported, and all compounds were characterized by ultraviolet, infrared, and nuclear magnetic resonance spectroscopy. Melting points were taken on a Kofler hot-stage microscope.

(6) H. Muxfeldt, *Angew. Chem.*, 74, 825 (1962).

(7) H. Meerwein, W. Florian, N. Schön, and G. Stopp, *Ann.*, **641**, 1 (1961); A. E. Wick, D. Felix, K. Steen, and A. Eschenmoser, *Helv. Chim. Acta*, 47, 2425 (1964).

(8) We wish to propose that this modification of the Claisen rearrangement be known as the Meerwein-Eschenmoser reaction.

(9) These isomeric amides were only slightly separated on thin layer chromatography.

(10) The formation of this sensitive compound is notable. Applications of this alternate course of the reaction are under investigation.