The products in Table I were converted to their methyl esters and analyzed by gc as described.[13]

Acknowledgment. Grateful acknowledgment is made to the National Science Foundation and the Petroleum Research Fund, administered by the American Chemical Society, for support of this work.

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[13] N. Deno, C. Pierson, and R. Fishbein, *J. Amer. Chem. Soc.*, **92**, 1451 (1970).

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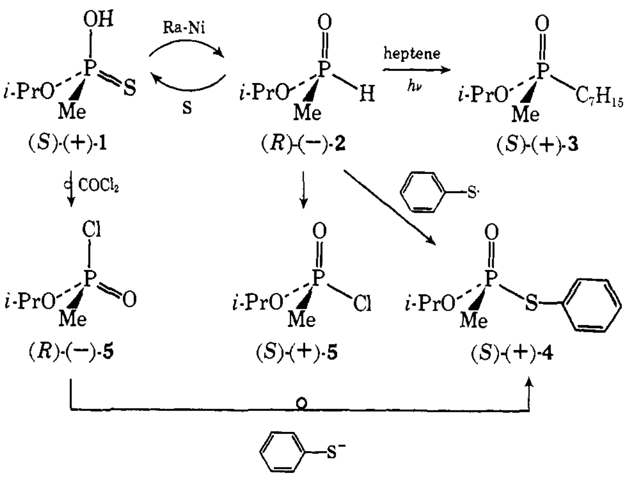
Stereospecific Synthesis and Reactions of Optically Active Isopropyl Methylphosphinate

Sir:

The recent publication of the resolution of a diastereoisomeric hydrogen phosphinate[1] and the separation of the geometric isomers of a cyclic hydrogen phosphite[2] prompts us to report our results on the stereospecific synthesis of an optically active acyclic hydrogen phosphinate (**2**), whose chirality is due solely to the presence of an asymmetric phosphorus atom. Hydrogen phosphinates are highly versatile synthetic intermediates that undergo a wide variety of interesting reactions.[3] We include here a preliminary report on the stereochemistry of a number of these reactions.

We find that (*S*)-(+)-isopropyl methylphosphonothioic acid (**1**), α_D +14.0° (neat) (100% optically pure),[4,5] is desulfurized on refluxing with Ra–Ni[6] in ethanol to give (*R*)-(−)-isopropyl methylphosphinate (**2**); similarly, (*S*)-(+)-**2** has been obtained from (*R*)-(−)-**1**. On a 20-mmol scale, after vacuum distillation at room temperature, a 60% yield of **2** (generally containing 5–10% ethanol) was regularly obtained: $[\alpha]_D$ −30° (EtOH), −19° (CCl_4), −14° (benzene). Once separated from nickel salts and acidic material in the reaction mixture, it was redistilled (bp 77° (7 mm)) with little or no racemization. The (−)-**2** is rapidly (if not instantaneously) racemized by traces of sodium methoxide in methanol, presumably *via* the anion (**7**) (see below). In contrast to the reported instability of the Ar(R)P(H)O system,[7] however, it appears stable toward acid-catalyzed racemization. Thus, it did not racemize in the presence of an equal weight of isopropyl methylphosphonic acid in ethanol solution. A slow loss of optical activity (half-life of about 5 days) was noted for (−)-**2** in 95% methanolic 0.05 *N* hydrochloric acid, probably due to hydrolysis of the ester function.

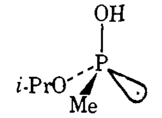
Chart I

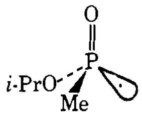


As shown in Chart I, (*R*)-(−)-**2** adds sulfur in dioxane in the presence of dicyclohexylamine, undoubtedly with retention of configuration[2] and apparently by a radical mechanism,[8] to return (*S*)-(+)-**1**, isolated as the dicyclohexylamine salt, $[\alpha]_D$ +6.80° (methanol), 89 ± 1% optically pure.[4] The desulfurization and the sulfur addition reactions are thus shown to be essentially stereospecific. Based on the assigned stereochemistry of the latter, the desulfurization must take place also with retention of configuration.

For studies of the stereochemistry of other reactions of **2**, the optically active compound was generally diluted with racemic material, synthesized essentially as described.[9]

In CH_3OD, (−)-**2** exchanged the hydrogen on phosphorus for deuterium, as followed by the decrease of the P–H band in the pmr spectrum. The exchange was accompanied by a slight increase in the specific rotation (from −13.57 to −13.61°), showing that the exchange occurred by a front-sided replacement of the hydrogen in (*R*)-**2**, presumably *via* its (*R*)-**2a** tautomer,[10] with overall retention of configuration.


(*R*)-**2a**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Photochemically initiated radical reactions of **2**, if run at or near room temperature, proceed stereoselectively (if not stereospecifically) with retention of configuration. Thus, (*S*)-(+)-**2**, $[\alpha]_D$ +18.8° (ethanol) (63% optically pure), with phenyl disulfide in the presence of uv light,[8] gave (*R*)-(−)-*O*-isopropyl *S*-phenyl methylphosphonothiolate (**4**), bp 94° (15 μ), 93% pure (glpc), $[\alpha]_D$ −52.2° (benzene), identical (ir, glpc) with the enantiomorph of the product obtained with predominant inversion of configuration from the reaction of (*R*)-(−)-isopropyl methylphosphonochloridate (**5**) with sodium thiophenoxide, as indicated in Chart I. Also, the radical addition of (−)-**2**, $[\alpha]_D$ −17.4° (eth-

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[1] H. P. Benschop, D. H. J. M. Platenburg, F. H. Meppelder, and H. L. Boter, *Chem. Commun.*, 33 (1970).

[2] M. Mikolajczyk, *ibid.*, 1221 (1969).

[3] A. W. Frank, *Chem. Rev.*, 61, 389 (1961).

[4] (a) H. S. Aaron, J. Braun, T. M. Shryne, H. F. Frack, G. E. Smith, R. T. Uyeda, and J. I. Miller, *J. Amer. Chem. Soc.*, **82**, 596 (1960); (b) H. L. Boter and D. H. J. M. Platenburg, *Recl. Trav. Chim. Pays-Bas*, **86**, 399 (1967).

[5] H. P. Benschop, G. R. van den Berg, and H. L. Boter, *ibid.*, **87**, 387 (1968).

[6] L. F. Fieser and M. Fieser, "Reagents for Organic Synthesis," Wiley, New York, N. Y., 1967, p 729.

[7] (a) T. L. Emmick and R. L. Letsinger, *J. Amer. Chem. Soc.*, **90**, 3459 (1968); (b) O. Cervinka, O. Belovsky, and M. Hepnerova, *Chem. Commun.*, 562 (1970).

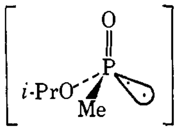
[8] W. A. Mosher and R. R. Irino, *J. Amer. Chem. Soc.*, **91**, 756 (1969).

[9] K. A. Petrov, N. K. Bliznyuk, Y. N. Studnev, and A. F. Kolomiets, *Zh. Obshch. Khim.*, 31, 179 (1961). We thank Thomas J. Barbish and David I. Rossman for samples of racemic **2**.

[10] See, for example, the summary discussion on p 612 in the review by S. G. Warren, *Angew. Chem.*, 7, 606 (1968).

anol) (58% optically pure), to heptene[11] gave (+)-isopropyl heptylmethylphosphinate (**3**), bp 119° (1.8 mm), $[\alpha]_{\mathrm{D}}$ +2.21° (ethanol), presumably with the (*S*) configuration, as shown. At least two possibilities exist for the configurationally stable radical intermediate in the former reaction [$\mathrm{Me}(i\text{-PrO})\dot{\mathrm{P}}(\mathrm{OH})\mathrm{SC_6H_5}$ by $\mathrm{C_6H_5S}\cdot$ addition to **2a**,[12] and **6** by $\mathrm{C_6H_5S}\cdot$ abstraction of H· from **2** or **2a**]. Only the phosphinyl radical (**6**) appears possible as an intermediate in the heptene addition reaction, however, if one assumes a radical chain process is involved. It follows, then, that the phosphinyl radical must be configurationally stable, at least as a transient intermediate.

Unlike the radical systems, reactions of the corresponding anion (**7**) lead to racemic products (however, see below). Here, the intermediate, as customarily prepared, is rapidly (possibly instantaneously) racemized. Thus, when (−)-**2** was treated with sodium or potassium in ether or benzene to form the Michaelis–Becker intermediate,[13] the resulting solutions had zero rotation, and the products of the reactions of these solutions with alkyl halides were optically inactive. Similarly, treatment of (+)-**2** with butyllithium and then benzyl bromide gave the racemic product.



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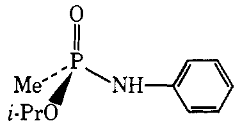

(*R*)-(−)-**8**

The (*R*)-(−)-**2**, $[\alpha]_{\mathrm{D}}$ −0.90° ($\mathrm{CCl_4}$) (4.6% optically pure), reacted rapidly and probably stereospecifically with *N*-chlorosuccinimide[14] in carbon tetrachloride to give the (*S*)-(+)-**5**. The product was identified by ir, then converted with inversion of configuration to the anilide, (*R*)-(−)-**8**, mp 91–95°, $[\alpha]_{\mathrm{D}}$ −9.2° (benzene) (8% optically pure).[15] Also (*R*)-(−)-**2** slowly reacted with carbon tetrachloride containing tributylamine[16] at 25° in the presence of added aniline to form (*S*)-(+)-**5**, which was converted *in situ* and isolated as the (*R*)-(−)-**8** anilide. In the absence of the added aniline, a racemized product mixture was obtained. Both the *N*-chlorosuccinimide and the amine–$\mathrm{CCl_4}$ reactions must take place with predominant if not complete retention of configuration (though not necessarily *via* similar mechanisms), based on the known[15] relationship of (*R*)-(−)-**5** to (*S*)-(+)-**1**, as indicated in Chart I. The stereoselectivity of the amine–$\mathrm{CCl_4}$ reaction indicates that either the suggested[16b] mechanism is incorrect, or else the postulated anion (**7**), like the phosphinyl radical, does maintain its configuration, if present only as a transient reaction intermediate. Other stereochemical studies of the reactions of **2** will be reported at a later date.

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[11] Compare, for example, A. N. Pudovik and I. V. Konovalova, *Zh. Obshch. Khim.*, **29**, 3342 (1959).

[12] Compare, for example, W. G. Bentrude, J. H. Hargis, and P. E. Rusek, Jr., *Chem. Commun.*, 296 (1969).

[13] A. Michaelis and T. Becker, *Chem. Ber.*, 30, 1003 (1897).

[14] G. W. Kenner, A. R. Todd, and F. J. Weymouth, *J. Chem. Soc.*, 3675 (1952).

[15] H. S. Aaron, R. T. Uyeda, H. F. Frack, and J. I. Miller, *J. Amer. Chem. Soc.*, **84**, 617 (1962). The apparent increase in optical purity in going from (−)-**2** *via* (+)-**5** to (−)-**8** is due to the fact that the (−)-**8** is more insoluble than the racemic compound.

[16] (a) F. R. Atherton, H. T. Openshaw, and A. R. Todd, *J. Chem. Soc.*, 660 (1945); (b) G. M. Steinberg, *J. Org. Chem.*, **15**, 637 (1950).

[17] To whom correspondence should be addressed.

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Received May 11, 1970

Reaction of Oxime *O*-Acetates with Chromous Acetate. A Method for the Conversion of Ketoximes to Ketones under Mild Conditions

Sir:

Despite the ready availability of ketoximes as synthetic intermediates and as derivatives for carbonyl protection, the utilization of oximes as precursors of ketones which are sensitive to acid and/or base has not been satisfactory.[1] In two instances recently encountered in these laboratories, none of the conventional or recently described procedures have shown promise.[2–4] This note describes a new reductive deoximation reaction which is highly effective even in the presence of acid- and base-sensitive functional groups such as ketal, hemithioketal, ester, and epoxide. The method involves the conversion of an oxime to the *O*-acetate derivative followed by reaction with >2 mol equiv of chromous acetate in 9:1 tetrahydrofuran–water (by weight) at temperatures between 25 and 65°. The selection of the reagent chromous acetate was based on the premise that it would cause reductive fission of the oxime N–O linkage to give an imine which then would suffer rapid hydrolysis to ketone at the pH (*ca.* 5) of the acetate ion buffered solution. The following procedure is illustrative of the new reaction.

Propiophenone. Propiophenone oxime *O*-acetate[5] (193 mg, 1.0 mmol) and excess chromous acetate (*ca.* 1 g)[6,7] were stirred in 10 ml of 9:1 tetrahydrofuran–

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[1] For a recent example see N. Finch and J. J. Fitt, *Tetrahedron Lett.*, 4639 (1969).

[2] Hydrolytic methods: (a) E. B. Hershberg, *J. Org. Chem.*, **13**, 542 (1948); (b) M. P. Cava, R. L. Little, and D. R. Napier, *J. Amer. Chem. Soc.*, **80**, 2260 (1958); (c) C. H. De Puy and B. W. Ponder, *ibid.*, **81**, 4629 (1959); (d) S. H. Pines, J. M. Chemerda, and M. A. Kozlowski, *J. Org. Chem.*, 31, 3446 (1966).

[3] Oxidative methods: (a) (nitrosating agents) D. T. Manning and H. A. Stansbury, Jr., *J. Amer. Chem. Soc.*, **81**, 4885 (1959), and references cited therein; (b) (lead tetraacetate) G. Just and K. Dahl, *Can. J. Chem.*, **48**, 966 (1970); (c) (Ce(IV)–$\mathrm{HNO_3}$) J. W. Bird and D. G. M. Diaper, *ibid.*, **47**, 145 (1969); (d) (ozone) R. E. Erickson, P. J. Andrulis, Jr., J. C. Collins, M. L. Lungle, and G. D. Mercer, *J. Org. Chem.*, **34**, 2961 (1969).

[4] Reductive methods: (a) (zinc–acetic acid, 100°) M. S. Ahmad and A. H. Siddiqui, *J. Indian Chem. Soc.*, **46**, 44 (1969); (b) (iron carbonyl–boron trifluoride) H. Alper and J. T. Edward, *J. Org. Chem.*, **32**, 2938 (1967).

[5] Oxime *O*-acetates were prepared by brief treatment of the ketoximes with acetic anhydride at 20°; see H. Metzger in "Methoden der Organischen Chemie," Vol. 10, No. 4, E. Muller, Ed., Georg Thieme Verlag, Stuttgart, 1968, p 182.

[6] An aqueous solution of Cr(II), prepared by reduction of chromic chloride by zinc–hydrochloric acid [J. H. Balthis, Jr., and J. C. Bailar, Jr., *Inorg. Syn.*, 1, 122 (1939)], was transferred by syringe into a filtering apparatus [L. R. Ocone and B. P. Block, *ibid.*, **8**, 125 (1966)] containing air-free sodium acetate solution. The precipitate of chromous acetate was collected, washed sequentially with air-free water, ethanol, and ether, and dried *in vacuo* to afford the dihydrate as a pink powder. The dried powder can be transferred with brief exposure to air with only slight oxidation.

[7] Most of the hydrolytic experiments which have been carried out in this work have been conducted on a 0.5–2-mmol scale using a substantial excess of chromous acetate. For larger scale work, where air oxidation of the reagent would be insignificant using approximately anaerobic techniques, a modest excess (*ca.* 20%) over the theoretical 2 mol equiv is preferred.