As might be expected from the structural relationship between **1a** and **1b**, labeling experiments provide support for an intramolecular insertion mechanism. We have prepared $[(n\text{-}C_4H_9)_4N]_3CH_3COCHMo_4O_{15}H$[9] (**2a**) by following the procedure outlined above for the preparation of compound **1a** but replacing glyoxal with methylglyoxal ($CH_3COCHO$). Compound **2a**, structurally related to **1a** by replacement of its aldehyde proton with a methyl group, reacts with HF in an analogous fashion to yield $[(n\text{-}C_4H_9)_4N]_3CH_3CCHMo_4O_{15}F$ (**2b**).[10] The $^1H$ NMR spectrum of pure compound **2b**, crystallized by slow (2 days) evaporation from $(CH_3)_2CO/CH_3C_6H_5$, in $CD_2Cl_2$, displays two acetal proton resonances at $\delta$ 6.05 and $\delta$ 5.83 having relative intensities of 3:2. These resonances presumably arise from the two isomers of **2b**, where the methyl group is bound to either the central or the peripheral acetal carbon (see Scheme II). The $^1H$ NMR spectrum of crude **2b** in $CD_2Cl_2$ displays only one acetal resonance at $\delta$ 6.05. If the NMR solution is allowed to stand, however, the second $\delta$ 5.83 acetal resonance appears and slowly grows in intensity as the $\delta$ 6.05 resonance loses intensity until a final intensity ratio of 3:2 is observed after 20–40 h. These observations show that the **2a** to **2b** transformation is regiospecific but that the product rearranges in solution. If one assumes that the methyl group in the kinetically favored product is bound to the peripheral carbon atom (see Scheme II), the NMR data support an insertion mechanism.

The conformational flexibility of the $F^-$ binding site in compounds **1b** and **2b** is evident from the anion structure of $[(n\text{-}C_4H_9)_4N]_3HCCHMo_4O_{17}CH$ (**1c**),[11] determined by an X-ray-diffraction study,[8] shown in Figure 1b. Compound **1c** is prepared according to eq 1, HX = $HCO_2H$, utilizing conditions similar to those employed for the synthesis of compound **1b** (see above). Comparison of Figure 1a,b and data given in Table I shows how the geometry of the $HCCHMo_4O_{15}{}^{2-}$ unit is adjusted to accommodate either the $F^-$ anion or the larger $HCO_2{}^-$ ion. Expansion of the $Mo_2$–$O_F$–$Mo_{2'}$ angle increases the $Mo_2$–$Mo_{2'}$ separation. As this Mo–Mo distance changes, however, the remainder of the anion geometry must be adjusted. The necessary flexibility is provided by rotation about the $C_{G1}$–$C_{G2}$ bond which varies the $Mo_1$–$Mo_{1'}$ distance and, together with expansion or contraction of the $Mo_2$–$O_F$–$Mo_{2'}$ angle, determines the size of the anion binding cavity.

**Acknowledgments.** W.G.K. acknowledges the National Science Foundation and the donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this research.

**Supplementary Material Available:** Tables of atomic positional and thermal parameters for compounds **1b** and **1c** (8 pages). Ordering information is given on any current masthead page.

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[9] Anal. Calcd for $C_{51}H_{113}N_3Mo_4O_{16}$: C, 43.50; H, 8.09; N, 2.98; Mo, 27.25. Found: C, 43.58; H, 8.30; N, 3.01; Mo, 27.49. $^1H$ NMR[5] ($CD_2Cl_2$): $\delta$ 5.77 (s, 1, $CH_3COCH$), 2.53 (s, 3, $CH_3COCH$). The IR spectra of **2a** and **1a** in Nujol mulls show the same pattern of absorptions in the 550–950-$cm^{-1}$ Mo–O and the 3610–3630-$cm^{-1}$ O–H stretching regions.

[10] Anal. Calcd for $C_{51}H_{112}N_3Mo_4O_{15}F$: C, 43.44; H, 8.01; N, 2.98; Mo, 27.21; F, 1.35. Found: C, 43.31; H, 8.08; N, 2.94; Mo, 27.10; F, 1.39.

[11] Anal. Calcd for $C_{51}H_{111}N_3Mo_4O_{17}$: C, 43.07; H, 7.87; N, 2.95; Mo, 26.98. Found: C, 43.18; H, 7.85; N, 3.12; Mo, 27.09. $^1H$ NMR[5] (80 MHz, $CD_2Cl_2$): $\delta$ 8.53 (s, 1, $HCO_2$), 6.05 (AB q, 2, $^3J_{AB}$ = 3.2 Hz, $\Delta\nu_{AB}$ = 7.9 Hz, $HCCH$).

[12] Camille and Henry Dreyfus Teacher-Scholar.

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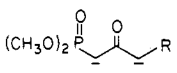
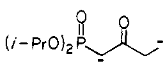
# A Novel β-Ketophosphonate 1,4-Dianion. Tin/Lithium Exchange

*Sir:*

In recent years, carbon–carbon bond formation by means of regiospecific reaction of dianions and dianion analogues has become an increasingly important synthetic tool.[1] Monoanions derived from β-ketophosphonate esters have been extremely useful in the synthesis of certain olefins from aldehydes and ketones.[2] Elegant uses of β-ketophosphonate 1,3-dianions (**1**) have been reported.[3] I report here the generation of β-ketophosphonate 1,4-dianion **2** via the tin/lithium exchange of the monoanion (**3**) derived from diisopropyl 4-tri-*n*-butylstannyl-2-oxobutylphosphonate (**4**). The generation of **2** provides a method of functionalizing the δ carbon of a β-ketophosphonate ester and shows for the first time that it is possible to generate a thermodynamically less stable 1,4-dicarbanion via tin/lithium transmetalation even when an alternative proton abstraction to produce a more stable 1,3-dicarbanion (**5**) is available.[4-6]



1



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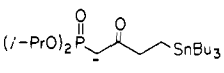

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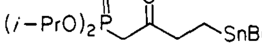

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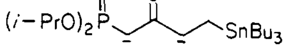

**5**

The generation of organolithium reagents from organotin compounds is a very well-known and widely used reaction.[7] These tin/lithium exchange reactions appear to be equilibrium processes, and they are usually successful only when the organolithium reagent to be generated is stabilized either by unsaturation or by a heteroatom.[8-10] For example, Seyferth and Weiner[8] were unable to prepare the corresponding lithio compound from (3-butenyl)tri-*n*-butyltin. Presence of a carbanionic center in the molecule also retards the tin/lithium transmetalation reactions.[11,12] The success of tin/lithium exchange in the case of **3** is possibly due

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[1] (a) For a review on dianions of β-dicarbonyl compounds, see: Harris, T. M.; Harris, C. M. *Org. React.* (*N.Y.*) **1969**, *17*, 155. (b) For a review on dianions and polyanions, see: Kaiser, E. M.; Petty, J. D.; Knutson, P. L. A. *Synthesis* **1977**, 509–550. (c) Hubbard, J. S.; Harris, T. M. *J. Am. Chem. Soc.* **1980**, *102*, 2110. (d) Trimitsis, G. B.; Hinkley, J. M.; Ten Brink, R.; Poli, M.; Gustafson, G.; Erdman, J.; Rop, D. *Ibid.* **1977**, *99*, 4838. (e) Weiler, L. *Ibid.* **1970**, *92*, 6702. (f) Bays, J. P. *J. Org. Chem.* **1978**, *43*, 38. (g) Cooke, M. P., Jr. *Ibid.* **1973**, *38*, 4062.

[2] (a) For a review, see: Boutagy, J.; Thomas, R. *Chem. Rev.* **1974**, *74*, 87–99. (b) For some recent uses, see: Meyers, A. I.; Smith, R. K. *Tetrahedron Lett.* **1979**, 2749. Stork, G.; Nakamura, E. *J. Org. Chem.* **1979**, *44*, 4010. Nicolaou, K. C.; Seitz, S. P.; Pavia, M. R.; Petasis, N. A. *Ibid.* **1979**, *44*, 4011.

[3] (a) Grieco, P. A.; Pogonowski, C. S. *J. Am. Chem. Soc.* **1973**, *95*, 3071. (b) *Synthesis* **1973**, 425. (c) Grieco, P. A.; Finkellor, R. S. *J. Org. Chem.* **1973**, *38*, 2909.

[4] Generation of the 1,4-dianion $LiCH_2CH_2CO_2Li$ from $BrCH_2CH_2CO_2Li$ and lithium naphthalenide via halogen/metal exchange has been reported; see: Caine, D.; Frobese, A. S. *Tetrahedron Lett.* **1978**, 883.

[5] It is assumed that the presence of tri-*n*-butyltin in the molecule did not greatly affect the stability of such a dianion. There is evidence in the literature to suggest that the presence of tri-*n*-butyltin in such a position of a carbanion does not change the behavior of the carbanion. See: Teratake, S.; Morikawa, S. I. *Chem. Lett.* **1975**, 1333. Still, W. C. *J. Am. Chem. Soc.* **1977**, *99*, 4836.

[6] Seebach, D.; Geiss, K. H. *J. Organomet. Chem. Libr.* **1976**, *1*, 5. In this example, Sn/Li exchange is faster than epoxide opening by BuLi at −100 °C.

[7] For a review, see ref 6, pp 188–190.

[8] Seyferth, D.; Weiner, M. A. *J. Am. Chem. Soc.* **1962**, *84*, 361.

[9] Still, W. C. *J. Am. Chem. Soc.* **1978**, *100*, 1481.

[10] Piers, E.; Morton, H. E. *J. Org. Chem.* **1979**, *44*, 3437.

[11] Seyferth, D.; Vick, S. C. *J. Organomet. Chem.* **1978**, *144*, 1.

[12] One example of a successful tin/lithium exchange of a lithio compound, $LiOCH_2SnBu_3$, has been reported: Seebach, D.; Meyer, N. *Angew. Chem., Int. Ed. Engl.* **1976**, *15*, 438. This was accomplished under forcing conditions (petroleum ether, room temperature, 6 h) in moderate yield.

0002-7863/80/1502-5973$01.00/0

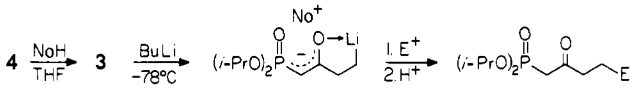
Table I

| electrophile | product | yield, %[a] |
|---|---|---|
| $CH_3OD$ | 7a, E = D | 70 |
| $CH_2{=}CHCH_2Br$ | 7b, E = $CH_2{=}CHCH_2$ | 75 |
| $CH_3CH_2CH_2I$ | 7c, E = $CH_3CH_2CH_2$ | 68 |
| $Me_3SiCl$ | 7d, E = $Me_3Si$ | 70 |
| $Ph_2CO$ | 7e, E = $Ph_2C(OH)$ | 72 |
| $CH_3CONMe_2$ | 7f, E = $CH_3CO$ | 52 |

[a] Yields refer to pure product after purification on silica gel.

to the stabilization of the organolithium reagent via the intramolecular chelation of lithium by the enolate oxygen to form a five-membered cyclic structure (**6**).[13]

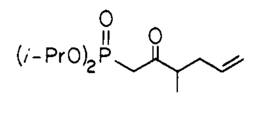
Phosphonate **4** is a stable compound[14] and was easily prepared in 75% yield by the reaction of diisopropyl lithiomethylphosphonate[2b,15] with methyl 3-(tri-*n*-butylstannyl)propionate.[16] The generation of **6** can be followed either by the disappearance of the starting phosphonate (**4**) or by the appearance of tetrabutyltin after acid workup of the reaction aliquots. The transmetalation reaction is essentially complete within 5 min at −78 °C. Lithio compound **6** reacts with various electrophiles (Table I) exclusively at the δ carbon, giving rise to terminally substituted phosphonate esters **7**.[17]



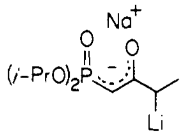
**6** **7**

The following experimental procedure is representative of the conversion. A dry 35-mL flask (equipped with a septum and a magnetic stirrer) containing 120 mg (2.5 mmol) of sodium hydride (50%, washed with hexanes to remove mineral oil) was flushed with argon and maintained under a positive pressure of argon. About 10 mL of freshly distilled dry THF was added, and then 1.05 g (2.0 mmol) of **4** was added dropwise. The reaction mixture was stirred at room temperature for 3 h to allow the formation of **3**. The reaction mixture was cooled to −78 °C, and 2.2 mmol (1.0 mL of a 2.2 M hexane solution) of *n*-butyllithium was added dropwise. The resulting light yellow solution was stirred at −78 °C for 10 min. The electrophile (2.2 mmol)[18] was added, and the reaction mixture was stirred at −78 °C for 15 min and at room temperature for 15 min. The reaction was quenched with 10% HCl (with dimethylacetamide as the electrophile, aqueous $NH_4Cl$ was used), and the mixture was extracted with ethyl acetate. The crude product[19] was purified by either modified flash chromatography[20] or preparative thin-layer chromatography.

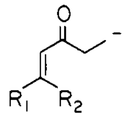
When the solution containing **6** (1,4-dianion) was stirred at 0 °C for 20 min, the solution turned red and on reaction with allyl bromide produced the γ-allyl compound (**8**) as the major product.



**8**



**9**



**10**

There was no evidence of **7b** being present in the product. This indicates that **6** is thermodynamically less stable and under conditions conducive to proton transfer gives rise to the more stable 1,3-dianion (**9**).

The generation of **6** shows for the first time that it is possible to generate a homoenolate anion equivalent by tin/lithium exchange when the carbonyl group is protected electronically from nucleophilic attack by butyllithium. The successful transformations reported here, in conjunction with the known reactions of β-ketophosphonates, allow the use of stannane **4** as a synthon for β′-substituted α,β-enones (**10**). The use of **6** to synthesize biologically useful organic molecules and the generation of similar δ-lithio derivatives of other functionalized systems[21] are being investigated.

**Acknowledgment.** I thank Dr. T. H. Whitesides for helpful discussions.

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[13] This kind of intramolecular chelated structure of organolithium reagents has been postulated in many cases: (a) Klumpp, G. W.; Kool, M.; Schakel, M.; Schmitz, R. F.; Boutkan, C. *J. Am. Chem. Soc.* **1979**, *101*, 7065. (b) Marino, J. P.; Kostusyk, J. L. *Tetrahedron Lett.* **1979**, 2489. (c) Beak, P.; McKinnie, B. G. *J. Am. Chem. Soc.* **1977**, *99*, 5213. (d) Still, W. C.; Macdonald, T. L. *Ibid.* **1974**, *96*, 5561. (e) Hartmann, J.; Stähle, M.; Schlosser, M. *Synthesis* **1974**, 888. (f) House, H. O.; Bare, T. M.; Hanners, W. E. *J. Org. Chem.* **1969**, *34*, 2209.

[14] Carbonyl compounds containing the trialkyltin group at the β position are usually stable to moisture and treatment with alkali.

[15] Ford-Moore, A. H.; Williams, J. H. *J. Chem. Soc.* **1947**, 1465.

[16] VanDerKerk, G. J. M.; Noltes, J. G.; Luijten, J. G. A. *J. Appl. Chem.* **1957**, *7*, 356.

[17] Yields have not been optimized. In most reactions, 10–20% of protonated compound **7** (E = H) was isolated as the byproduct. As expected, γ-hydroxy ketone **7e** exists predominantly in the cyclic hemiketal structure: Kyrides, L. P.; Zienty, F. B. *J. Am. Chem. Soc.* **1946**, *68*, 1385. The $^1H$ NMR, IR, and analytical data of all compounds were in accord with the assigned structures.

[18] Excess chlorotrimethylsilane (5.2 mmol) was used for the preparation of **7d**.

[19] The crude residue can be partly purified by partitioning between acetonitrile and hexanes; see: Berge, J. M.; Roberts, S. M. *Synthesis* **1979**, 471.

[20] Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

[21] Preliminary experiments show that it is possible to generate $PH_3P^+{-}^-CHCOCH_2CH_2Li$ similarly. This work will soon be submitted for publication.

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## The First Practical Method for Asymmetric Epoxidation

*Sir:*

As revealed in Scheme I, we have discovered a new metal-catalyzed asymmetric epoxidation process which is far more selective than any of the previously described methods[1] for this type of asymmetric transformation. The simplicity of this new method is one of its more attractive aspects; the necessary components [(+) or (−)-diethyl tartrate,[2] titanium tetraisopropoxide, and

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[1] (a) J. D. Morrison and H. S. Mosher, "Asymmetric Organic Reactions", Prentice-Hall, Englewood Cliffs, NJ, 1971, pp 258-62; (b) S. Yamada, T. Mashiko, and S. Terashima, *J. Am. Chem. Soc.*, **99**, 1988 (1977); (c) R. C. Michaelson, R. E. Palermo, and K. B. Sharpless, *ibid.*, **99**, 1990 (1977); (d) H. B. Kagan, H. Mimoun, C. Mark, and V. Schurig, *Angew. Chem., Int. Ed. Engl.*, **18**, 485 (1979) [records the highest ee (35%) for a hydrocarbon olefin]; (e) K. Tani, M. Hanafusa, and S. Otsuka, *Tetrahedron Lett.*, 3017 (1979); (f) H. Wynberg and B. Marsman, *J. Org. Chem.*, **45**, 158 (1980); (g) K. Takai, K. Oshima, and H. Nozaki, *Tetrahedron Lett.*, 1659 (1980); (h) J. Rebek, *Heterocycles*, in press.

[2] We had earlier examined the effect of chiral alcohols and chiral diols (including L(+)-diethyl tartrate) on the molybdenum- and vanadium-catalyzed TBHP epoxidation of isolated olefins as well as of allylic alcohols. Small (i.e., <10% ee) asymmetric inductions were noted, but they were not deemed worth reporting: R. C. Michaelson and K. B. Sharpless, unpublished results, Massachusetts Institute of Technology, 1974. Otsuka and co-workers have recently described[1e] low (<11% ee) asymmetric inductions in the epoxidation of hydrocarbon olefins with TBHP in the presence of dialkyl tartrate esters and a molybdenum(VI) catalyst.