(CH_3OH–HCl); the quantity of fumaric acid recovered indicates that 80% of the available sites in 7 have covalently bound the new template molecule.[5]

The sequence of transformations serves to illustrate several important points. The fractional recovery of template molecules (30%), even after prolonged hydrolysis, establishes that a significant number of template assemblies occupy inaccessible regions of the polymer. Unlike Merrifield polymers which, at least in their swollen state, undergo reaction throughout the polymer network,[6] hydrolysis occurs largely in the region that may be loosely defined as the surface of a solid polymer particle. This finding is undoubtedly a consequence of the higher degree of cross-linking in poly(divinylbenzene). Second, the uptake of fumaryl chloride is approximately equal to the theoretical number of *difunctional* sites and suggests that, at least in a significant number of cases, rebinding can occur in a manner similar to that which was found in the original polymer (two site).

The region in which the hydrolysis and rebinding occur is rather poorly defined. The area is at the interface between solvent phase and the highly cross-linked "nucleus" of the solid poly(divinylbenzene). Located in this region are pendant polymer and vinyl groups, template assemblies, rebinding sites, and more lightly cross-linked segments of the polymer.[7] If the hydrolyzed polymer is to exhibit a "memory" for the template molecule (T), the template assembly must "imprint" stereochemical information at the polymerization stage. Our first test for this "memory" is illustrated in Scheme II. The sequence involves at the penultimate step a methylene transfer to a prochiral alkene (fumaric acid) covalently bound to the macromolecule. When racemic template (**5**) is used for the polymer synthesis, racemic cyclopropanedicarboxylic acid would be the product from the methylenation step; however, when a chiral template is used for the polymer synthesis the "memory" can take the form of local asymmetry in the region of the functional groups; this asymmetry may induce formation of a chiral product in the methylenation step. The polymer-bound fumaric ester (**8**) was reacted with methylene transfer reagents to form 1,2-cyclopropanedicarboxylic acid ester (**9**). This transformation was successfully executed using (dimethylamino)phenyloxosulfonium methylide as the nucleophilic methylene transfer reagent.[8] Synthetic cyclopropanedicarboxylic acid is liberated by hydrolysis in 34% overall yield based upon available sites of the hydrolyzed polymer (**7**).

The preceding sequence was repeated using (−)-*trans*-1,2-cyclobutanedicarboxylic acid ($[\alpha]^{25}{}_{D}$ −158.7° (CH_3OH)) as the template.[9] After hydrolysis, rebinding of fumaryl chloride, cyclopropanation, and hydrolysis, *trans*-1,2-cyclopropanedicarboxylic acid was recovered as the dimethyl ester by preparative VPC. The diester exhibited a specific rotation, $[\alpha]^{21}{}_{D}$ 0.1°, which corresponds to a 0.05% enantiomeric excess.[10] The slight enantiomeric excess arises in the methylene transfer step and is the result of a chiral environment (of some unspecified nature) surrounding the reaction zone. Considering the severity of the hydrolysis conditions, the observed asymmetric induction is encouraging. Work is continuing in an effort to understand those factors which will influence the magnitude of asymmetric induction and to define the degree of stereochemical control available by the template synthesis approach.

Acknowledgment. We thank the donors of the Research Corporation and the National Institutes of Health for generous support of this work.

References and Notes

(1) See references cited in review articles such as: (a) R. Breslow, *Chem. Soc. Rev.*, **1**, 553 (1972); (b) D. W. Griffiths and M. L. Bender, *Adv. Catal.*, **23**, 209 (1973); V. A. Kabanov in "Advances in Polymer Science", Z. A. Rogovin, Ed., Wiley, New York, N.Y., 1974, p 263; (d) T. Kunitake and Y. Okahata, *Fortschr. Hochpolym.-Forsch.*, **20**, 159 (1976); (e) T. Shimidzu, *ibid.*, **23**, 56 (1977); (f) M. L. Bender and M. Komiyama *Bioorg. Chem.*, **1**, 19 (1977); (g) J. H. Fendler and E. J. Fendler, "Catalysis in Micellar and Macromolecular Systems", Academic Press, New York, N.Y., (1975); (h) E. Tsuchida and H. Nishide, *Fortschr. Hochpolym.-Forsch.*, **24**, 1 (1977).

(2) (a) G. Wulff, A. Sarhan, and K. Zabrocki, *Tetrahedron Lett.*, 4329 (1973); (b) G. Wulff, W. Vesper, R. Grobe-Einsler, and A. Sarhan, *Makromol. Chem.*, **178**, 2799, 2817 (1977).

(3) The polymerization conditions result in the formation of an insoluble, highly porous (macroreticular) polymer with an average surface area of 200 m^2/g.

(4) Development of analytical procedures and detection of nonspecific reactions with the polymer was facilitated by a parallel series of reactions performed with a "blank" polymer; that is, one prepared in an identical manner only without template assemblies.

(5) In our idealized representation (Scheme II) we have assumed that two-point rebinding reconnects two functional groups that were previously connected by a template assembly (intersite) as opposed to two "unrelated" functional groups (intrasite). At present we have no evidence to confirm this assumption. Additional studies are underway to distinguish between these possibilities.

(6) (a) G. R. Stark, "Biochemical Aspects of Reactions on Solid Supports", Academic Press, New York, N.Y., 1971; (b) W. Heitz, *Fortschr. Hochpolym.-Forsch.*, **23**, 1 (1977).

(7) Characterization of the surface of solid organic polymers continues to be a very active area of investigation. For recent studies of the generation, characterization, and functionalization of the surface of a solid polymer, see J. R. Rasmussen, E. R. Stedronsky, and G. M. Whitesides, *J. Am. Chem. Soc.*, **99**, 4736 (1977), and references cited therein.

(8) C. R. Johnson, E. R. Janiga, and M. Haake, *J. Am. Chem. Soc.*, **90**, 3890 (1968).

(9) This material is assumed to be optically pure; Y. Inouye, S. Sawada, M. Ohno, and H. M. Walborsky, *Tetrahedron*, **23**, 3237 (1967).

(10) Y. Inouye, T. Sugita, and H. M. Walborsky, *Tetrahedron*, **20**, 1695 (1964).

Kenneth J. Shea,* Evan A. Thompson
Department of Chemistry
University of California, Irvine
Irvine, California 92717

Received June 27, 1978

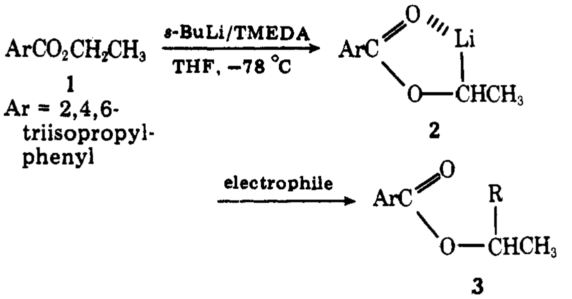
Lithiation of Ethyl 2,4,6-Triisopropylbenzoate Adjacent to Oxygen: The α-Lithioalkyl Alcohol Synthon

Summary: Metalation of ethyl 2,4,6-triisopropylbenzoate (**1**) with *sec*-butyllithium/tetramethylethylenediamine in tetrahydrofuran provides α-lithioethyl 2,4,6-triisopropylbenzoate (**2**). Reaction of **2** with carbonyl and halide electrophiles provides the expected products **3a–g.** Reduction of typical products with lithium aluminum hydride gives the corresponding alcohols. Overall this sequence provides the α-lithioalkyl alcohol synthon from a primary alcohol.

Sir: The formation and use of α-heteroatom carbanions has been widely explored and exploited in recent years. In conjunction with our studies of prospectively dipole-stabilized carbanions, we have reported metalations adjacent to the heteroatom of methyl 2,4,6-triisopropylbenzoate, methyl and ethyl 2,4,6-trialkylthiobenzoates, and methyl- and ethyl-2,4,6-triisopropylbenzamides.[1,2] The metalations of the ester and thioesters have been shown to be key steps in providing the α-lithiomethyl alcohol and the α-lithiomethyl and α-lithioethyl thiol synthons, respectively. More recently Seebach et al. have observed similar metalations of 2,4,6-trialkylbenzoate derivatives and also have shown that dimethyltriphenylacetamide provides the (α-lithiomethyl)alkylamine synthon.[3] We now wish to report that ethyl 2,4,6-triisopropylbenzoate can be metalated adjacent to oxygen and to suggest that this approach will provide α-lithioalkyl alcohol synthons for the corresponding primary alcohols.

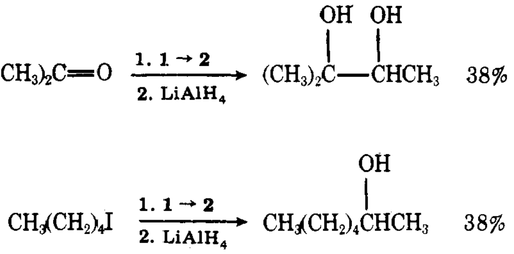
Reaction of ethyl 2,4,6-triisopropylbenzoate (**1**) with 2–4 equiv of *sec*-butyllithium/tetramethylethylenediamine (*s*-BuLi/TMEDA) in tetrahydrofuran (THF) at −78 °C for 3–6

Scheme I



a, R = $HOC(CH_3)_2$ 41% (64%)
b, R = $HOC(CH_2)_5$ 31% (50%)
c, R = $CH_2CH{=}CH_2$ 42% (79%)
d, R = $Si(CH_3)_3$ 64% (94%)
e, R = $Sn(C_4H_9)_3$ 53% (85%)
f, R = $HOC(CD_3)_2$
g, R = D

Scheme II



$$(CH_3)_2C{=}O \xrightarrow[\text{2. LiAlH}_4]{\text{1. 1}\rightarrow\text{2}} (CH_3)_2C(OH)\text{—}CH(OH)CH_3 \quad 38\%$$

$$CH_3(CH_2)_4I \xrightarrow[\text{2. LiAlH}_4]{\text{1. 1}\rightarrow\text{2}} CH_3(CH_2)_4CH(OH)CH_3 \quad 38\%$$

h gives **2**, which can be trapped by addition of acetone, cyclohexanone, allyl bromide, trimethylsilyl chloride, and tri-*n*-butyltin chloride to give the expected products, **3a–e**, in the purified (and crude) yields indicated in Scheme I.[5] When hexadeuterioacetone is used as the electrophile and the composition of the products determined by NMR, the product **3f** is obtained in 67% yield, while the ethyl ester is observed to be 58% deuterated material, **3g**. This result, as well as the 85% crude yield of **3e**, suggests that metalation is satisfactorily complete under these conditions and that the relatively low yields obtained with the ketones are due to competing enolizations.

On a preparative scale the metalation can be a key step in the preparation of the α-lithioethyl alcohol synthon. Thus formation of **2** from **1** on a several gram scale, followed by addition of hexamethylphosphoric triamide (HMPA) just prior to addition of the electrophile followed by reduction with lithium aluminum hydride in THF or dimethoxyethane, yields the substituted alcohols as shown in Scheme II. The isolated yields are based on **1**.

It is reasonable that corresponding α-lithio derivatives of other primary alcohols will be available by metalation of the esters of 2,4,6-trisubstituted benzoates or closely related compounds.[6] For some situations the presence of excess *s*-BuLi/TMEDA or unmetalated ester may be inconvenient. In that case the tin compound **3d** can be reacted with methyllithium to provide **2** in high yields; subsequent additions of deuteriomethanol, methyl iodide, and methyl benzoate give the expected products in 80–100% crude yield. An imaginative alternative route to α-lithioalkyl alcohol synthons by stannylation of the corresponding aldehydes has recently been reported by Still.[7]

Activation by the benzoate carbonyl has now been shown to facilitate direct metalative preparation of primary and secondary organolithiums adjacent to oxygen, sulfur, and nitrogen.[1-3] While such organometallics can be considered dipole-stabilized carbanions, further information on that point, as well as development of the synthetic potential of these species, is being studied.

Procedure. To a solution of 1:1 *s*-BuLi/TMEDA (25.3 mmol) in THF stirring at −78 °C under nitrogen was added a solution of 3.98 g (14.4 mmol) of ethyl 2,4,6-triisopropylbenzoate (**1**) in THF. After the reaction mixture was allowed to stir at −78 °C for 6 h, 4 mL of HMPA was added, followed by 20 mL of 1-iodopentane. The reaction mixture was allowed to stir at −78 °C for 20 min, and then allowed to warm to room temperature. Ether was added and the organic phase was washed with aqueous saturated NH_4Cl, concentrated, dissolved in ether, and washed with aqueous 10% HCl and 10% NaOH. The organic layer was dried ($CaSO_4$) and concentrated under vacuum to give 4.8 g of a clear, orange oil. This material and 5.0 g (0.13 mol) of $LiAlH_4$ in 75 mL of dimethoxyethane (DME) were heated at reflux for 2.5 h. The heterogeneous reaction mixture was cooled to room temperature and treated with a minimal amount of H_2O. The insoluble salts were removed by filtration and washed with ether. The filtrates were combined, dried ($MgSO_4$), and concentrated under vacuum to give a clear, yellow oil which was distilled at atmospheric pressure to afford 0.64 g (5.51 mmol, 38%) of 2-heptanol.

Acknowledgment. We are grateful to the National Institutes of Health—Institute of General Medicine for support of this work.

References and Notes

(1) (a) P. Beak and B. G. McKinnie, *J. Am. Chem. Soc.*, **99**, 5213 (1977); (b) D. B. Reitz, P. Beak, R. F. Farney, and L. S. Helmick, *ibid.*, **100**, 5428 (1978); (c) P. Beak, B. G. McKinnie, and D. B. Reitz, *Tetrahedron Lett.*, 1839 (1977).
(2) P. Beak and D. B. Reitz, *Chem. Rev.*, **78**, 275 (1978).
(3) R. Schecker, D. Seebach, and W. Lubosch, *Helv. Chim. Acta*, **61**, 512 (1978).
(4) Prepared from the corresponding acid chloride and ethanol: R. C. Fuson and E. C. Horning, *J. Am. Chem. Soc.*, **62**, 2962 (1940). An alternative route from 2,4,6-triisopropylphenyllithium and diethyl carbonate is also useful.
(5) All new compounds were characterized by IR, NMR, and satisfactory combustion analysis except for **3b**, which was 0.5% low for hydrogen. Previously known compounds were identified by comparison of NMR and IR spectra with published data.
(6) For example, metalation of *n*-octyl 2,4,6-triisopropylbenzoate under similar conditions followed by separate reactions with deuteriomethanol, acetone, or allyl bromide gives the expected products in crude yields of 90, 45, and 95%, respectively.
(7) W. C. Still, *J. Am. Chem. Soc.*, **100**, 1481 (1978).

Peter Beak,* Maurice Baillargeon, Linda G. Carter
Roger Adams Laboratory, University of Illinois
Urbana, Illinois 61801

Received July 10, 1978

Photochemical Transformations of Chalcone Oxides

Summary: Close examination of the photobehavior of several chalcone oxides has demonstrated that aryl ring substituents control whether the C_α–O or C_α–C_β bond of the oxirane ring will be cleaved.

Sir: Photochemical rearrangements of α,β-epoxy ketones have received extensive study and have been the subject of several reviews.[1-4] These compounds generally display two types of photobehavior: (a) photoisomerization of arylcyclopentenone oxides to pyrylium oxides,[5,6] and (b) photoisomerization of α,β-epoxy ketones to β-diketones.[8-10] Although much data have been accumulated to show that C_α–O bond cleavage is the predominant mode of photofragmentation in α,β-epoxy ketones, Muzart and Pète[11] have demonstrated that cleavage of the oxirane C_α–C_β bond also can occur in certain optically active derivatives. Interestingly, epoxynaphthoquinones have been shown to undergo two types of photocycloaddition reactions with olefins arising either from n,π^* excited-state addition of the carbonyl group to form oxetanes, or from C–C bond fission of the oxirane ring followed by 1,3-dipolar addi-