or well-buffered, produces in a controlled fashion *monomeric* SeO_2 which then serves as the active oxidant.[12]

Whatever the mechanism it is clear that this system can accomplish efficient, selective hydroxylation of sensitive and heretofore intractible substrates.

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[12] Preliminary studies of the effects of "pH" and of water are consistent with this interpretation.

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Sterically Directed Conjugate Addition Reactions of Unsaturated Esters

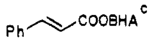
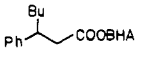
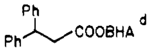
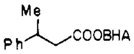
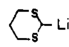
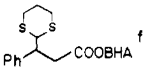
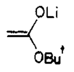
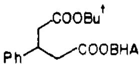
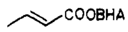
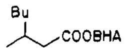
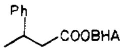
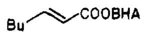
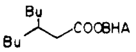
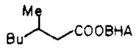
Summary: Unsaturated esters of 2,6-di-*tert*-butyl-4-methoxyphenol undergo conjugate addition reactions with a variety of organolithium reagents. Oxidation of adducts with ceric ammonium nitrate provides substituted carboxylic acids.

Sir: The reaction of strong nucleophiles with α,β-unsaturated esters usually results in the formation of products resulting from carbonyl addition.[1] Products resulting from the alternate 1,4 or conjugate addition mode generally require the use of organocopper reagents derived from reactive nucleophiles.[2] Recent reports suggest that lithium enolates of some esters also reliably undergo conjugate addition reactions with unsaturated acyclic esters.[3]

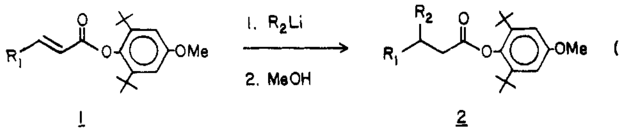
It was observed some time ago that conjugate addition reactions of unsaturated ketones can be promoted by steric interference with the 1,2-addition process. DeMeester and Fuson[4] found that Grignard reagents undergo predominantly 1,4-addition reactions with mesityl vinyl ketone and more recently Seebach and co-workers have demonstrated similar selectivity for 1,4-addition with organolithium reagents and unsaturated trityl ketones as well as amide acceptors derived from a highly hindered amine.[5]

While occassional reports of conjugate addition reactions of organometallic reagents to unsaturated *sec*-butyl[1c,6] and *tert*-butyl esters[7] have appeared, no general method for the steric suppression of carboxyl reactivity in unsaturated esters has been reported. A recent report by Seebach[8] noting the resistance of 2,6-di-*tert*-butyl-4-methylphenyl esters (BHT esters) to carboxyl attack by alkyllithium reagents suggested that conjugate addition reactions might be favored in unsaturated acceptors having this type of carbonyl steric protection. We now report that α,β-unsaturated esters of 2,6-di-*tert*-butylphenol derivatives cleanly undergo conjugate addition reactions with a range of organolithium reagents (eq 1). Results of nucleophilic additions to unsaturated esters of 2,6-di-*tert*-butyl-4-methoxyphenol (BHA esters, 1) chosen for their ease of oxidative hydrolysis (vide infra) are shown in Table I.[9]

Table I. Addition of Lithium Reagents to Unsaturated BHA Esters[a,b]

entry	acceptor	RLi (equiv)	product	yield (%)
1	 [c] 3	n-BuLi (1.1)	 4	99
2		PhLi (1.3)	 [d] 5	87
3		MeLi (1.3)	 6	96
4		 Li (1.4)[e]	 [f] 7	91
5		 (1.3)[e]	 [g] 8	93
6	 9	n-BuLi (1.2)	 10	75
7		PhLi (1.2)	 11	91
8	 12	n-BuLi (1.2)	 13	95
9		MeLi (1.1)	 14	92

[a] All structures are supported by spectral and analytical data. [b] See ref 11 for a typical procedure. [c] mp 120–121 °C. [d] mp 145.5–147.0 °C. [e] Inverse addition. [f] mp 149.0–150.5 °C. [g] mp 84.5–85.5 °C.



1 2 (1)

Typical unsaturated BHA esters (**3**, **9**, and **12**), prepared from the corresponding acid chlorides and lithium 2,6-di-*tert*-butyl-4-methoxyphenoxide in the manner previously described for the preparation of saturated BHA esters[10] undergo exceptionally clean 1,4-addition reaction reactions with lithium reagents in THF at −78 °C over the course of several minutes giving enolates which, when

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[1] (a) Negishi, E. In *Organometallics in Organic Synthesis*; Wiley: New York, 1980; Vol. 1, p 127. (b) Wakefield, B. J. In *The Chemistry of Organolithium Compounds*; Pergamon Press: New York, 1974; p 139. (c) Munch-Peterson, J. *J. Org. Chem.* **1957**, *22*, 170.

[2] Posner, G. H. *Org. React.* (*N.Y.*) 1972, *19*, 1.

[3] Yamaguchi, M.; Tsukamoto, M.; Hirao, I. *Tetrahedron Lett.* **1985**, *26*, 1723. Yamaguchi, M.; Tsukamoto, M.; Tanaka, S.; Hirao, I. *Ibid.* **1984**, *25*, 5661. Yamaguchi, M.; Tsukamoto, M.; Hirao, I. *Chem. Lett.* **1984**, 375.

[4] DeMeester, W. A.; Fuson, R. C. *J. Org. Chem.* **1965**, *30*, 4332.

[5] (a) Seebach, D.; Ertas, M.; Schweizer, W. B. *Helv. Chim. Acta* **1985**, *68*, 264. (b) Seebach, D.; Locher, R. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 957. (c) Locher, R.; Seebach, D. *Ibid.* **1981**, *20*, 569.

[6] Munch-Peterson, J. *Org. Synth.* **1961**, *41*, 60.

[7] (a) A phenyl-Grignard reagent reportedly gives only 1,4-addition with *tert*-butyl cinnamate: Hauser, C. R.; Yost, R. S.; Ringler, B. I. *J. Org. Chem.* **1949**, *14*, 261. (b) A significant amount of 1,4-addition has been noted in the addition of *n*-BuLi to *tert*-butyl 2-heptenoate: Cooke, M. P., Jr. *Ibid.* **1984**, *49*, 1144.

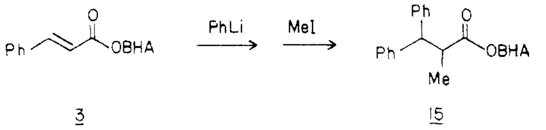
[8] Haner, R.; Laube, T.; Seebach, D. *J. Am. Chem. Soc.* **1985**, *107*, 5396.

[9] Similar results are obtained from additions to unsaturated BHT esters.

[10] Heathcock, C. H.; Pirrung, M. C.; Montgomery, S. H.; Lampe, J. *Tetrahedron* **1981**, *37*, 4087.

0022-3263/86/1951-1637$01.50/0

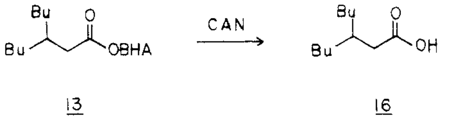
quenched with a proton source (MeOH), give high yields of saturated BHA esters **2**.[11] As in the case of BHT ester enolates,[8] the enolates resulting from additions to 1 are unstable at temperatures above approximately −20 °C but may be intercepted by electrophiles below −20 °C as illustrated in eq 2. where phenyllithium addition to **3** (−78 °C, 11 min) followed by alkylation with MeI (5 equiv, 5 min at −78 °C, 5 min at −20 °C) gave α-methylated ester **15** in 88% yield. Both BHA and BHT ester enolates have previously been shown to be highly useful in stereoselective aldol condensations[8,10] and the decomposition of BHT ester enolates in the presence of alkyllithium reagents has been shown to give ketones, presumably through additions to intermediate ketenes.[8]



(2)

Our success with nucleophiles not normally successfully employed as Gilman reagents through their copper derivatives (entries 4 and 5) is noteworthy. Thus far our only unsuccessful addition with an alkyllithium reagent has been in the case of *tert*-butyllithium where complex products were obtained with both BHA and BHT esters. Interestingly, Grignard reagents appear not to undergo these additions: no reaction was observed with **3** and *n*-BuMgCl at temperatures up to −10 °C.

While both BHT and BHA esters are extremely resistant to hydrolysis,[10] BHT esters (and presumably BHA esters as well) may be reduced to primary alcohols with $LiAlH_4$ and BHA esters, upon oxidation with ceric ammonium nitrate (CAN), give corresponding carboxylic acids.[10] An example of the CAN oxidation of an addition product (**13**), is shown in eq 3 where the corresponding carboxylic acid (**16**) was obtained in 90% yield.[12]



(3)

In summary, sterically protected unsaturated esters containing the 2,6-di-*tert*-butylphenyl moiety appear to be exceptionally good Michael acceptors for a wide range of lithium reagents.

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[11] In a typical procedure 160 mg (0.47 mmol) of **12** (prepared in 71% yield from 2-heptenoyl chloride) in 4 mL of THF was treated with stirring at −78 °C with 0.37 mL (0.58 mmol) of 1.55 M *n*-BuLi in hexane over 0.5 min. The yellow solution was stirred for 7 min and then quenched by the addition of 100 μL of MeOH. After solvent removal in vacuo and treatment of the residue with CH_2Cl_2–H_2O, the oil obtained from the dried (Na_2SO_4) organic phase gave after PTLC (silica gel, 1:1 CH_2Cl_2–CCl_4) and vacuum drying 182 mg (95%) of **13**. An analytical sample was obtained after bulb-to-bulb distillation (210 °C (air), 0.05 mm); Anal. C, H.

[12] In a manner similar to that previously described,[10] 208 mg (0.51 mmol) of **13** in 2 mL of acetonitrile was treated under vigorous stirring with 1.0 mL (1.2 mmol) of 1.2 M ceric ammonium nitrate solution. After 50 min 300 mg of mannitol was added with continued stirring for 2 min followed by the addition of 1 mL of water and further stirring for 1 min. The mixture was poured into 15 mL of H_2O, made acidic by the addition of 2 mL of 4 N HCl and then twice extracted with 15 mL of Et_2O. The combined extracts were washed twice with 0.5 N NaOH (10 mL) and the combined aqueous layers were extracted with Et_2O. Acidification of the aqueous layer gave upon extraction with pentane (2 × 10 mL) an oil which after bulb-to-bulb distillation (150 °C (air), 0.05 mm) gave 86 mg (90%) of **16**; Anal. C, H. 2,6-Di-*tert*-butylquinone was recovered from the ethereal extracts.

Effect of Metal Loading and Triphenylphosphine on Product Selectivities in the Hydrogenation of Di-*tert*-butylacetylene and 3-Hexyne over Palladium/Alumina

Summary: The effect of triphenylphosphine and metal loading and/or dispersion on the product distributions from di-*tert*-butylacetylene indicates that the surface structure of the metal particles also may affect stereospecificities by promoting different catalytic mechanisms at different sites.

Sir: Recently, the claim was made "that the poisons used in the preparation of Lindlar and Rosenmund catalysts do not block active sites but act to rearrange the surface structure of the catalyst".[1] The authors cited the cis stereospecificity of the hydrogenation (26–76% conversion) of disubstituted alkynes on palladium foil and the physical change of palladium black when heated with diethylamine and D_2O at 150 °C for 20 h. However, the slowness of the hydrogenation, which is consistent with the small fraction of the palladium atoms which are exposed to the reactants, and the foil's lack of porous structure minimize the effect of diffusion in modifying the intrinsic selectivity of the surface reaction.[2-4] The quinoline used with a Lindlar catalyst lowers the rate of the surface reactions by competing with the alkyne for reactive sites and, because the strength of its adsorption on palladium falls between that of the alkyne and the product alkene, it almost excludes the latter from the surface even when the conversion of the alkyne to alkene is complete.[3,5-7]

We report evidence that the hydrogenation of alkynes on palladium occurs by at least two mechanisms at structurally differen surface sites. The reaction conditions were chosen to avoid diffusion-limited kinetics as judged from prior experiments with cyclohexene and norbornene and by the constancy of the turnover frequency for the hydrogenation of both 3-hexyne and di-*tert*-butylacetylene (DTBA) on 1% to 5% Pd/Al_2O_3 catalysts which also varied in dispersion.[8-12] On these catalysts the initial

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[1] McEwen, A. B.; Guttieri, N. J.; Maier, W. F.; Laine, R. M.; Shvo, Y. *J. Org. Chem.* **1983**, *48*, 4436–4438.

[2] Lindlar, H.; Dubois, R. *Organic Syntheses*; Wiley: New York, 1973; Collect. Vol. 5, pp 880–883.

[3] Rylander, P. *Catalytic Hydrogenation in Organic Synthesis*; Academic Press: New York, 1979; Chapter 2.

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[5] Kieboom, A. P. G.; van Rantwijk, F. *Hydrogenation and Hydrogenolysis in Synthetic Organic Chemistry*; Delft University Press: The Netherlands, 1977; pp 62–68.

[6] Steenhock, A.; van Wijngaarden, B. H.; Pabon, H. J. J. *Recl. Trav. Chim. Pays-Bas* **1971**, *90*, 961–973.

[7] Bond, G. C.; Wells, P. B. *Adv. Catal.* **1964**, *15*, 155–184.

[8] Hawkins, J. A., Doctoral Dissertation, University of Arkansas, Fayetteville, AR 1983.

[9] The catalyst support was prepared from Catapal SB alumina (CONOCO) according to procedures in ref. 10. The 1–5% Pd/Al_2O_3 catalysts were prepared by impregnating the above alumina (≤325 mesh) with palladium chloride following procedures of Aben (ref 11). Reactions were performed at 30 °C in a small (30 mL) vortically stirred reactor using procedures similar to those described by Kung, Pellet, and Burwell (ref 10) to establish that reactants were free of poisons and that the rates of hydrogenation were free of diffusional limitations. Generally 10–50 mg of catalyst (1–5% Pd on alumina) and 0.1–0.3 mL of alkyne in 1–3 mL of cyclhexane were used.