ic acids by superoxide seems applicable to a spectrum of substrates, including not only α-keto and α-hydroxy carbonyl compounds but α-halo ketones, esters, and acids as well. This latter reaction, in particular, provides a convenient and unique procedure for the degradative cleavage of α-halo carbonyl compounds. Second, the fact that both 1-hydroxycycloheptanecarboxylic acid and α-cyclohexylmandelic acid can be quantitatively recovered after treatment with potassium superoxide suggests that the successful oxidative cleavage of α-hydroxy carbonyl compounds requires the presence of an α hydrogen on the hydroxy-bearing carbon. Third, the reaction of superoxide with α-keto and α-hydroxy carbonyl compounds resembles, in several respects, the behavior of certain dioxygenases. Specifically, the oxidative cleavage of α-keto carboxylic acids is reminiscent of the reaction of those enzymes which use α-ketoglutarate as a cosubstrate.[8] This oxygenase catalyzes the overall reaction

$$\mathrm{S + O_2 + HO_2CCH_2CH_2C(O)CO_2H} \xrightarrow{\text{enzyme}} \mathrm{SO + HO_2CCH_2CH_2CO_2H + CO_2}$$

where one atom of oxygen is introduced into the substrate (S) and another into the resulting succinic acid. Typical substrates oxidized by such enzymes are alkane derivatives such as proline peptides, betaines, and the methyl group of thiamine. Hamilton[9] has proposed that these reactions proceed through the intermediacy of persuccinic acid formed by the oxidative decarboxylation of α-ketoglutaric acid. The attractiveness of this proposal is enhanced by the fact that peracids are putative intermediates resulting from the demonstrated reaction of superoxide with carboxylic esters.[2b] What relevancy, if any, these observations have to the mechanism of dioxygenase action in these instances remain uncorroborated and is currently under further investigation. However, the possibility that superoxide, either free or coordinated, is involved in these processes is made more reasonable by the fact that these oxygenases are Fe(II)-containing enzymes whose reaction with molecular oxygen provides a plausible means for the biosynthesis of the requisite superoxide.

Aside from their synthetic utility[10] and their possible relevancy to the mechanisms of oxidation by certain dioxygenase enzymes, the results reported here may offer some insight into the role of superoxide in biological disorders. Further observations related to the scope and mechanism(s) of these reactions will be presented in future papers.

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(9) G. A. Hamilton in "Progress in Bioorganic Chemistry", Vol. 1, E. T. Kaiser and F. J. Kezdy, Ed., Wiley, New York, N.Y., 1971, p 83.

(10) The principal reagents used for the selective cleavage of α-keto and α-hydroxy carbonyl compounds are periodic acid and lead tetraacetate. Unlike lead tetraacetate, periodic acid requires an aqueous solvent media; however, lead tetraacetate has the disadvantage that the side reactions which frequently accompany the use of this reagent can sometimes become the dominant reaction pathway. The oxidative cleavage of α-halo carbonyl compounds has not been reported for either of these reagents. For a discussion and comparison of the relative merits of both periodic acid and lead tetraacetate in oxidative cleavage reactions, see H. O. House in "Modern Synthetic Reactions", 2nd ed, W. A. Benjamin, Menlo Park, Calif., 1971, Chapter 7.

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Synthesis of Unsymmetrical Conjugated Diynes via the Reaction of Lithium Dialkynyldialkylborates with Iodine

Summary: Unsymmetrical conjugated diynes may be prepared in satisfactory yield by the reaction of iodine in tetrahydrofuran with lithium dialkynyldisiamylborates, $\mathrm{Li^+[Sia_2BC{\equiv}CR(C{\equiv}CR')]}$; a convenient, essentially one-pot procedure for the preparation of unsymmetrical conjugated diynes from commercially available borane–methyl sulfide and acetylenes is presented.

Sir: Treatment of lithium 1-alkynyltrialkylborates and lithium ethynyltrialkylborates with iodine under very mild conditions produces the corresponding acetylenes in essentially quantitative yields (eq 1).[1,2] More recently, it has

$$\mathrm{Li^+[R_3BC{\equiv}CR']^-} \xrightarrow[\text{THF, }-78°]{\mathrm{I_2}} \mathrm{RC{\equiv}CR'} \tag{1}$$

been reported that symmetrical diynes and enynes may be prepared in excellent yield from lithium dialkynyldialkylborates (eq 2)[3] or lithium alkynylalkenyldialkylborates (eq 3),[4] respectively.

$$\mathrm{Li^+[R_2B(C{\equiv}CR')_2]^-} \xrightarrow[\text{THF, }-78°]{\mathrm{I_2}} \mathrm{R'C{\equiv}CC{\equiv}CR'} \tag{2}$$

$$\mathrm{Li^+[R_2B(C{\equiv}CR')(CH{=}CHR'')]^-} \xrightarrow[\text{THF, }-78°]{\mathrm{I_2}} \mathrm{R'C{\equiv}CCH{=}CHR''} \tag{3}$$

Investigations in our laboratory into the synthesis and reactions of alkynyldialkylboranes have led to the development of a convenient, general, and quantitative method for the synthesis of base-free alkynyldialkylboranes from methyl dialkylborinates. Treatment of the 1-alkynyldisiamylboranes with lithium alkynes produces cleanly the corresponding lithium dialkynyldisiamylborates. This procedure, in contrast to the earlier one,[3] makes possible the synthesis of lithium dialkynyldisiamylborates containing two different alkynyl groups. Treatment of this "ate" complex with iodine gives the corresponding diyne, symmetrical or unsymmetrical as desired, in excellent yield (eq 4).

$$\mathrm{Sia_2BC{\equiv}CR + LiC{\equiv}CR'} \xrightarrow[-78°]{\text{THF}} \mathrm{Li^+[Sia_2B(C{\equiv}CR)(C{\equiv}CR')]^-}$$

$$\mathrm{Li^+[Sia_2B(C{\equiv}CR)(C{\equiv}CR')]^-} \xrightarrow[\text{THF, }-78^\circ]{\mathrm{I_2}} \mathrm{RC{\equiv}CC{\equiv}CR'} \qquad (4)$$

It proved possible to carry through the synthesis without the isolation of the intermediate 1-alkynyldisiamylborane. Consequently, the synthesis of the symmetrical or unsymmetrical conjugated diynes may be carried out in an essentially one-pot process, as outlined in reactions 5.

$$\mathrm{BH_3{\cdot}S(CH_3)_2 + 2(CH_3)_2C{=}CHCH_3} \xrightarrow[0^\circ\text{ to }25^\circ]{\text{THF}} \mathrm{Sia_2BH + S(CH_3)_2}$$

$$\mathrm{Sia_2BH + MeOH} \xrightarrow[25^\circ]{\text{THF}} \mathrm{Sia_2BOMe + H_2}$$

$$\mathrm{Sia_2BOMe + LiC{\equiv}CR} \xrightarrow[-78^\circ]{\text{THF}} \mathrm{Li^+[Sia_2BC{\equiv}CR(OMe)]^-}$$

$$\mathrm{3Li^+[Sia_2BC{\equiv}CR(OMe)]^- + 4BF_3{\cdot}OEt_2} \xrightarrow[-78^\circ\text{ to }25^\circ]{\text{THF}} \mathrm{3Sia_2BC{\equiv}CR + (MeO)_3B + 3LiBF_4}$$

$$\mathrm{Sia_2BC{\equiv}CR + LiC{\equiv}CR'} \xrightarrow[-78^\circ]{\text{THF}} \mathrm{Li^+[Sia_2BC{\equiv}CR(C{\equiv}CR')]^-}$$

$$\mathrm{Li^+[Sia_2BC{\equiv}CR(C{\equiv}CR')]^-} \xrightarrow[\text{THF, }-78^\circ]{\mathrm{I_2}} \mathrm{RC{\equiv}CC{\equiv}CR'} \qquad (5)$$

The results are summarized in Table I.

Table I. Preparation of Unsymmetrical Conjugated Diynes, RC≡CC≡CR′, via Iodination of Lithium Disiamyldialkynylborates, Li$^+$[Sia$_2$BC≡CR(C≡CR′)]$^-$

R	R′	Yield, %[a]	
		Procedure A[b]	Procedure B[c]
n-Hexyl	Ethyl	95	61
n-Hexyl	Cyclohexyl	80	73
n-Hexyl	*tert*-Butyl	79	60
n-Hexyl	Phenyl	79	61
Cyclohexyl	*tert*-Butyl		70

[a] By GLC on a 10% Dow 710 or 10% SE-30 column. [b] From isolated Sia$_2$BC≡CR. Sia$_2$BC≡C-*n*-Hex isolated quantitatively from Sia$_2$BOMe. [c] "One-pot" procedure not involving isolation of any intermediate.

The procedure for the preparation of 1-cyclohexyl-1,3-decadiyne is representative. In a dry, nitrogen-flushed, 500-ml flask, fitted with a gas inlet tube with stopcock, septum inlet, and magnetic stirring bar, are placed 50 ml of tetrahydrofuran and 100 mmol (10.2 ml of 9.8 M) borane–methyl sulfide.[5] The stopcock in the gas inlet tube is closed and the flask immersed in an ice–salt bath. 2-Methyl-2-butene (14.7 g, 210 mmol) is added via syringe and the reaction mixture stirred at room temperature for 2 h. Methanol (3.2 g, 100 mmol) is added dropwise, the hydrogen evolved is safely vented, and the solution is stirred for an additional hour.

Meanwhile, in a separate 250-ml flask, fitted as before, is generated lithium 1-octyne (100 mmol) by the dropwise addition of *n*-butyllithium (40 ml of a 2.5 M solution) to a dry ice–acetone cooled solution of 1-octyne (11 g, 100 mmol) in 75 ml of tetrahydrofuran.

The 500-ml flask containing the freshly prepared methyl disiamylborinate is cooled to −78 °C and the lithium 1-octyne solution added via double-ended needle.[5] The 250-ml flask is rinsed with 5 ml of tetrahydrofuran to ensure complete transfer, and the solution stirred 30 min at −78°. Boron trifluoride etherate (18.8 g, 133 mmol) is added to the reaction via syringe and the mixture stirred for 15 min at −78°, warmed to room temperature, and recooled to −78°. To this mixture is added a solution of 100 mmol of lithium cyclohexylethyne in tetrahydrofuran prepared as was the lithium 1-octyne above.

The reaction mixture is stirred at −78° for 30 min. Iodine (25.7 g, 100 mmol), dissolved in 50 ml of tetrahydrofuran, is added dropwise to the cold reaction mixture. The resulting solution with an orange suspension is stirred for 1 h at −78° and then warmed to room temperature. The reaction mixture is washed twice with 25 ml of 3 M sodium hydroxide. Oxidation to remove residual organoborane is accomplished by the addition of 35 ml of 3 M sodium hydroxide and the addition of 35 ml of 30% hydrogen peroxide at such a rate so as to maintain the temperature under 50°. The aqueous layer is then saturated with potassium carbonate and the organic layer separated. The aqueous layer is extracted once with ether and the combined organic layers dried over anhydrous potassium carbonate. The volatiles are evaporated. Distillation under reduced pressure gave 1-cyclohexyl-1,3-decadiyne (12.1 g, 56% from borane–methyl sulfide): bp 129–131 °C (0.5 mm); $n^{20}\mathrm{D}$ 1.5102. Mass spectroscopic examination showed a parent ion of 216.816 (calcd for $C_{16}H_{24}$: 216.817).

The reaction of iodine with lithium disiamyldialkynylborates represents a new method for the preparation of both symmetrical and unsymmetrical conjugated diynes. The procedure presented here provides a direct route to unsymmetrical conjugated diynes, circumventing the more limited scope of the previous procedure[6] as well as the need to isolate either a 1-bromoalkyne[6] or a borane intermediate.[3]

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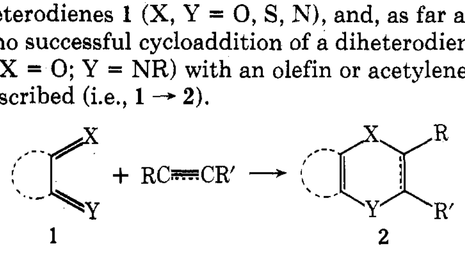
Metal Complexes in Organic Synthesis. I. Cycloaddition of Dimethyl Acetylenedicarboxylate with the Bis Copper(II) Complexes Formed from *o*-Nitrosophenols. Synthesis of 2,3-Dicarbomethoxy-4-hydroxy-1,4-benzoxazines

Summary: The heterodiene system in the bis copper(II) complexes formed from *o*-nitrosophenols undergoes smooth [4 + 2] cycloaddition with dimethyl acetylenedicarboxylate to give 1,4-benzoxazines in excellent yield.

Sir: Cycloadditions of diheterodienes with olefins and acetylenes constitute simple procedures for the preparation of a wide range of 1,2-, 1,3- and 1,4-heterocyclic systems.[1,2] The least investigated of these three processes is that involving 1,4-diheterodienes **1** (X, Y = O, S, N), and, as far as we are aware, no successful cycloaddition of a diheterodiene of the type **1** (X = O; Y = NR) with an olefin or acetylene has yet been described (i.e., **1** → **2**).



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