

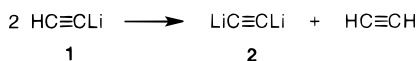
Disproportionation of Monolithium Acetylide into Dilithium Carbide and Acetylene Is a Reversible Reaction in Tetrahydrofuran at 0 °C

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The monolithium acetylide method is probably the most widely used ethynylation and alkynylation reaction.¹ Monolithium acetylide (**1**) disproportionates readily above -25 °C into the more stable dilithium carbide (**2**) and acetylene.² Liquid ammonia which is utilized in processes claimed to have industrial economics^{1,3} serves not only as a solvent but also as a stabilizing agent. When ammonia is removed completely, disproportionation occurs. The use of the monolithium acetylide–ethylenediamine complex which is produced by allowing *N*-lithioethylenediamine to react with acetylene in various solvents permits isolation and eliminates the need for liquid ammonia.^{4,5} **1** may also be prepared from acetylene and lithium in benzene/hexamethylphosphoric triamide.⁶ However, the stabilizing effect of all of these complexing agents and solvents greatly diminishes the reactivity of the acetylide toward alkylating agents.



In 1975 Midland reported on a procedure for the preparation and use of a reactive amine-free monolithium acetylide in tetrahydrofuran.^{7,8} Addition of *n*-butyllithium to acetylene (1:1 ratio) in THF at -78 °C results in a clear and stable solution of $\text{HC}\equiv\text{CLi}$ from which a number of aldehydes and ketones can be added to give good yields (>90%) of the desired propargylic alcohols (Scheme 1 and Table 1). When the THF solution is warmed at 0 °C prior to the addition of the electrophile, monolithium acetylide disproportionates into the snow-

Scheme 1

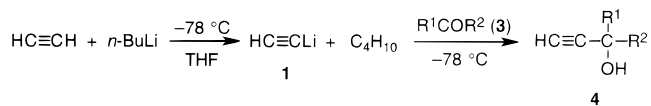
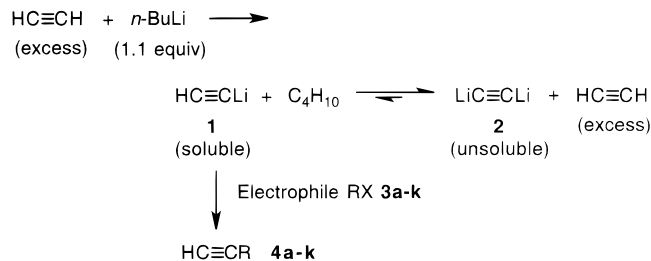


Table 1. Addition of Monolithium Acetylide to Electrophiles in THF

electrophile (3)	RC≡CH (4), yield (%) ^{a,b}	
	-78 °C (ref 7)	0 °C
a acetone	94	99 (82)
b hexanal	98	99 (92)
c 2-hexanone	92	95
d di- <i>tert</i> -butyl ketone	66	80
e acetophenone	75	80 (75)
f acetophenone		95 ^c
g benzaldehyde	93	100 (90)
h cyclopentanone	94	97
i cyclohexanone	95	95
j cinnamaldehyde	96	100
k chlorobis(diisopropylamino)borane	35 ^d	95 (85)
k 1-iodooctane	0	20

^a By VPC based on carbonyl compounds. All products exhibit consistent IR, ¹H and ¹³C NMR, and mass spectra. Isolated yields are in parentheses. ^b 1.1 equiv of *n*-butyllithium was used. ^c 2 Equiv of *n*-butyllithium was used. ^d A saturated solution of acetylene was used.

Scheme 2



white insoluble dilithium carbide (**2**).⁷ When *n*-butyllithium is added at 0 °C to a solution of acetylene (1:1 ratio) in THF, **1** produces the same precipitate **2** and treatment of the reaction mixture with acetone at 0 °C gives only a poor yield (32%) of the carbinol **4a** (R¹ = R² = Me).⁷

This Note establishes for the first time that disproportionation of lithium acetylide into dilithium carbide and acetylene is a reversible process in THF at 0 °C and that such an equilibrium may be readily displaced by addition of an electrophile (Scheme 2).

Addition of a 1.6 M solution of *n*-butyllithium in hexanes to a saturated tetrahydrofuran solution of acetylene cooled at 0 °C⁹ yields, as expected, dilithium carbide (**2**). *The white precipitate slowly dissolves when an electrophile 3 is added dropwise affording a clear solution at the end of the addition.* The reactants are stirred at 0 °C for 30 additional min and brought to ambient temperature. With a variety of aldehydes and ketones (Table 1), the reaction appears to be essentially complete under these conditions. Since comparable yields have heretofore not been approached, this one-step procedure con-

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stitutes a much improved route to propargylic alcohols. Most compounds give satisfactory results with a 1.1:1 ratio of *n*-butyllithium to electrophiles. Acetophenone reacts in higher yield when 2 equiv of *n*-butyllithium is used. With less reactive electrophiles such as chlorobis(diisopropylamino)borane [ClB(*i*-Pr)₂] (**3j**), reaction takes place efficiently at 0 °C to deliver boracetylene **4j** in excellent yield. The latter transformation is particularly worthy of note since the reaction is by far less effective at -78 °C. Monolithium acetylide does not react with alkyl halides at -78 °C.⁷ At 0 °C, 1-iodooctane produces 1-decyne (**4k**) in low yield (20%).

This new process should be a welcome addition to anyone interested in ethynylation and alkynylation reaction. The method is generally applicable to a wide variety of ketones and aldehydes and appears to be particularly advantageous with less reactive electrophiles. The procedure should be exceptionally suitable for industrial purposes since a reactive nonstabilized monolithium acetylide is available for the first time in reaction conditions compatible with industrial requirements.

Experimental Section

Reactions are performed in oven-dried glassware under an argon atmosphere. Tetrahydrofuran (THF) is distilled from deep blue solutions of sodium/benzophenone ketyl prior to use. *n*-BuLi, 1.6 M in hexanes, purchased from Aldrich Chemical Co., Inc., is titrated as indicated by Watson and Eastham.¹⁰ Acetylene (welding grade) is purified by passage through a gas

washing bottle containing a concentrated sulfuric trap and through a calcium chloride drying tube. All ketones and aldehydes are obtained commercially and are distilled under nitrogen prior to use.

General Procedure for Monolithium Acetylide Preparation. 3-Phenyl-1-propyn-3-ol. In a 250-mL, septum-capped, round-bottomed flask, equipped with a magnetic stir bar and purged under Ar is charged 40 mL of dry THF. The apparatus is cooled at 0 °C, and the solution is saturated with acetylene by means of a 10-mm glass tube approximately 30 cm in length inserted through the septum of the flask. *n*-Butyllithium (10 mmol, 6.3 mL of a 1.6 M solution in hexanes) is transferred dropwise into the reaction flask over a period of 20 min by means of a 10-mL syringe. The inlet end of the needle is pushed *below* the surface of the liquid to avoid contact of the organolithium with the acetylene atmosphere and formation of dilithium carbide on the needle tip. The contents are resaturated with acetylene, and benzaldehyde (9 mmol, 0.88 mL) in THF (10 mL) is added dropwise over a 20-min period. The solution is warmed to ambient temperature, and 20 mL of water is added. Anhydrous potassium carbonate is added until the aqueous phase becomes pasty. The organic layer is decanted, and the aqueous phase is extracted with 2 × 50 mL of ether. The combined organic layer is dried (MgSO₄), filtrated, and concentrated in vacuo to give a yellow oil which is purified by Kugelrohr distillation to obtain 1.19 g (90%) of the alcohol as a pale oil. ¹H NMR (CDCl₃, TMS) δ: 2.63 (s, C≡CH), 5.38 (s, 1H), 7.27–7.53 (m, 5H). ¹³C NMR (CDCl₃) δ: 64.2; 74.9 (internal acetylene); 83.7 (terminal acetylene); 126.7; 128.7; 140.1; 148.5. HMRS calcd for C₈H₉O: 132.0575. Found: 132.0570.

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