Reaction of 1,3-Dilithioacetylides with Carbonyl Electrophiles: Preparation of Allene-1,3-dicarboxylic Acids

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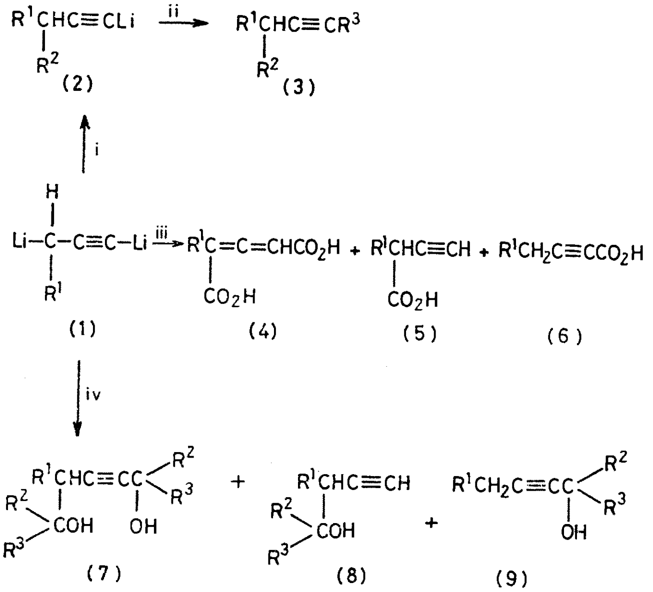
Summary 1,3-Dilithioalk-1-ynes react with carbon dioxide and give alk-2,3-dien-1,5-dioic acids; in contrast the acetylenes, alk-2-yn-1,5-diols are isolated on reaction with aldehydes and ketones.

1,3-Dilithioalk-1-ynes[1] (**1**) can be used to prepare branched[1,2] and linear[3] acetylenes by regioselective alkylations with alkyl halides [Scheme, (**1**) → (**2**) → (**3**)]. These studies have now been extended by treating 1,3-dilithioacetylides with carbon dioxide, formaldehyde, and cyclic ketones.



Scheme. i, R^2Br; ii, R^3Br, hexamethylphosphoric triamide; iii, CO_2; iv, CH_2O or $[CH_2]_nC{=}O$ (n = 4, 5, or 6).

Previous work on the carboxylation of 1,3-dilithiobut-1-yne led to the isolation of 2-methylglutaric acid from hydrogenation of the reaction product, but the unsaturated intermediate was not identified.[4]

Reaction of 1,3-dilithiohex-1-yne (**1**; $R^1 = n\text{-}C_3H_7$) with a slurry of dry carbon dioxide led to the isolation of an allenic dicarboxylic acid (33%), m.p. 144—145 °C [ν 1950 cm⁻¹; δ ¹H: 6·03 (CH, *J ca.* 2 Hz); δ ¹³C: 91·86 (d), 217·71 (s), and 103·69 (s) p.p.m.]. That carboxylation had occurred at C-1 and C-3 to give the allene (**4**; $R^1 = n\text{-}C_3H_7$) was supported by the long range coupling of the proton at C-1 with methylene group at C-4[5] and confirmed by catalytic hydrogenation in the presence of palladium–charcoal to give the known 3-propylglutaric acid.[6] Two acetylenic monocarboxylic acids (**5** and **6**; $R^1 = n\text{-}C_3H_7$) were also detected after the carboxylation reaction. Similar results were obtained from the carboxylation of dilithiopent-1-yne (**1**; R^1 = Et) and dilithiohept-1-yne (**1**; R^1 = Buⁿ) (Table 1). When the order of addition was reversed and carbon dioxide gas was passed into hexane solutions of dilithio-oct-1-yne (**1**; $R^1 = n\text{-}C_5H_{11}$) and also the lower homologues at *ca.* −40 °C only poor yields of allene dicarboxylic acids were obtained. The isolation of allene-1,3-dicarboxylic acids was unexpected since with other carbonyl electrophiles,[1,2] *e.g.* formaldehyde, cyclopentanone, cyclohexanone, and cycloheptanone, the expected prop-2-ynylic and terminal acetylenic substitutions occurs and alk-2-yne-1,5-diols (**7**) are formed together with some of the monohydric alcohols (**8** and **9**) (Table 2). However, our results are in accord with previous attempts to prepare pent-2-yn-1,5-dioic acid ('glutinic acid')[7] or its dimethyl ester[8] which led to the isolation of penta-2,3-dien-1,5-dioic acid[7] or its dimethyl ester.[8] Thus our approach provides a new general method for the synthesis of allene-1,3-dicarboxylic acids.

Table 1. Allene products, $R^1C(CO_2H){=}C{=}CHCO_2H$ (**4**), from dicarboxylation of 1,3-dilithioalk-1-ynes (**1**).[a]

R	Et	Prⁿ	Buⁿ	$n\text{-}C_5H_{11}$
Isolated yield/%	33	37	31·5	13·5[b]
M.p./°C	170—172	144—145	136—138	146—147

[a] Good analytical data were obtained for the reaction products but the yields were not optimised. [b] This reaction was carried out by passing carbon dioxide gas into the reaction mixture.

Table 2. Alk-2-yn-1,5-diols, $R^1C(R^2R^3COH)H{-}C{\equiv}C{-}C(OH)R^2R^3$ (**7**), from reactions of formaldehyde and cyclic ketones with 1,3-dilithioalk-1-ynes (**1**).[a]

	R^2R^3 (Yield/%)			
R^1	H,H	$[CH_2]_4$	$[CH_2]_5$	$[CH_2]_6$
Et	35 (b.p. 54—56 at 0·04 mmHg)	6 (m.p. 120—121)		
Prⁿ	46·5 (b.p. 42—45 at 0·1 mmHg)	32 (m.p. 115—116)	23 (m.p. 90)	
Buⁿ	28 (b.p. 59 at 0·02 mmHg)		16 (m.p. 96)	21 (m.p. 95)

[a] Good analytical data were obtained for the reaction products but the yields were not optimised. All b.p.s and m.p.s are in °C.

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