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Syntheses of Enynes, Homopropargylic Alcohols, and Propargylic Carboxylic Acids from Allenes

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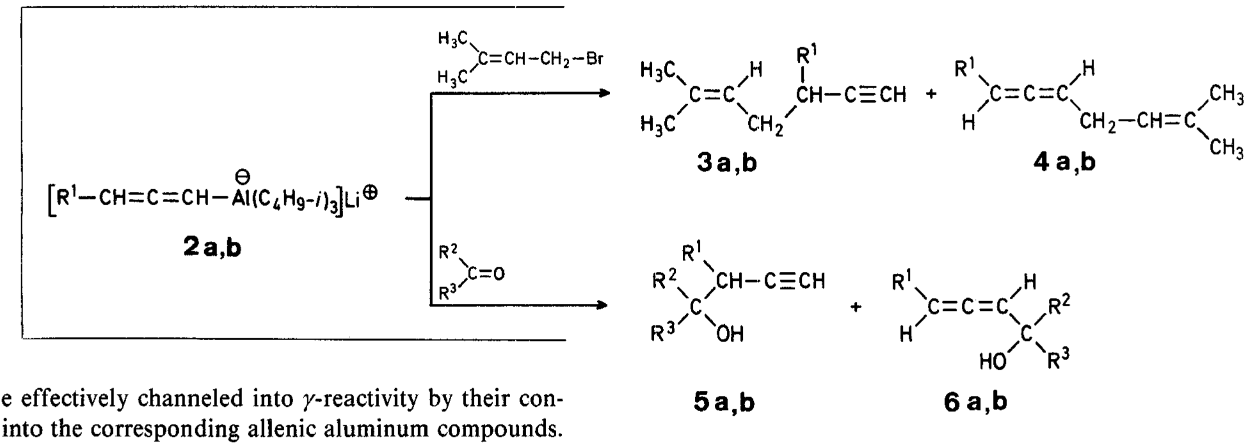
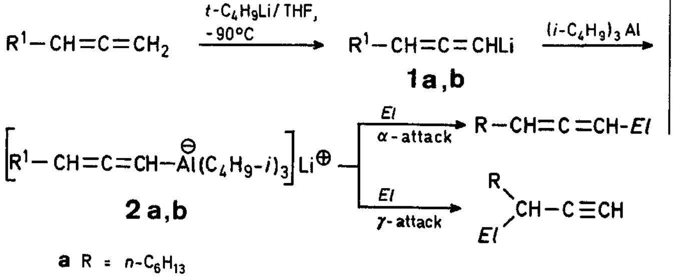
A variety of allenic lithium reagents are readily obtained through metalation of allenes with alkyllithiums[1,2]. Their reactions with electrophilic reagents often proceed without rearrangement of the allenic structure to furnish α-substituted allenes[1,2,3]. On the other hand, we have recently observed that propargylic aluminum derivatives react regioselectively with electrophilic reagents in the γ-positions via rearrangement[4]. This suggested that the α-reactivity of allenic lithium reagents might be effectively channeled into γ-reactivity by their conversion into the corresponding allenic aluminum compounds. In accord with this, we have now found that allenic lithium-derived organoaluminum compounds react with allylic halides as well as with carbonyl reagents to afford nearly exclusively γ-substituted 1-alkynes.



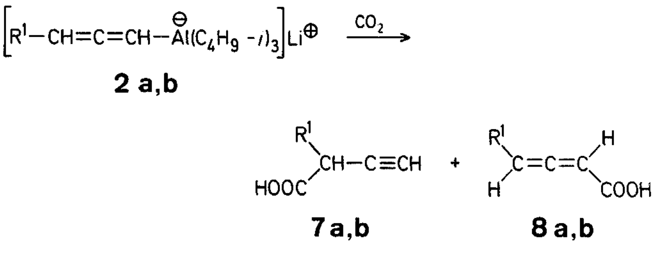
Lithiation of monosubstituted allenes[5] in tetrahydrofuran with *t*-butyllithium at −90 °C followed by treatment of the resultant 1-lithio-1,2-dienes **1**[6] with triisobutylalane produced the corresponding allenic alanates **2**[8]. The allenic alanates **2** possess two potential sites for reaction with electrophiles. Attack of an electrophile (*El*) at the α-carbon should afford an allenic derivative, whereas attack at the γ-carbon should produce, via bond transposition, the propargylic derivative.



Treatment of **2a** in tetrahydrofuran at −78 °C with prenyl bromide (1-bromo-3-methyl-2-butene) furnished, after hydrolytic workup, the enyne **3a** of γ-attack containing only 1% of the allylic allene α-coupling product **4a**. Interestingly, substitution of the *n*-hexyl group on the γ-carbon in **2a** by the larger cyclohexyl group **2b** did not decrease the amount of γ-prenylation product **3b**. However, the reaction proceeded at a much slower rate. In marked contrast to the nearly exclusive formation of the enyne **3a** from the allenic alanate **2a**, treatment of the corresponding allenic lithium reagent **1a** with prenyl bromide yielded the allyl allene **4a** as the major product (75 to 25 mixture of **4a** and **3a**).

The alanates **2** also exhibited high γ-selectivities in their reactions with aldehydes and ketones[9]. Thus, treatment of **2a, b** with variously substituted aldehydes furnished the corresponding homopropargylic alcohols **5a, b** in at least 97% isomeric purities, regardless of the size of the alkyl group at the carbonyl moiety[10]. No loss in γ-selectivity was observed when acetone was used as the electrophile.

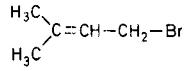
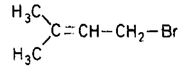
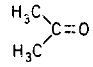
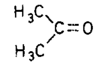
The reaction of allenic alanates with carbon dioxide should provide an attractive synthesis for propargylic carboxylic acids. Thus, carbonation of **2a, b** resulted in regioselective γ-carboxylation forming the acids **7a, b** containing only a small amount of the isomeric allenic acids **8a, b**. On the other hand, it has been reported[2] that allenic lithium reagents react with carbon dioxide to afford predominately the allenic acids **8**.



5-*n*-Hexyl-2-methylhept-2-en-6-yne (3a); Typical Procedure:

To a well-stirred solution of 1,2-nonadiene (0.62 g, 5.0 mmol) in tetrahydrofuran (12 ml) under a nitrogen atmosphere is added dropwise a 2.7 molar solution of *t*-butyllithium (1.85 ml, 5.0 mmol) while maintaining the temperature during the addition at −90 °C (methanol/liquid nitrogen bath)[6]. The resultant yellow solution is stirred at −90° to −95 °C for 1 h, warmed gradually to −78 °C (acetone/Dry Ice bath), stirred for 15 min at this temperature, and then treated with neat triisobutylalane (1.4 ml, 3.96 molar, 5.5 mmol) over a 5 min period. The mixture is stirred for 15 min at −78 °C; then the allenic alanate **2a** formed is treated with prenyl bromide (0.82 g, 5.5 mmol). The result-

Table. Enynes (3), Homopropargylic Alcohols (5), and Propargylic Carboxylic Acids (7) prepared

Allenic alanate No. R^1		Electrophile	Reaction time[a] [h]	Yield [%] of product[b]			Isomeric purity [%][c]	b.p. [°C]/torr	n_D (temp. [°C])	Molecular formula[d]
				3	5	7				
2a	n-C_6H_{13}	 $(H_3C)_2C=CH-CH_2-Br$	2	76	—	—	99	83–84°/0.4	1.4569 (25°)	$C_{14}H_{24}$ (192.3)
2b	c-C_6H_{11}	 $(H_3C)_2C=CH-CH_2-Br$	16	86	—	—	99	85°/0.5[g]	1.4811 (25°)	$C_{14}H_{22}$ (190.3)
2a	n-C_6H_{13}	$C_2H_5-CH=O$	2	—	83[e]	—	98	77–78°/0.6	1.4524 (25°)	$C_{12}H_{22}O$ (182.3)
2b	c-C_6H_{11}	$C_2H_5-CH=O$	2	—	76[e]	—	97	80°/0.5[g]	1.4830 (26°)	$C_{12}H_{20}O$ (180.3)
2a	n-C_6H_{13}	i-$C_3H_7-CH=O$	2	—	97[e,f]	—	99	79–80°/0.5	1.4518 (24°)	$C_{13}H_{24}O$ (196.3)
2a	n-C_6H_{13}	t-$C_4H_9-CH=O$	2	—	80[e]	—	99	90–91°/0.8	1.4563 (23°)	$C_{14}H_{26}O$ (210.4)
2a	n-C_6H_{13}	 $(H_3C)_2C=O$	16	—	76	—	98	87–89°/0.5	1.4521 (24°)	$C_{12}H_{22}O$ (182.3)
2b	c-C_6H_{11}	 $(H_3C)_2C=O$	16	—	58	—	99	70–71°/0.7	1.4805 (25°)	$C_{12}H_{20}O$ (180.3)
2a	n-C_6H_{13}	CO_2	0.5	—	—	73	97	110°/10^{-4}[g]	1.4518 (24°)	$C_{10}H_{16}O_2$ (168.2)
2b	c-C_6H_{11}	CO_2	0.5	—	—	71	97	165°/0.5[g]	1.4861 (28°)	$C_{10}H_{14}O_2$ (166.2)

[a] The electrophile was added to the alanate **2** at −78 °C followed by maintaining the reaction mixture at 25 °C for the time indicated.

[b] The products contained 2–5% of the corresponding 3-substituted allenes (Ref. 6).

[c] The isomeric purities of the products were determined on a SE-54 glass capillary column (30 m).

[d] Microanalytical results showed the following deviations from the calculated values: C, ±0.14; H, ±0.11.

[e] Mixtures of diastereomers.

[f] Yield determined by G.L.C.

[g] Kugelrohr distillation.

ing mixture is gradually warmed to 25 °C, stirred for 2 h at this temperature, and then is poured into ice-cold 3 molar hydrochloric acid (25 ml). The aqueous phase is extracted with ether (3 × 10 ml), and the combined extracts are washed with 3 molar hydrochloric acid (10 ml) and with a saturated solution of sodium chloride (10 ml), then dried with magnesium sulfate. The solvents are removed and the residue is distilled through a short-path column; yield: 0.73 g (76%); b.p. 83–84 °C/0.4 torr; n_D^{25}: 1.4569.

$C_{14}H_{24}$ (192.1879).

M.S.: $m/e = 177.1644$ ($M^+ - 15$).

I.R. (neat): $\nu = 3325, 2120, 1670, 845$ cm^{-1}.

^{1}H-N.M.R. (CCl_4): $\delta = 5.1$ [m, 1H, $(CH_3)_2C=C\underline{H}$]; 2.1 (m, 3H); 1.9 (s, 1H, $C\equiv C\underline{H}$); 1.6 (d, 6H, $J = 7$ Hz); 1.5–1.0 (m, 10H); 0.9 ppm (t, 3H, $J = 6$ Hz).

4-*n*-Hexylhex-5-yn-3-ol (5a, $R^2 = C_2H_5$, $R^3 = H$); Typical Procedure:

The 1,2-nonadiene (0.62 g, 5.0 mmol) is converted into the allenic alanate **2a** as described above. To the organoaluminum compound, propanal (0.32 g, 5.5 mmol) is added at −78 °C. The resultant clear solution is warmed gradually to 25 °C, stirred for 2 h, and then poured into ice-cold 3 molar hydrochloric acid (25 ml). The layers are separated, and the aqueous phase is extracted with ether (3 × 10 ml). The combined extracts are washed with 3 molar hydrochloric acid (10 ml) and with saturated aqueous sodium chloride (10 ml), then dried with magnesium sulfate. The filtrate is concentrated and the residue obtained is distilled through a short-path column; yield: 0.76 g (83%); b.p. 77–78 °C/0.6 torr; n_D^{25}: 1.4524.

M.S.: $m/e = 182.1666$ (M^+; $C_{12}H_{22}O$ requires 182.1672).

I.R. (neat): $\nu = 3420, 3320, 2110$ cm^{-1}.

^{1}H-N.M.R. (CCl_4): $\delta = 3.3$ (m, 1H, $C\underline{H}OH$); 2.3 (m, 1H, $C\underline{H}C\equiv C$); 2.0–1.8 (m, 2H); 1.7–1.1 (m, 12H); 1.1–0.7 ppm (m, 6H).

2-*n*-Hexylbut-3-ynoic acid (7a); Typical Procedure:

The alanate **2a** (5 mmol), prepared as described above, is carbonated at −78 °C by introducing a steady stream of dry carbon dioxide. The mixture is then slowly brought to room temperature while continuing the addition of carbon dioxide for an additional 30 min. The reaction mixture is poured into ice-cold 3 normal hydrochloric acid (25 ml) and the aqueous phase is extracted with ether (3 × 10 ml). The combined extracts are washed with 3 molar hydrochloric acid (10 ml) and with a saturated solution of sodium chloride (10 ml), then dried with magnesium sulfate. The solvents are removed and the residue is distilled (Kugelrohr); yield: 0.61 g (73%); b.p. 110 °C/10^{-4} torr; n_D^{25}: 1.4525.

M.S.: $m/e = 168.1155$ (M^+; $C_{10}H_{16}O_2$ requires 168.1151).

I.R. (neat): $\nu = 3320, 2130, 1710$ cm^{-1}.

^{1}H-N.M.R. (CCl_4): $\delta = 11.3$ (s, 1H, $COO\underline{H}$); 3.3 (dt, 1H, $J = 9$ Hz, 3 Hz, $C\underline{H}C\equiv C$); 2.2 (d, 1H, $J = 3$ Hz, $C\equiv C\underline{H}$); 2.1–0.6 ppm (m, 13H).

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[4] N. R. Pearson, G. Hahn, G. Zweifel, *J. Org. Chem.* **47**, 3364 (1982).

[5] The allenes were obtained in 80–90% yields by the reaction of methyl propargyl ether with the appropriate Grignard reagent in the presence of copper(I) bromide: J. L. Moreau, M. Gaudemar, *J. Organometal. Chem.* **108**, 159 (1976).

[6] Metalation of the allenes with *t*-butyllithium produced besides the desired 1-lithio-1,2-dienes some of the C-3 lithiated allenes[7]. This side-reaction could be decreased to 2–5% by carrying out the lithiation at −90 °C.

[7] L. Brandsma, H. D. Verkruijsse, *Synthesis of Acetylenes, Allenes and Cumulenes*, Elsevier Scientific Publishing Co., Amsterdam, 1981, p. 7.

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[9] For alternative syntheses of homopropargylic alcohols **3** using allenic or propargylic organometallics, see:
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[10] It is noteworthy that even the 3,3-dialkyl substituted allenic alanates derived from 3-*n*-pentyl-1,2-nonadiene reacted with propanal nearly exclusively (99%) at the more hindered γ-position.