Allenyllithium Reagents; V[1]. An Efficient Route to Functionalised Allenes

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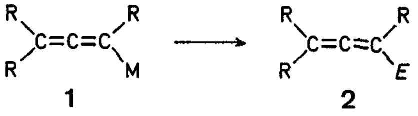
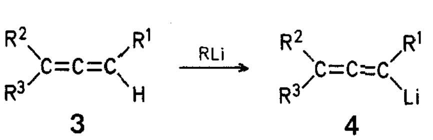
A potentially direct route for the introduction of the allenyl moiety into a molecule might be expected by reaction of allenyl organometallic reagents **1** with electrophiles (Scheme **A**).



Scheme **A**

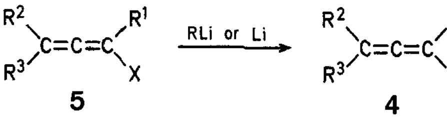
Although this reaction (Scheme **A**) appears simple, the different organometallic reagents thus far studied[3] have not proved very efficient for the synthesis of pure allenic compounds **2**. As a result of the propargyl rearrangement, a mixture of allenes and acetylenes was generally obtained. The corresponding lithium derivatives **1** (M = Li), obtained previously by addition of alkyllithium reagents to vinylacetylenes[4] have received little attention in synthesis.

We recently described a highly regioselective preparation of allenyllithium reagents **4** by (a) metallation of allenic hydrocarbons[5] **3** (Scheme **B**)



Scheme **B**

or (b) by halogen/metal exchange[5,6] in the haloallenes **5** (Scheme **C**).



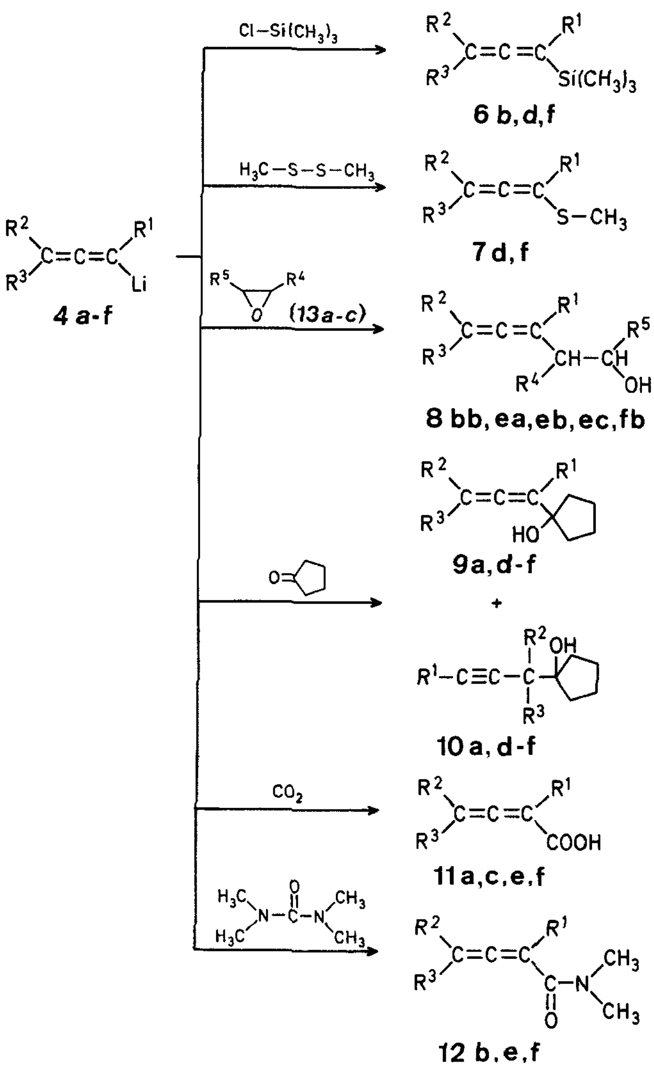
Scheme **C**

We now report a simple synthesis of functionalised allenes **6–12** by reaction of the organometallic reagents **4** with a variety of electrophiles; the reaction takes place in most cases with retention of the allenic structure (Scheme **D**).

When treated with chlorotrimethylsilane or dimethyl disulphide, the substituted reagents **4** reacted to give respectively the allenylsilanes **6** and the allenyl sulphides **7**. Reactions of **4** with oxiranes **13** in the presence of hexamethylphosphoric triamide[7,8] afforded the β-allenic alcohols **8**.

The reactions with aliphatic ketones were dependent upon the degree of substitution in the organometallic reagents **4**, the substituted allenyllithium reagents led mainly to allenic alcohols (e.g. of type **9**). However, propargylic alcohols (e.g. of type **10**) were obtained from unhindered aromatic carbonyl compounds[5,9].

When treated with carbon dioxide, the substituted reagents **4** reacted to give the allenic acids **11** and with tetramethylurea, after mild acid hydrolysis, they reacted to give the dialkylamides **12** in good yields.



4	R^1	R^2	R^3
a	H	H	H
b	H	H	n-C_3H_7
c	H	H	n-C_5H_{11}
d	H	H	n-C_8H_{17}
e	H	CH_3	CH_3
f	n-C_4H_9	CH_3	CH_3

13	R^4	R^5
a	H	H
b	H	CH_3
c	$-(CH_2)_4-$	

Scheme **D**

The above examples illustrate the scope and utility of the allenyllithium reagents **4** for the synthesis of a large variety of substituted allenic compounds.

Allenyllithium Reagents 4:

Method A: Metallation of Allenic Hydrocarbons **3**: Under nitrogen, a 1.5 normal solution of butyllithium in hexane (20 mmol) is added with stirring to the allene **3**[5] (20 mmol) in anhydrous tetrahydrofuran (50 ml) at −78 °C. The mixture is stirred at this temperature for 30 min[10] and the reagent is used immediately.

In the case of *trisubstituted allenes* **3** (R^1, R^2, R^3 = alkyl), metallation is carried out in the same way with t-butyllithium (1 equiv), 30 min at −78 °C, then 1 h at −40 °C or with n-butyllithium (1.05 equiv) + *hexamethylphosphoric triamide (1.4 equiv), 30 min at −78 °C, and 6 h* at −30 °C.

Table. Reactions of Allenyllithium Compounds **4** with Electrophiles (Scheme **D**)

Product No.	Yield [%]	b.p. [°C]/ torr or m.p. [°C]	Molecular formula[a] or Lit. data	I.R. (neat) ν [cm^{-1}]	^{1}H-N.M.R. δ [ppm]	^{13}C-N.M.R. (CDCl$_3$/TMS) δ [ppm]	Mass Spectra *m/e*
6b	90[b]	40–50°/20	$C_9H_{18}Si$ (154.3)	1940, 1245, 840, 755	0.05 (s, 9H); 0.7–1.0 (m, 3H); 1.1–1.6 (m, 2H); 1.7–2.1 (m, 2H); 4.6–5.0 (m, 2H)	−0.9 (3C), 13.5, 14.4, 22.3, 31.6, 89.0, 97.4, 198.9	154, 139, 83, 75, 74, 73 (100)
6d	85[b]	75°/0.2	$C_{14}H_{28}Si$ (224.3)	1938, 1247, 841, 756	0.05 (s, 9H); 0.7–1.7 (m, 15H); 4.6–4.9 (m, 2H)	−0.74 (3C), 14.21, 22.82, 28.00, 29.36 (2C), 29.62, 29.88, 32.01, 82.24, 83.28, 209.70	224, 209, 168, 150, 126, 111, 73
6f	95	—[c]	$C_{12}H_{21}Si$ (196.3)	1925, 1250, 850, 765	0.05 (s, 9H); 0.75–1.0 (m, 3H); 1.63 (s, 6H); 1.7–2.1 (m, 2H)	1.39 (3C), 13.82, 19.84 (2C), 22.24, 29.23, 31.43, 88.72, 94.35, 203.94	196, 181, 149, 139, 74, 73
7d	76	80–90°/1	$C_{12}H_{22}S$ (198.3)	1943, 695	0.65–1.7 (m, 15H); 1.8–2.4 (m, 2H); 2.07 (s, 3H); 5.43 (dd, $J=6.4$ Hz, $J=3.2$ Hz); 5.70 (dt, 1H, $J=6.4$ Hz, $J=3.2$ Hz)	14.0, 15.1, 21.2 (2C), 22.5, 31.8, 101.9, 102.4, 193.5	198, 183, 113, 100, 85, 67
7f	96	—[c]	$C_{10}H_{18}S$ (170.2)	1940	0.7–1.65 (m, 7H); 1.75 (s, 6H); 2.00 (s, 3H); 1.8–2.3 (m, 2H)	13.43, 14.66, 20.94, 21.66, 30.13, 33.05, 101.53, 102.31, 193.38	170, 155, 123, 113, 93, 90, 81, 79, 43, 41 (100)
8bb	83	—[c]	$C_9H_{16}O$ (140.2)	3330, 1960	0.93 (t, 3H, $J_1=7.5$ Hz); 1.15 (d, 3H, $J_2=6$ Hz); 1.3–1.7 (m, 2H); 1.7–2.3 (m, 4H); 3.5–4.0 (qd, 1H, $J_2=6$ Hz, $J_3=7$ Hz)	13.63, 22.30 (2C), 38.81, 67.23, 86.77, 90.27, 204.39	140, 111, 81, 67, 55, 45, 43, 41
8ea	85	80°/20	$C_7H_{12}O$ (112.2)	3300, 1960	1.62 (d, 6H, $J=3$ Hz); 1.95–2.4 (m, 2H); 3.35 (t, 2H, $J=6.5$ Hz); 4.65–5.2 (m, 1H)	20.62 (2C), 32.53, 61.98, 84.90, 95.19, 201.99	112, 97, 79, 70, 69, 67, 53, 41
8eb	82	—[c]	$C_8H_{14}O$ (126.2)	3320, 1960	1.15 (d, 3H, $J_1=6$ Hz); 1.65 (d, 6H, $J_2=3$ Hz); 2.05 (t, 2H, $J_3=7$ Hz); 3.50–4.00 (qd, 1H, $J_1=6$ Hz, $J_3=7$ Hz)	20.43 (2C), 22.30, 39.00, 67.23, 84.83, 94.54, 202.32	126, 111, 93, 83, 67, 54, 45, 43, 41
8ec	78	—[c]	$C_{11}H_{18}O$ (166.2)	3340, 1960	1.0–2.1 (m, 15H); 2.9–3.4 (m, 1H); 4.7–5.2 (m, 1H)	20.49, 20.62, 24.57, 25.22, 31.30, 33.95, 46.06, 73.63, 90.92, 95.25, 200.89	166, 133, 123, 81, 79, 67, 41
8fb	88	—[c]	$C_{12}H_{22}O$ (182.2)	3340, 1960	0.8–1.05 (m, 3H); 1.05–1.5 (m, 7H); 1.65 (s, 6H); 1.75–2.3 (m, 5H); 3.50–4.00 (qd, 1H, $J_1=6$ Hz, $J_2=7$ Hz)	13.95, 20.62, 20.81, 21.01, 22.24, 29.75, 33.05, 42.89, 66.06, 95.90, 99.01, 198.17	182, 167, 140, 125, 107, 96, 81, 43
9a	50	—[c]	$C_8H_{12}O$ (124.1)	3350, 1938, 855	1.6–2.1 (m, 9H); 4.85 (d, 2H, $J=7$ Hz); 5.42 (t, 1H, $J=7$ Hz)	23.79 (2C), 40.43 (2C), 78.17, 79.65, 98.43, 205.04	124, 95, 86, 85, 82, 67, 57, 56, 55 (100)
9d	80[d]	—[c]	$C_{16}H_{28}O$ (236.3)	3340, 1940	0.7–1.05 (m, 3H); 1.8–2.25 (m, 22H); 2.35 (1H); 5.1–5.4 (m, 2H)	14.15, 22.69, 23.73, 24.24, 28.97, 29.23 (2C), 29.48 (2C), 40.17, 40.36, 79.85, 94.35, 99.14, 200.12	236, 218, 137, 84 (100)
9e	95	60°/1.5	$C_{10}H_{16}O$ (152.2)	3320, 1945	1.5–2.0 (m, 8H), 1.70 (d, 6H, $J=3$ Hz); 2.50 (s, 1H); 5.20 (sept, 1H, $J=3$ Hz)	20.49 (2C), 23.47 (2C), 40.10 (2C), 80.11, 97.13, 98.17, 197.79	152, 134, 109, 85, 67 (100), 41
9f	92	—[c]	$C_{14}H_{24}O$ (208.2)	3400, 1945	0.75–1.05 (m, 3H); 1.15–2.25 (m, 15H); 1.70 (s, 6H)	13.89, 20.43 (2C), 22.30, 23.34 (2C), 27.29, 30.33, 38.94 (2C), 82.24, 97.39, 108.26, 194.91	208, 165, 95, 85, 82 (100), 67, 55, 41
10a	50	—[c]	$C_8H_{12}O$ (124.1)	3380, 3290, 2135	1.6–2.0 (m, 8H); 2.05 (t, 1H, $J=3$ Hz); 2.15 (s, 1H); 2.52 (d, 2H, $J=3$ Hz)	24.18 (2C), 31.49, 39.20 (2C), 70.27, 80.69, 81.40	124, 106, 95, 91, 85 (100), 81, 67
10d	10[d]	—[c]	$C_{16}H_{28}O$ (236.3)	3400, 3300, 2125	2.00 (d, 1H, $J=2$ Hz); 2.1–2.5 (m, 2H)	14.28, 22.82, 24.05, 24.31, 27.29, 28.13, 29.42, 29.62 (2C), 30.01, 32.01, 37.58, 39.07, 42.89, 83.47, 85.48	—
11a	62	65–66° (pentane)	65–66°[15]	3500, 1970, 1934, 1680 (1934, 1970)[15]	5.26 (d, 2H, $J=6$ Hz); 5.62 (t, 1H, $J=6$ Hz); 10.85 (s, 1H)	79.46, 87.49, 171.44, 216.30	84, 69, 67, 66, 45, 43, 39 (100)
11c	75	—[e]	$C_9H_8O_2$ (154.1)	3100, 1955, 1685	0.7–1.15 (m, 3H); 1.15–1.7 (m, 6H); 1.75–2.40 (m, 2H); 5.3–5.9 (m, 2H); 11.6 (s, 1H)	15.04, 22.99, 27.85, 29.18, 31.83, 87.50, 95.46, 169.70, 218.30	154, 139, 125, 97, 41 (100)
11f	88	70–72° (pentane)	$C_{10}H_{16}O_2$ (168.2)	3450, 1965, 1675	0.7–1.0 (m, 3H); 1.1–1.55 (m, 4H); 1.77 (s, 6H); 2.0–2.3 (2H, m); 10.13 (s, 1H)	14.53, 20.23, 22.58, 27.40, 28.73, 30.94, 97.23, 98.99, 171.46, 205.49	168, 143, 126, 111, 81, 67, 55, 43 (100)

Table (continued)

Product No.	Yield [%]	b.p. [°C]/ torr or m.p. [°C]	Molecular formula[a] or Lit. data	I.R. (neat) ν [cm^{-1}]	^{1}H-N.M.R. δ [ppm]	^{13}C-N.M.R. (CDCl$_3$/TMS) δ [ppm]	Mass Spectra *m/e*
12b	66	—[c]	$C_9H_{25}NO$ (153.2)	1945, 1620	0.7-1.1 (m, 3H); 1.1-1.7 (m, 2H); 2.0-2.4 (m, 2H); 3.00 (s, 6H); 4.8-4.95 (m, 2H)	13.63, 20.88, 22.30, 32.01, 35.38, 77.32 (C), 164.49, 205.68	153, 138, 124, 111 (100), 96, 72
12e	72	—[b]	$C_8H_{13}NO$ (139.2)	1960, 1620	1.75 (d, 6H, $J=3$ Hz); 3.00 (s, 6H); 5.65 (sept, 1H, $J=3$ Hz)	19.01, 34.92, 37.12, 85.30, 98.11, 147.60, 206.81	139, 124, 111, 72 (100), 67
12f	81	—[b]	$C_{12}H_{21}NO$ (195.2)	1960, 1620	0.75-1.1 (m, 3H); 1.1-1.6 (m, 4H); 1.71 (s, 6H); 2.0-3.0 (m, 8H)	13.24, 19.06 (2C), 21.59, 29.42, 29.61, 34.66, 37.90, 96.74, 97.71, 167.94, 199.02	195, 152, 124, 81, 72 (100)

[a] The microanalyses were in satisfactory agreement with the calculated values (C ±0.31, H ±0.21).

[b] Containing ~5% of an isomer resulting from metallation at C-3 of **3** ($R^1=R^3=H$)[11] (G.L.C., SE 52, 80°).

[c] Chromatographed on silica gel (20 g), elution pentane, then pentane-ether 92:8.

[d] A mixture (84:12:4) of alcohols **9d**:**10d**:x (G.L.C. analysis) was formed in 95% yield. The alcohols **9d** and **10d** were separated by chromatography on neutral Merck alumina (elution: pentane/ether 92/8).

[e] Crude product.

In the case of *monosubstituted allenes* **3** ($R^1=R^2=H$), some metallation (~5%) occurs at C-3[11] and further derivatisation leads to a side product. When highly pure (>96%) lithium reagents are desired, the Method B should be used.

Method B: Halogen/Metal Exchange in Haloallenes **5** (X = Br, J): The halide **5** is filtered with suction before use through a small amount of alumina (Merck, activity IV). To a flask, cooled in a bath at −40 °C, containing powdered lithium (2.0 g, 0.3 mol) and anhydrous ether (20 ml), 1,2-dibromoethane (5 drops) is added. Then, a solution of 1-bromobuta-1,2-diene (6.7 g, 0.05 mol in ether (40 ml) is added dropwise while maintaining the temperature of the mixture at −20 °C. The mixture is maintained for 2 h at −5 °C and filtered through glass wool.

Reaction of Allenyllithium Reagents 4 with Electrophiles; General Procedure for Derivatives 6, 9, and 10:

To the allenyllithium reagent **4** (20 mmol) in tetrahydrofuran (50 ml) at −78 °C, the electrophile (20 mmol) is added dropwise with stirring. After 15 min at −78 °C, the reaction mixture is allowed to warm to room temperature and hydrolysed with saturated ammonium chloride solution. The aqueous layer is extracted with ether (3 x 100 ml), the extracts are dried with magnesium sulphate, and the product distilled or chromatographed as indicated in the Table.

Allenyl Methyl Sulphides[14] 7:

The allenyllithium reagent **4** (10 mmol) is added dropwise to a solution of dimethyl disulphide (15 mmol) in tetrahydrofuran (40 ml) at −20 °C. The reaction mixture is maintained at −20 °C for 1 h and allowed to warm to room temperature within 2 h. After hydrolysis with saturated ammonium chloride solution, extraction with ether (3 x 100 ml), the organic solution is washed with aqueous sodium hydrogen carbonate solution (100 ml), water (100 ml), and dried with magnesium sulphate. After evaporation of the solvent, the product is distilled in vacuo.

β-Allenic Alcohols 8:

Under nitrogen, hexamethylphosphoric triamide (4 ml, 23 mmol) is slowly added to the lithium reagent **4** (20 mmol) in tetrahydrofuran (50 ml) below −50 °C. Then, the oxirane **13** (30 mmol) is slowly added. After 30 min, the reaction mixture is allowed to warm to room temperature, hydrolysed with aqueous ammonium chloride solution, and extracted with ether (3 x 100 ml). The organic extracts are washed with water (30 ml) and dried with magnesium sulphate. The solvents are evaporated and the product is distilled or filtered through silica gel as indicated in the Table.

Allenic Acids 11:

A stream of carbon dioxide (10 ml/min) is passed over a tetrahydrofuran solution (50 ml) of the lithium reagent **4** (20 mmol) at −78 °C. After 1 h at −78 °C, the reaction mixture is allowed to warm to room temperature, hydrolysed with aqueous hydrochloric acid, and extracted with ether. The organic solution is dried with magnesium sulphate and the solvent is evaporated in vacuo.

In the case of **4a**, a mixture of *2,3-butadienoic* and *3-butynoic acid* is formed. This mixture is stirred with an aqueous solution of potassium carbonate at 40 °C for 3 h[12] and gives, after acidification, pure allenic acid **11a**.

In the case of **11d**, the acid cyclised on standing overnight into *4-hydroxy-4-methylpent-2-enoic lactone*[13].

Allenic Amides 12:

Tetramethylurea (2.32 g, 20 mmol) is added with stirring at −78 °C to the allenyllithium reagent **4** (20 mmol) in tetrahydrofuran (50 ml). The mixture is maintained at −78 °C for 3 h and then transfered by canula to ice-cooled 1 normal hydrochloric acid (30 ml). The aqueous layer is extracted with ether (3 x 100 ml), the organic extracts are washed with water (3 x 30 ml), and dried with magnesium sulphate. The solvent is removed in vacuo and the residual product is filtered through silica gel (20 g) using pentane/ether (92:8) as eluent.

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