A New Access to Sterically Shielded Allenes

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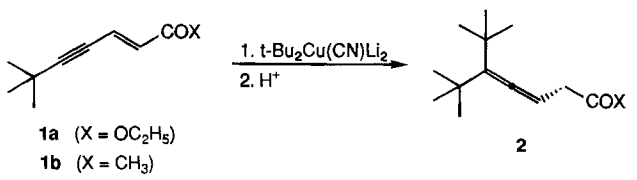
The synthesis of the sterically shielded allenes **2** and **5** by 1,6- and 1,4-addition of organocuprates to acceptor-substituted enynes and diynes, respectively, is described. Treatment of the di-*tert*-butyl-substituted allenes **2** with aqueous base does not cause double bond isomerization; whereas ester **2a** is converted into the corresponding β-allenic acid, ketone **2b** yields the 2*H*-pyran **6**.

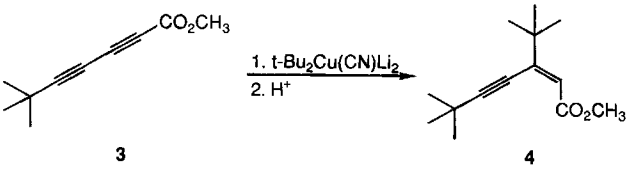
The use of sterically demanding substituents for the kinetic stabilization of reactive and normally unstable molecules or intermediates is well established in organic chemistry; this is also true for sterically shielded allenes bearing *tert*-butyl groups as bulky substituents[1-3]. The simplest non-functionalized allenes of this type, tri-*tert*-butylallene[2] and tetra-*tert*-butylallene[3], are known for some time and have been used for the stabilization of reactive allene oxides and allene radical cations, respectively. Recently, a new access to allenes bearing a variety of functional groups has been opened by the 1,6-addition of organocuprates to acceptor-substituted enynes[4]; thus, it has seemed attractive to examine the scope of this method for the synthesis of functionalized sterically shielded allenes which should exhibit an enhanced chemical reactivity compared to the non-functionalized sterically shielded allenes mentioned above.

The reaction of the *tert*-butyl-substituted 2-en-4-ynoate **1a** with lithium di-*tert*-butylcyanocuprate under the usual conditions (diethyl ether, −20°C, 1 h[4]) proceeds as expected by 1,6-addition; after protonation with diluted sulfuric acid the di-*tert*-butyl-substituted allene **2a** is isolated in 91% yield. Likewise, 2-en-4-ynone **1b** gives the β-allenic ketone **2b** in 69% yield. In both cases the protonation of the initially formed allenyl enolate[4] takes place regioselectively at C-2 and not at C-4, since the latter position is shielded by the adjacent *tert*-butyl groups.

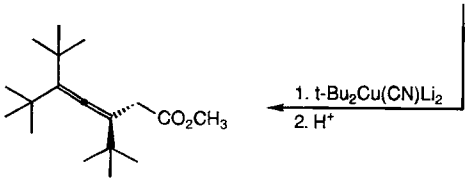


1a (X = OC_2H_5)
1b (X = CH_3)

2



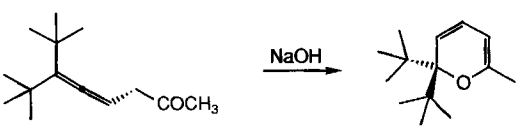
3 **4**



5

In order to synthesize a threefold *tert*-butyl-substituted allene by this method, the enynoate **4** has to be prepared; for this purpose, it has seemed attractive to use a diynoate as Michael acceptor. Whereas the 1,4-addition of organocuprates to acetylenic esters is well-known[5], the reaction of diynoates with cuprates (which could occur by 1,4- or 1,6-addition) has not been examined yet. The reaction of diynoate **3** with $tBu_2Cu(CN)Li_2$ in diethyl ether at −80°C proceeds exclusively by 1,4-addition to give the desired enynoate **4** in 68% yield; the configuration of the double bond of **4** is established to be *Z*[5] by an NOE experiment (see Experimental Section). Not surprisingly, the 1,6-addition of lithium di-*tert*-butylcyanocuprate to this sterically shielded enynoate proceeds sluggishly; nevertheless, the threefold *tert*-butyl-substituted allene **5** is obtained in 36% yield. Thus, the combination of 1,4- and 1,6-addition enhances the flexibility of this allene synthesis since two substituents can be incorporated into the allene by organocuprate addition reactions.

These sterically shielded β-allenic carbonyl compounds show a reactivity strongly different from related unhindered allenes. It is well-known that the latter are readily isomerized to the thermodynamically more stable conjugated 2,4-dienoates or 2,4-dienones[4,6]; in contrast to this, treatment of ester **2a** with aqueous sodium hydroxide does not cause double bond isomerization, but simple hydrolysis yielding the corresponding β-allenic acid. This behavior is caused by steric hindrance of the protonation at C-4 by the *tert*-butyl groups attached to C-5. Likewise, ketone **2b** does not react by double bond isomerization; rather, treatment with aqueous sodium hydroxide induces cyclization to give the 2*H*-pyran **6** in 45% yield. This cyclization occurs formally by enolization of **2b** and intramolecular attack of the enolate oxygen atom at C-5. Further work is in progress in order to examine the chemical reactivity of these sterically shielded allenes.



2b **6**

  0009–2940/91/1111–2633 $ 3.50+.25/0

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Experimental

IR: Perkin-Elmer IR spectrometer 197. – ^1H, ^{13}C NMR: Bruker WM-300 with $CDCl_3$ as solvent and internal standard (δ = 7.27 [^1H NMR], 77.05 [^{13}C NMR]). Abbreviations for the DEPT spectra: + = CH_3, CH; – = CH_2; x = C(quart.). – MS: Varian MAT 311 A.

All reactions were carried out in thoroughly dried glassware under nitrogen. Diethyl ether and THF were distilled from $LiAlH_4$ and potassium/benzophenone, respectively, prior to use. All other reagents were used without further purification.

Ethyl 5-(1,1-Dimethylethyl)-6,6-dimethyl-3,4-heptadienoate (**2a**): To a suspension of 0.31 g (3.5 mmol) of copper(I) cyanide in 10 ml of diethyl ether was added dropwise at –30°C 4.1 ml (7.0 mmol) of *t*BuLi (1.7 M solution in pentane). The mixture was stirred at –30°C for 30 min and treated with a solution of 0.45 g (2.5 mmol) of ethyl 6,6-dimethyl-2-hepten-4-ynoate (**1a**[7]) in 10 ml of diethyl ether. After stirring at –20°C for 1 h, the mixture was poured into vigorously stirred 2 N H_2SO_4 (10 ml), and the copper salts and excess of acid were removed by filtration through Celite. The filtrate was dried with $MgSO_4$ and the solvent removed in vacuo. The obtained crude product was purified by kugelrohr distillation (70–80°C/0.001 Torr); yield 0.54 g of **2a** (91%, colorless liquid.). – IR: $\tilde{\nu}$ = 1940 (w, C=C=C), 1735 cm^{-1} (s, C=O). – ^1H NMR: δ = 1.16 [s, 18H, $C(CH_3)_3$], 1.22 (t, 3H, J = 7.1 Hz, $CO_2CH_2CH_3$), 2.94 (d, 2H, J = 7.2 Hz, 2-H), 4.12 (q, 2H, J = 7.1 Hz, CO_2CH_2), 5.12 (t, 1H, J = 7.2 Hz, 3-H). – ^{13}C NMR: δ = 14.2 (+, $CO_2CH_2CH_3$), 32.1 [+, $C(CH_3)_3$], 3.48 [x, $C(CH_3)_3$], 35.7 (–, C-2), 60.4 (–, CO_2CH_2), 84.6 (+, C-3), 122.6 (x, C-5), 171.9 (x, C-1), 203.5 (x, C-4). – MS: m/z (%) = 238 (5) [M^+], 57 (100).

$C_{15}H_{26}O_2$ (238.4) Calcd. C 75.58 H 10.99
Found C 75.35 H 11.31

6-(1,1-Dimethylethyl)-7,7-dimethyl-4,5-octadien-2-one (**2b**): From 0.36 g (4.0 mmol) of copper(I) cyanide, 4.7 ml (8.0 mmol) of *t*BuLi (1.7 M solution in pentane), and 0.38 g (2.5 mmol) of 7,7-dimethyl-3-octen-5-yn-2-one (**1b**[8]) as described for the preparation of **2a**. Purification of the crude product by kugelrohr distillation (60–70°C/0.1 Torr) yielded 0.36 g of **2b** (69%, colorless liquid). – IR: $\tilde{\nu}$ = 1940 (w, C=C=C), 1715 cm^{-1} (s, C=O). – ^1H NMR: δ = 1.15 [s, 18H, $C(CH_3)_3$], 2.16 (s, 3H, 1–H), 3.03 (d, 2H, J = 7.3 Hz, 3-H), 5.13 (t, 1H, J = 7.3 Hz, 4-H). – ^{13}C NMR: δ = 29.5 (+, C-1), 32.1 [+, $C(CH_3)_3$], 34.9 [x, $C(CH_3)_3$], 44.8 (–, C-3), 84.5 (+, C-4), 122.4 (x, C-6), 203.7 (x, C-5), 206.8 (x, C-2). – MS: m/z (%) = 208 (7) [M^+], 43 (100).

$C_{14}H_{24}O$ (208.3) Calcd. C 80.71 H 11.61
Found C 78.87 H 11.49

Methyl 6,6-Dimethyl-2,4-heptadiynoate (**3**)[9]: To a solution of 8.22 g (0.1 mol) of 3,3-dimethyl-1-butyne in 25 ml of methanol was added a solution of 1.0 g of copper(I) chloride and 1.0 g of hydroxylammonium chloride in 20 ml of 70% aqueous ethylamine. To this mixture was added with stirring a solution of 14.90 g (0.1 mol) of bromopropynoic acid[10] in 15 ml of methanol; during the addition the temp. was kept below 30°C by occasional cooling. The mixture was stirred at room temp. for 1 h, diluted with 300 ml of water, acidified with 2 N H_2SO_4, and extracted with diethyl ether. The combined extracts were dried with $MgSO_4$, and the solvent was removed in vacuo. The brown oil thus obtained was dissolved in 100 ml of methanol; after addition of 6 ml of conc. H_2SO_4, the mixture was allowed to stand at room temp. for 10 d. The reaction was quenched by pouring the mixture into ice/water; neutralization with saturated aqueous $NaHCO_3$ solution was followed by extraction with pentane. The combined extracts were dried with $MgSO_4$, and the solvent was removed in vacuo. The crude product was purified by kugelrohr distillation (50–60°C/0.5 Torr); yield 2.90 g of **3** (18%, colorless liquid, that turns dark rapidly). – IR: $\tilde{\nu}$ = 2240 (s, C≡C), 1710 cm^{-1} (s, C=O). – ^1H NMR: δ = 1.26 [s, 9H, $C(CH_3)_3$], 3.76 (s, 3H, CO_2CH_3). – ^{13}C NMR: δ = 28.3 (x, C-6), 30.0 [+, $C(CH_3)_3$], 52.8 (+, CO_2CH_3), 62.4 (x), 66.4 (x), 71.9 (x, C-2/C-3/C-4), 95.0 (x, C-5), 153.4 (x, C-1). – MS: m/z (%) = 164 (36) [M^+], 133 (100).

$C_{10}H_{12}O_2$ (164.2) Calcd. C 73.15 H 7.37
Found C 71.69 H 7.41

Methyl (Z)-3-(1,1-Dimethylethyl)-6,6-dimethyl-2-hepten-4-ynoate (**4**): As described for the preparation of **2a**, a solution of $tBu_2Cu(CN)Li_2$ was prepared from 0.63 g (7.0 mmol) of copper(I) cyanide in 20 ml of diethyl ether and 8.2 ml (14.0 mmol) of *t*BuLi (1.7 M solution in pentane). This solution was treated at –80°C with a solution of 0.82 g (5.0 mmol) of **3** in 20 ml of diethyl ether. The mixture was stirred at –80°C for 1 h; after quenching the reaction with 5 ml of saturated aqueous NH_4Cl solution, the mixture was warmed up to room temp. and filtered through Celite. Removal of the solvent in vacuo and column chromatography (SiO_2, diethyl ether/hexane 1:20) furnished 0.76 g of **4** (68%, bright yellow liquid). – IR: $\tilde{\nu}$ = 2220 (m, C≡C), 1700 cm^{-1} (s, C=O). – ^1H NMR: δ = 1.15 [s, 9H, 3-$C(CH_3)_3$], 1.30 [s, 9H, 5-$C(CH_3)_3$], 3.70 (s, 3H, CO_2CH_3), 5.94 (s, 1H, 2-H). – NOE experiment: Irradiation at δ = 1.15 [3-$C(CH_3)_3$] gave an intensity enhancement of the resonance at δ = 5.94 (2-H). – ^{13}C NMR: δ = 28.5 (x, C-6), 29.0 [+, $C(CH_3)_3$], 30.6 [+, $C(CH_3)_3$], 37.7 [x, 3-$C(CH_3)_3$], 51.0 (+, CO_2CH_3), 76.5 (x, C-4), 111.8 (x, C-5) 119.3 (+, C-2), 149.3 (x, C-3), 166.4 (x, C-1). – MS: m/z (%) = 221 (2) [M^+ – 1], 155 (100).

$C_{14}H_{22}O_2$ (222.3) Calcd. C 75.63 H 9.97
Found C 75.90 H 10.02

Methyl 3,5-Bis(1,1-dimethylethyl)-6,6-dimethyl-3,4-heptadienoate (**5**): From 0.27 g (3.0 mmol) of copper(I) cyanide, 3.5 ml (6.0 mmol) of *t*BuLi (1.7 M solution in pentane), and 0.31 g (1.4 mmol) of **4**; procedure as described for the preparation of **2a**. Purification of the crude product by column chromatography (SiO_2, diethyl ether/hexane 1:20) gave 0.14 g of **5** (36%, bright yellow liquid). – IR: $\tilde{\nu}$ = 1935 (w, C=C=C), 1740 cm^{-1} (s, C=O). – ^1H NMR: δ = 1.02 [s, 9H, 3-$C(CH_3)_3$], 1.13 [s, 18H, 5-$C(CH_3)_3$], 2.94 (s, 2H, 2-H), 3.60 (s, 3H, CO_2CH_3). – ^{13}C NMR: δ = 29.0 [+, 3-$C(CH_3)_3$], 32.1 [+, 5-$C(CH_3)_3$], 34.1 [x, 3-$C(CH_3)_3$], 35.3 (–, C-2), 35.5 [x, 5-$C(CH_3)_3$], 51.2 (+, CO_2CH_3), 106.1 (x, C-3), 123.2 (x, C-5), 172.4 (x, C-1), 198.3 (x, C-4). – MS: m/z (%) = 280 (5) [M^+], 57 (100).

$C_{18}H_{32}O_2$ (280.5) Calcd. C 77.09 H 11.50
Found C 77.26 H 11.49

2,2-Bis-(1,1-dimethylethyl)-6-methyl-2H-pyran (**6**): A solution of 208 mg (1.0 mmol) of **2b** in 5 ml of methanol was treated with 3 drops of 1% aqueous sodium hydroxide and stirred at room temp. for 3 d. After dilution with water, the mixture was extracted with diethyl ether; the combined extracts were dried with $MgSO_4$, and the solvent was removed in vacuo. The obtained crude product was purified by column chromatography (Al_2O_3 B II–III, diethyl ether/hexane 1:20); yield 94 mg (45%, colorless liquid). – IR: $\tilde{\nu}$ = 1660 (s), 1600 cm^{-1} (s, C=C). – ^1H NMR: δ = 1.06 [s, 18H, $C(CH_3)_3$], 1.74 (s, 3H, 6-CH_3), 4.60 (d, 1H, J = 5.8 Hz, 5-H), 5.21 (d, 1H, J = 10.6 Hz, 3-H), 5.77 (dd, 1H, J = 5.8/10.6 Hz, 4-H). – ^{13}C NMR: δ = 19.6 (+, 6-CH_3), 27.6 [+, $C(CH_3)_3$], 43.3 [x, $C(CH_3)_3$], 89.5 (x,

C-2), 93.0 (+, C-5), 116.0 (+), 120.3 (+, C-3/C-4), 153.9 (x, C-6). – MS: *m/z* (%) = 209 (2) [M^+ + 1], 57 (100).

$C_{14}H_{24}O$ (208.3) Calcd. C 80.71 H 11.61
Found C 78.53 H 11.28

CAS Registry Numbers

1a: 60739-66-4 / **1b**: 60739-71-1 / **2a**: 135774-44-6 / **2b**: 135774-45-7 / **3**: 135774-46-8 / **4**: 135774-47-9 / **5**: 135774-48-0 / **6**: 135774-49-1 / 3,3-dimethyl-1-butyne: 917-92-0 / bromopropynoic acid: 16900-53-1

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