Selective Non-catalytic Cyclopropanation of Methyl (*E*)-Pent-3-en-1-yn-3-ylcarboxylates with Diazomethane

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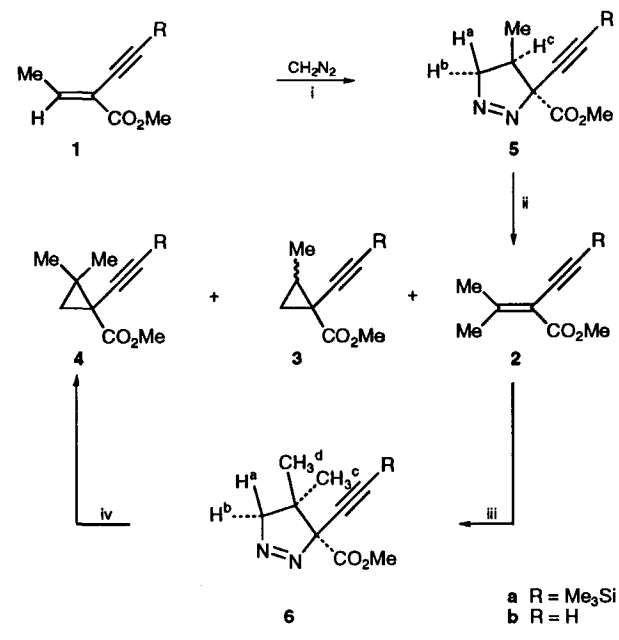
1,3-Dipolar cycloaddition of diazomethane to methyl (*E*)-pent-3-en-1-yn-3-ylcarboxylates proceeds selectively with participation of only the double bond, resulting in unstable methyl 3-alkynylpyrazolinylcarboxylates, thermolysis of which leads to methyl 1-alkynylcyclopropanecarboxylates and 4-methylpent-3-en-1-yn-3-ylcarboxylates.

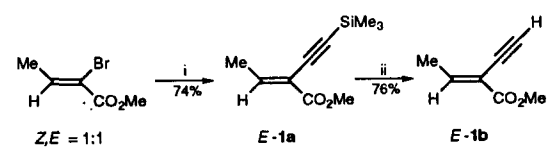
1,3-Dipolar cycloaddition of diazomethane to enyne hydrocarbons proceeds non-selectively and leads to mixtures of alkenylpyrazoles and alkynylpyrazolines, dediazatation of which, on heating and irradiation, results in alkenylcyclopropenes and alkynylcyclopropanes, respectively.[1] At the same time, methyl 5-methylhex-4-en-2-ynoate, the triple bond of which is activated by the methoxycarbonyl group, reacts with diazopropane with participation of only the triple bond, forming the corresponding methyl alkenylpyrazolylcarboxylates. These compounds were used as precursors for the synthesis of the corresponding alkenylcyclopropene-3-carboxylates.[2] We have therefore examined the possibility of the synthesis of 1-ethynylcyclopropanecarboxylates by 1,3-cycloaddition of diazoalkanes to enynes with the double bond activated by the methoxycarbonyl group.

We have found that methyl (*E*)-1-trimethylsilylpent-3-en-1-yn-3-ylcarboxylate† **1a** reacts with ~1 equivalent of CH_2N_2 at 20 °C with participation of only the double bond, furnishing methyl 1-trimethylsilyl-4-methylpent-3-en-1-yn-3-ylcarboxylate **2a** along with small quantities of methyl 1-trimethylsilylethynyl-2-methylcyclopropanecarboxylate **3a**, as a mixture of (*E*)- and (*Z*)-isomers (ratio 9:1), and methyl 1-trimethylsilylethynyl-2,2-dimethylcyclopropanecarboxylate **4a** (product ratio 81:12:7).‡ The reaction was monitored in the detector of a ^1H NMR spectrometer at −20 °C and it was shown that *trans*-methyl-1-trimethylsilylethynyl-4-methyl-1-pyrazolinyl-3-carboxylate **5a**§ is the initial–and the only–product under these conditions. At 5–20 °C **5a** is decomposed to give the observed mixture of **2a–4a**.

We consider the formation of **4a** to be the result of 1,3-dipolar cycloaddition of excess CH_2N_2 to **2a**. This was demonstrated by treatment of a **2a–4a** mixture with a further equivalent of CH_2N_2 at 20 °C, leading to the appearance of 3-trimethylsilylethynyl-4,4-dimethyl-1-pyrazolinyl-3-carboxylate **6a**¶ in the reaction mixture and an increase in the proportion of **4a**. Finally, only **4a** and **3a** in 9:1 ratio with 95% total yield were detected in the reaction mixture.



Scheme 1 *Reagents and conditions:* i, 1 equiv. CH_2N_2, CH_2Cl_2, −20 °C; ii, CH_2Cl_2, −20 °C → 20 °C; iii, 1 equiv. CH_2N_2, CH_2Cl_2, 20 °C; iv, CH_2Cl_2, 20 °C



Scheme 2 *Reagents and conditions:* i, 5% mol. $PdCl_2(PPh_3)_2$, 5% mol. CuCl, 3 equiv. NEt_3, 1.3 equiv. $Me_3SiC{\equiv}CH$, THF, 25 °C; ii, 1.5 equiv. $KF{\cdot}2H_2O$, $DMF–H_2O$, 25 °C.

† The synthesis of **1a** was carried out according to ref. 3 by $PdCl_2(PPh_3)_2$-promoted cross-coupling of methyl (*E,Z*)-2-bromobut-2-enoate with $HC{\equiv}CSiMe_3$, Scheme 2.

‡ *Spectroscopic data* for **2a**: IR ν/cm^{-1} 2144 (C≡C), 1736 (C=O), 1613 (C=C); ^1H NMR (300 MHz, $CDCl_3$) δ 3.65 (s, 3H, OMe), 2.11 (s, 3H, *cis*-Me), 2.03 (s, 3H, *trans*-Me), 0.11 (s, 9H, $SiMe_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.38 (C=O), 161.05 (Me_2C), 112.38 (=C<), 100.87 (−C≡), 99.01 (≡CSi), 51.64 (OMe), 25.70 (*trans*-Me), 22.19 (*cis*-Me), −0.18 ($SiMe_3$).

Spectroscopic data for **3a**: IR ν/cm^{-1} 2168 (C≡C), 1751 and 1743 (C=O); MS (*trans*-isomer) *m/z* 210 (M^+), 195 (M^+ − Me), 179 (M^+ − OMe), 151 (M^+ − CO_2Me), 106, 89, 73, 59.

Spectroscopic data for **4a**: IR ν/cm^{-1} 2168 (C≡C), 1743 (C=O); ^1H NMR (300 MHz, $CDCl_3$, *J*/Hz) δ 3.62 (s, 3H, OMe), 1.56 and 0.94 (2 d, 2H, CH_2, ^3J = 4.4), 1.27 and 1.09 (2 s, 6H, Me), 0.07 (s, 9H, $SiMe_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.21 (C=O), 105.03 (−C≡), 85.55 (≡CSi), 52.70 (OMe), 31.09 (CH_2), 30.94 and 28.56 (2 C), 24.05 and 19.87 (2Me), 0.38 ($SiMe_3$).

§ *Spectroscopic data* for **5a**: ^1H NMR (−20 °C, 300 MHz, CD_2Cl_2, *J*/Hz) δ 4.79 (d.d, 1H, H^b, J_{ab} = 17.4, J_{bd} = 7.8), 4.21 (d.d., 1H, H^a, J_{ad} = 6.6), 3.78 (s, 3H, OMe), 2.47 (m, 1H, H^d, J_{dc} = 7.1), 1.05 (d, 3H, H^c), 0.16 (s, 9H, $SiMe_3$); ^{13}C NMR (−20 °C, 75 MHz, CD_2Cl_2) δ 167.52 (C=O), 97.58 (≡CSi), 94.89 (−C≡), 94.62 (C), 84.95 (CH_2), 53.80 (OMe), 34.79 (CH), 14.80 (Me), −0.62 ($SiMe_3$).

¶ *Spectroscopic data* for **6a**: ^1H NMR (300 MHz, CD_2Cl_2, *J*/Hz) δ 4.39 (d, 1H, H^a, J_{ab} = 16.8), 4.26 (d, 1H, H^b), 3.78 (s, 3H, OMe), 1.19 (s, 3H, H^c), 0.89 (s, 3H, H^d), 0.18 (s, 9H, $SiMe_3$). The configurations of **5a** and **6a** were established by NOE observation.

The same reaction of (*E*)-pent-3-en-1-yn-3-ylcarboxylate **1b*** with 2 equiv. of CH_2N_2 led to a mixture of **2b**,‡ **3b** and **4b** in the ratio 73:24:3 (according to GC–MS analysis) in 90% total yield. Attempts to convert **2b** further by treatment of the reaction mixture with an additional quantity of CH_2N_2 failed, and an intractible tar mixture formed. At the same time, the proportion of **4b** in the reaction mixture did not increase.

This new transformation of 1-trimethylsilylpent-3-en-1-yn-3-ylcarboxylate into 1-trimethylsilylethynyl-2,2-dimethylcyclopropanecarboxylate opens the way to a direct synthesis of 2-substituted 1-ethynylcyclopropanecarboxylates from the corresponding enynylcarboxylates and diazoalkanes.

References

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* The synthesis of **1b** was carried out by **1a** desilylation with KF/DMF–H_2O.

For **1b**: b.p. 65–67 °C (17 Torr), n_D^{20} 1.4799. IR ν/cm^{-1} 3282 (≡CH), 2106 (C≡C), 1724 (C=O), 1622 (C=C); ^{1}H NMR (90 MHz, $CDCl_3$, *J*/Hz) δ 7.40 (q.d., 1H, =CH, ^3J = 7.3, ^5J = 0.9), 3.81 (s, 3H, OMe), 3.36 (br. s, 1H, ≡CH), 2.08 (d, 3H, Me, ^6J = 0.8); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 164.65 (C=O), 150.40 (=CH), 117.19 (=C<), 84.47 (≡CH), 76.83 (–C≡), 52.18 (OMe), 16.42 (Me).

‡ *Spectroscopic data* for **2b**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.74 (s, 3H, OMe), 3.22 (br. s, 1H, ≡CH), 2.22 and 2.13 (2 s, 6H, 2Me).