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ELEMENT-SUBSTITUTED PROPYNALS IN THE BIGINELLI REACTION

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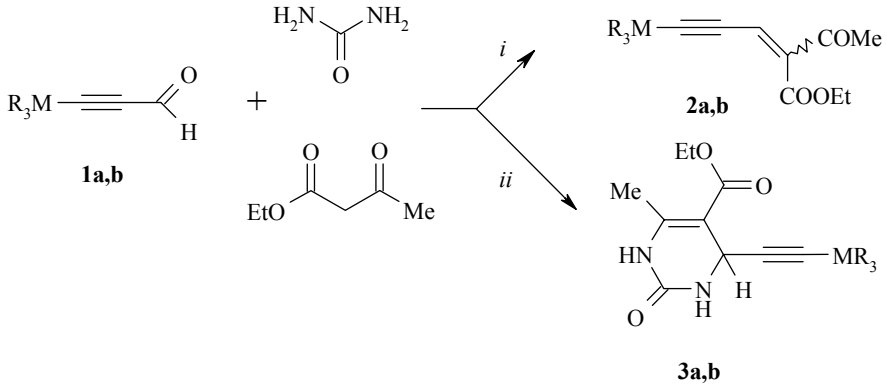
The Biginelli reaction is actively studied at this time with the aim of preparing 3,4-dihydropyrimidin-2-ones which are widely used in pharmacology [1-3]. This multicomponent reaction has been applied to aromatic, unsaturated, and aliphatic aldehydes [4-6] but not realized until now for the case of propynals. It is known that efficient catalysts in the Biginelli reaction can be both Brönsted [7, 8] or Lewis acids, including $LiClO_4$ [9].

We have shown that the single reaction products of the 3-trimethylsilyl-2-propyn-1-al (**1a**) and 3-triethylgermyl-2-propyn-1-al (**1b)** with acetoacetic ester and urea in the presence of $LiClO_4$ (20 mol %) are the Knoevenagel *Z*,*E*-enyne adducts **2a** and **2b** in 95 and 79% yields respectively. The expected dihydropyrimidinones are not formed under these conditions. Enyne **2a** has been obtained before by treating the aldehyde **1a** with acetoacetic ester in the presence of piperidine as catalyst [10].



i MeCN, LiClO4 (20 mol %), 80°C, 10 h; *ii* MeOH, HCl (5 mol %), 60°C, 25 h;
1–3 a $R_3M = Me_3Si$, **b** $R_3M = Et_3Ge$

The previously unknown ethyl 6-methyl-2-oxo-4-(2-trimethylsilylethynyl)-1,2,3,4-tetrahydropyrimidine-5-carboxylate **3a** and its germyl analog **3b** were prepared in high yield (78-81%) by refluxing the propynals **1a,b** with urea and acetoacetic ester in methanol medium for 25 h in the presence of 5 mol % of hydrochloric acid.

* Dedicated to Academician M. G. Voronkov, Russian Academy of Sciences in his 85th year.

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The structure of compounds **2a,b** and **3a,b** has been confirmed from IR, ^{1}H NMR, and ^{13}C NMR spectroscopic data and the composition from elemental analysis.

Hence in the example of the element containing propynals **1a,b** we have shown for the first time the possibility of using acetylene aldehydes in the Biginelli reaction and the marked effect of the catalyst on its realization.

IR spectra were recorded on a Specord IR-75 spectrometer. ^{1}H NMR and ^{13}C NMR spectra were taken on a Bruker DPX-400 instrument (400 and 100 MHz respectively) using $CDCl_3$ and with HMDS as internal standard.

Ethyl *Z*,*E*-2-acetyl-5-trimethylsilyl-2-penten-4-ynoate (2a). A mixture of the aldehyde **1a** (0.4 g, 3 mmole), urea (0.36 g, 6 mmol), acetoacetic ester (0.39 g, 3 mmol), $LiClO_4$ (20 mol %, 0.07 g), and acetonitrile (8 ml) was stirred for 10 h at 80°C. After removal of solvent at reduced pressure, water (5 ml) and ether (10 ml) were added. The organic layer was separated and the aqueous fraction was saturated with NaCl and extracted with ether. The combined organic phase was washed with water and dried over $MgSO_4$. Removal of ether gave the product as a yellowish oil (0.68 g, 95%). IR spectrum, ν, cm^{-1}: 2170 (C≡C), 1720, 1215 (COO), 1670 (C=O), 1595 (C=C), 1245, 845 ($SiCH_3$). ^{1}H NMR spectrum, *Z*-isomer, δ, ppm (*J*, Hz): 0.17 (9H, s, Si(C$\underline{H}_3$)$_3$); 1.33 (3H, t, $^3J_{H,H}$ = 7.0, C$\underline{H}_3$CH$_2$O); 2.31 (3H, s, COCH$_3$); 4.32 (2H, q, $^3J_{H,H}$ = 7.0, OC$\underline{H}_2$CH$_3$); 6.71 (1H, s, $^3J_{COOEt,H}$ = 7.3, CH). ^{13}C NMR spectrum, *Z*-isomer, δ, ppm: -0.55 (Si(CH$_3$)$_3$); 14.16 (C$\underline{H}_3$CH$_2$O); 30.02 (CO$\underline{C}$H$_3$); 61.21 (CH$_3$$\underline{C}H_2$O), 99.62 (C$\underline{C}$≡C); 111.95 (C≡$\underline{C}$Si); 121.77 ($\underline{C}$H=C); 144.17 (CH=$\underline{C}$); 164.27 (COO); 197.21 (C=O). ^{1}H NMR spectrum, *E*-isomer, δ, ppm (*J*, Hz): 0.17 (9H, s Si(C$\underline{H}_3$)$_3$); 1.25 (3H, t, $^3J_{H,H}$ = 7.0, C$\underline{H}_3$CH$_2$O); 2.42 (3H, s COCH$_3$); 4.21 (2H, q, $^3J_{H,H}$ = 7.0, OC$\underline{H}_2$CH$_3$); 6.72 (1H, s, $^3J_{COOEt,H}$ = 11,4, CH). ^{13}C NMR spectrum, *E*-isomer, δ, ppm: -0.49 (Si(CH$_3$)$_3$); 14.16 (C$\underline{H}_3$CH$_2$O); 27.39 (CO$\underline{C}$H$_3$); 61.42 (CH$_3$$\underline{C}H_2$O); 99.96 (C$\underline{C}$≡C); 112.95 (C≡$\underline{C}$Si); 123.35 ($\underline{C}$H=C). 142.46 (CH=$\underline{C}$); 164.83 (COO); 192.72 (C=O). Ratio of isomers *Z*: *E* = 40: 60. Found, %: C 60.39; H 7.49; Si 11.53. $C_{12}H_{18}O_3Si$. Calculated, %: C 60.45; H 7.61; Si 11.78.

Ethyl *Z*,*E*-2-acetyl-5-triethylgermyl-2-penten-4-ynoate (2b) was obtained similarly as a yellow oil in 79% yield. IR spectrum, ν, cm^{-1}: 2165 (C≡C), 1720, 1215 (COO), 1665 (C=O), 1595 (C=C). ^{1}H NMR spectrum, *Z*-isomer, δ, ppm (*J*, Hz): 0.91 (6H, q, $^3J_{H,H}$ = 7.0, GeC$\underline{H}_2$CH$_3$); 1.10 (9H, t, $^3J_{H,H}$ = 7.0, GeCH$_2$C$\underline{H}_3$); 1.29 (3H, t, $^3J_{H,H}$ = 7.0, C$\underline{H}_3$CH$_2$O); 2.33 (3H, s, COCH$_3$); 4.24 (2H, q, $^3J_{H,H}$ = 7.0, OC$\underline{H}_2$CH$_3$); 6.76 (1H, s, $^3J_{COOEt,H}$ = 7.0, CH). ^{13}C NMR spectrum, *Z*-isomer, δ, ppm: 5.83 (Ge$\underline{C}$H$_2$CH$_3$); 9.07 (GeCH$_2$$\underline{C}H_3$); 14.25 (C$\underline{H}_3CH_2$O); 30.41 (CO$\underline{C}H_3$); 61.57 (CH$_3$$\underline{C}H_2$O); 100.77 (C$\underline{C}$≡C); 112.34 (C≡$\underline{C}$Ge); 122.68 ($\underline{C}$H=C); 143.52 (CH=$\underline{C}$); 163.83 (COO); 198.43 (C=O). ^{1}H NMR spectrum, *E*-isomer, δ, ppm (*J*, Hz): 0.91 (6H, q, $^3J_{H,H}$ = 7.0, GeC$\underline{H}_2$CH$_3$); 1.10 (9H, t, $^3J_{H,H}$ = 7.0, GeCH$_2$C$\underline{H}_3$); 1.34 (3H, t, $^3J_{H,H}$ = 7.0, C$\underline{H}_3$CH$_2$O); 2.46 (3H, s, COCH$_3$); 4.30 (2H, q, $^3J_{H,H}$ = 7.0, OC$\underline{H}_2$CH$_3$); 6.78 (1H, s, $^3J_{COOEt,H}$ = 11.4, CH). ^{13}C NMR spectrum, *E*-isomer, δ, ppm: 5.83 (Ge$\underline{C}$H$_2$CH$_3$); 9.07 (GeCH$_2$$\underline{C}H_3$); 14.25 (C$\underline{H}_3CH_2$O); 27.38 (CO$\underline{C}H_3$); 61.48 (CH$_3$$\underline{C}H_2$O); 100.97 (C$\underline{C}$≡C); 113.54 (C≡$\underline{C}$Ge); 124.04 ($\underline{C}$H=C); 142.36 (CH=$\underline{C}$); 165.46 (COO); 193.46 (C=O). Ratio of isomers *Z*: *E* = 45:55. Found, %: C 55.18; H 7.26; Ge 22.23. $C_{15}H_{24}GeO_3$. Calculated, %: C 55.44; H 7.44; Ge 22.34.

Ethyl 6-methyl-2-oxo-4-(2-trimethylsilylethynyl)-1,2,3,4-tetrahydropyrimidine-5-carboxylate (3a). A mixture of aldehyde **1a** (2.61 g, 21 mmol), urea (2.48 g, 43 mmol), acetoacetic ester (2.69 g, 21 mmol), conc. HCl (0.11 g, 5 mol %), and methanol (10 ml) was stirred for 25 h at 60°C. Work up of the reaction mixture as described in the previous experiment and recrystallization from ethanol gave **3a** (4.56 g, 81%) as colorless crystals with mp 210-212°C. IR spectrum, ν, cm^{-1}: 3210, 3095 (NH), 2155 (C≡C), 1695, 1200 (COO), 1640 (C=O), 1630 (C=C), 1270 (SiC). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.28 (9H, s, Si(CH$_3$)$_3$); 1.28 (3H, t, $^3J_{H,H}$ = 7.1, C$\underline{H}_3$CH$_2$O); 2.31 (3H, s, C=CCH$_3$); 4.20 (2H, q, $^3J_{H,H}$ = 7.1, OC$\underline{H}_2$CH$_3$); 5.14 (1H, s, CH); 6.07 (1H, br. s, NH), 8.75 (1H, br. s, NH). ^{13}C NMR spectrum, δ, ppm: 0.02 (Si(CH$_3$)$_3$); 14.48 (C$\underline{H}_3$CH$_2$O); 18.66 (C=C$\underline{C}$H$_3$); 43.85 (CH); 50.33 (CH$_3$$\underline{C}H_2$O); 87.61 (C≡$\underline{C}$Si); 98.88 (C=$\underline{C}$COO); 104.31 (C$\underline{C}$≡C); 147.43 (CH$_3$$\underline{C}$=C); 153.82 (C=O); 165.11 (COO). Found, %: C 56.38; H 6.98; N 9.84; Si 9.82. $C_{13}H_{20}N_2O_3Si$. Calculated, %: C 56.69; H 7.18; N 9.99; Si 10.02.

Ethyl 6-methyl-2-oxo-4-(2-triethylgermylethynyl)-1,2,3,4-tetrahydropyrimidine-5-carboxylate (3b) was prepared similarly as colorless crystals (78%) with mp 221-222°C. IR spectrum, ν, cm^{-1}: 3200, 3070 (NH), 2140 (C≡C), 1700, 1205 (COO), 1640 (C=O), 1630 (C=C). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.82 (6H, q, $^3J_{H,H}$ = 7.8, $GeC\underline{H}_2CH_3$); 1.04 (9H, t, $^3J_{H,H}$ = 7.8, $GeCH_2C\underline{H}_3$); 1.28 (3H, t, $^3J_{H,H}$ = 7.1, $C\underline{H}_3CH_2O$); 2.15 (3H, s, $C{=}CCH_3$); 4.20 (2H, q, $^3J_{H,H}$ = 7.1, $OC\underline{H}_2CH_3$); 5.12 (1H, s, CH); 5.71 (1H, br s, NH); 8.62 (1H, br. s, NH). ^{13}C NMR spectrum, δ, ppm: 5.92 ($Ge\underline{C}H_2CH_3$); 9.18 ($GeCH_2\underline{C}H_3$); 14.60 ($\underline{C}H_3CH_2O$); 18.54 ($C{=}C\underline{C}H_3$); 43.89 (CH); 60.19 ($CH_3\underline{C}H_2O$); 85.24 (C≡CSi); 99.44 (C==CCOO); 105.50 (C$\underline{C}$≡C); 147.37 ($CH_3\underline{C}$=C); 154.05 (C=O). 165.03 (COO). Found, %: C 52.18; H 7.08; N 7.55, Ge 19.61. $C_{16}H_{26}GeN_2O_3$. Calculated, %: C 52.36; H 7.14; N 7.63; Ge 19.78.

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