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Vinylation of trialkylamines with acyl- and cyanoacetylenes *via* C–N bond cleavage in the presence of water

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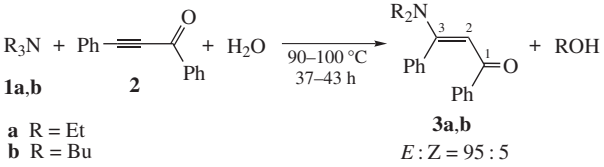
Trialkylamines react with acyl- and cyanoacetylenes in the presence of water (90–100 °C, 37–43 h) to give functionalized *N*,*N*-dialkylvinylamines, the products of N-dealkylation of the starting amines, in 22–44% yields.

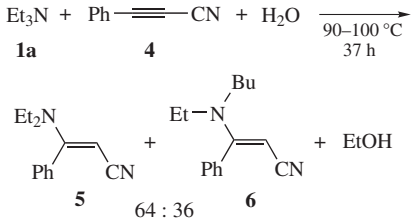
N-Vinylamines are commonly synthesized by base-,[1] transition metal-catalyzed[2] or non-catalyzed[3] hydroamination of alkynes with secondary amines. Vinylation of tertiary amines *via* the C–N bond cleavage by alkynes is less studied. The known cases are limited by the addition of tertiary amines to acetylenecarboxylates. Perhaps, the earliest example of such a vinylation is the reaction of triethylamine with dimethyl acetylenedicarboxylate (DMAD) in the presence of hydrogen bromide (reflux in CH_2Cl_2, 4 h) to yield a mixture of diethylaminomaleate- and fumarate.[4] Triethylamine with ethyl propiolate gave the corresponding betaine (H_2O/CH_2Cl_2, room temperature, 1 h), which upon pyrolysis (175 °C) decomposed to diethylaminoacrylate (17% yield).[5] In the presence of metal (La, Ce, Sb, Sn) chlorides, trialkylamines were vinylated (dioxane, 80 °C, 5 h) with DMAD or diethyl acetylenedicarboxylate (DEAD) to dialkylaminomaleates in 15–90% yields, in the presence of water the yields being appreciably dropped.[6] The C–N bond cleavage in cyclic tertiary amines under the action of DMAD, DEAD and methyl propiolate was elegantly introduced into the synthesis of heterocyclic compounds by Varlamov's group.[7] The Tröger's bases as representatives of fused cyclic tertiary amines reacted with acetylene carboxylates in the presence of Lewis acids ($ZnBr_2$, $BF_3{\cdot}Et_2O$) to split the C–N bond and expand the heterocyclic system.[8]

Herein we demonstrate that acetylenecarboxylates are not the only acetylenes which are able to vinylate tertiary amines *via* the C–N bond cleavage. Indeed, when excess trialkylamines **1a**,**b** were heated (90–100 °C, 37–43 h) with 1,3-diphenylprop-2-yn-1-one **2** in the presence of 2 equiv. of water, the corresponding dialkylamino derivatives **3a**,**b** were isolated in up to 44% yield (Scheme 1).† The reaction proved to be stereoselective: mainly *E*-isomers were formed. The content of *Z*-isomers was within 5%.



Scheme 1

In the case of 3-phenylprop-2-ynenitrile **4** and amine **1a**, the crude product consisted of the expected *N*,*N*-diethylamino- and unexpected *N*-butyl-*N*-ethylamino derivatives **5** and **6** both of the *E*-configuration in 44% total yield (Scheme 2).‡



Scheme 2

The reaction route is rationalized as triggered by the vinyl zwitterionic intermediate **A**, the primary adduct of trialkylamine with acetylene, which is quenched with water to deliver the quaternary ammonium hydroxide **B**. The latter decomposes to functionalized *N*,*N*-dialkyl-*N*-vinylamines **3a**,**b** and **5** with elimination of alcohol (Scheme 3).

† *(*E*)-3-Diethylamino-1,3-diphenylprop-2-en-1-one* **3a**. The solution of acetylene **2** (0.103 g, 0.500 mmol) (prepared according to reported procedure[10]) and water (0.018 g, 1.000 mmol) in Et_3N **1a** (2 ml) was stirred at 90–100 °C for 37 h. The reaction was monitored with IR spectroscopy by disappearance of the C≡C absorption band at 2200 cm^{-1}. The solvent was distilled off *in vacuo*, column chromatography [neutral Al_2O_3, chloroform–benzene–ethanol (20 : 4 : 1) as an eluent] afforded vinylamine **3a** (0.061 g, 44%) as a dark-orange oil. The ^1H, ^{13}C NMR (AV-400 Bruker BioSpin) and IR (Bruker Vertex 70) spectra correspond to reported data.[3(b)]

*(*E*)-3-Dibutylamino-1,3-diphenylprop-2-en-1-one* **3b**. Analogously, from acetylene **2** (0.103 g, 0.500 mmol) and water (0.018 g, 1.000 mmol) in Bu_3N **1b** (2 ml) (90–100 °C, 43 h) vinylamine **3b** (0.037 g, 22%) was obtained as a brown oil. IR (microlayer, ν/cm^{-1}): 1664 (C=C, C=O). ^1H NMR (400.13 MHz, $CDCl_3$) δ: 0.87 [m, 6H, 2$(CH_2)_3Me$], 1.27 [m, 4H, 2$(CH_2)_2CH_2$Me], 1.59 (m, 4H, 2CH_2CH_2Et), 3.19 (m, 4H, 2CH_2Pr), 5.92 (s, 1H, H-2), 7.20 (m, 2H, *o*-H_{Ph}), 7.30–7.40 (m, 6H, *m*-H_{Ph}, *m'*-H_{Bz}, *p*-H_{Ph}, *p'*-H_{Bz}), 7.80 (m, 2H, *o'*-H_{Bz}). ^{13}C NMR (100.62 MHz, $CDCl_3$) δ: 14.0 [2$(CH_2)_3Me$], 20.3 [2$(CH_2)_2CH_2$Me], 30.1 (2CH_2CH_2Et), 50.4 (2CH_2Pr), 93.9 (C-2), 127.8 (*o'*-C_{Bz}), 128.1 (*o*-C_{Ph}), 128.4 (*m*-C_{Ph}), 128.6 (*p*-C_{Ph}), 128.8 (*m'*-C_{Bz}), 130.6 (*p'*-C_{Bz}), 137.4 (*i*-C_{Ph}), 142.3 (*i'*-C_{Bz}), 163.8 (C-3), 187.3 (C-1). Found (%): C, 81.95; H, 8.43; N, 4.33. Calc. for $C_{23}H_{29}NO$ (%): C, 82.34; H, 8.71; N, 4.18.

‡ *(*E*)-3-Diethylamino-3-phenylprop-2-enenitrile* **5** *and (*E*)-3-(*N*-butyl-*N*-ethylamino)-3-phenylprop-2-enenitrile* **6**. Similarly, from acetylene **4** (0.064 g, 0.500 mmol) and water (0.018 g, 1.000 mmol) in Et_3N **1a** (2 ml) (90–100 °C, 37 h) vinylamines **5** (0.018 g, 28%) and **6** (0.08 g, 16%) were obtained as a dark-orange oil (**5**:**6** ratio of 64 : 36). Ethanol was detected in the reaction mixture using GLC (Agilent 6890N). The separation was performed on a column HP-5MS (30 m×0.25 mm×0.25 μm) at constant flow rate, helium was used as the carrier gas, temperature of evaporator was 200 °C, the column was heated from 60 to 200 °C at a rate of 10 K min^{-1}. The starting acetylene **4** was recovered (0.027 g, conversion is 58%). IR (microlayer, ν/cm^{-1}): 2194 (C≡N), 1593 (C=C).

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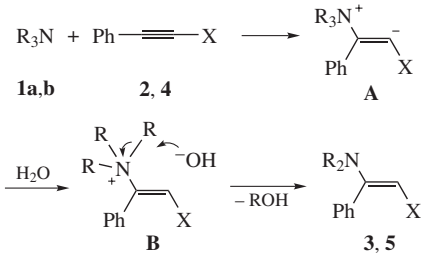
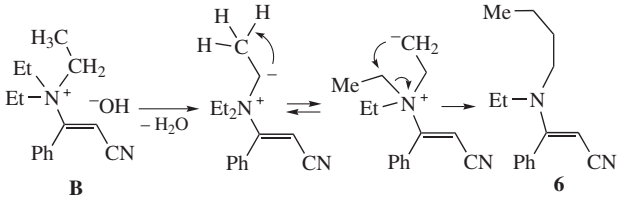


Scheme 3

The abnormal adduct **6** is likely formed *via* the Stevens/Sommelet type rearrangement of intermediate **B**, which includes the α-deprotonation of an ethyl substituent followed by the β-proton transfer and the migration of ethyl cation towards the terminal carbanionic center (Scheme 4).



Scheme 4

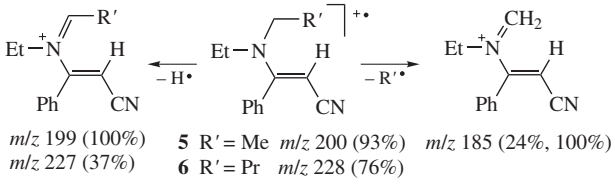
In the reaction with acetylene **2**, the rearranged adducts similar to **6** were formed in trace amounts (^{1}H NMR). The pronounced rearrangement of the ethyl substituents for the reaction with nitrile **4** may be explained by a higher electron-withdrawing power of the cyano group compared to the benzoyl one that facilitates the α-deprotonation in triethylammonium moiety.

The high *E*-stereoselectivity of the vinylation may be due to the attractive interaction between the carbanionic center and positively charged ammonium nitrogen in the primary intermediate **A**.

The structures of compounds **5** and **6** in the mixture unambiguously follows from their ^{1}H and ^{13}C NMR spectra. In the ^{1}H NMR spectra, there are two signals of olefinic protons H-2 (4.02 and 4.03 ppm) and in the ^{13}C NMR spectra, four signals of olefinic carbons (63.9, 64.1, 164.5 and 164.6 ppm). In the 2D NOESY spectrum, signals of olefinic protons correlate with the *N*-CH_2 signals thus indicating the *E*-configuration of the olefin moiety. Moreover, the cross-peaks of the 2D NOESY and 2D COSY spectra allow the signals of *N*-Bu group protons to be assigned (0.85, 1.19, 1.51 and 3.03 ppm, respectively, counting from methyl group towards nitrogen). These signals are not overlapped with the signals of the Et groups (1.09 and 3.12 ppm).

Compound **5**: ^{1}H NMR (400.13 MHz, $CDCl_3$) δ: 1.09 (m, 3H, CH_2*Me*), 3.12 (m, 2H, NC*H*$_2$Me), 4.03 (s, 1H, H-2), 7.29–7.42 (m, 5H, H_{Ar}). ^{13}C NMR (100.62 MHz, $CDCl_3$) δ: 12.7 (CH_2*Me*), 44.4 (*C*H_2Me), 63.9 (C-2), 122.1 (CN), 128.5 (*m*-C_{Ph}), 128.8 (*o*-C_{Ph}), 129.5 (*p*-C_{Ph}), 135.4 (*i*-C_{Ph}), 164.5 (C-1). MS (EI), *m/z* (%): 201 (34) $[M+H]^+$, 200 (93) $[M]^{+\cdot}$, 199 (100) $[M-H]^+$, 185 (24) $[M-Me]^+$, 171 (42) $[M-H-C_2H_4]^+$, 160 (18), 132 (28), 128 (45) $[M-Et_2N]^+$, 116 (18), 105 (15), 104 (49), 103 (18), 102 (17), 101 (26), 91 (16), 89 (9), 77 (56), 68 (63).

Compound **6**: ^{1}H NMR (400.13 MHz, $CDCl_3$) δ: 0.85 [m, 3H, $(CH_2)_3$*Me*], 1.09 (m, 3H, CH_2*Me*), 1.19 [m, 2H, $(CH_2)_2$*C*H_2Me], 1.51 (m, 2H, CH_2*C*H_2Et), 3.03 (m, 2H, *C*H_2Pr), 3.12 (m, 2H, *C*H_2Me), 4.02 (s, 1H, H-2), 7.29–7.42 (m, 5H, H_{Ar}). ^{13}C NMR (100.62 MHz, $CDCl_3$) δ: 11.3 [$(CH_2)_3$*Me*], 13.8 (CH_2*Me*), 20.1 [$(CH_2)_2$*C*H_2Me], 28.7 (CH_2*C*H_2Et), 45.0 (*C*H_2Me), 49.7 (*C*H_2Pr), 64.1 (C-2), 122.1 (CN), 128.4 (*m*-C_{Ph}), 128.7 (*o*-C_{Ph}), 129.5 (*p*-C_{Ph}), 135.4 (*i*-C_{Ph}), 164.6 (C-1). MS (EI), *m/z* (%): 229 (35) $[M+H]^+$, 228 (76) $[M]^{+\cdot}$, 227 (37) $[M-H]^+$, 213 (11) $[M-Me]^+$, 200 (10), 199 (15) $[M-H-C_2H_4]^+$, 188 (36), 185 (100) $[M-C_3H_7]^+$, 172 (12), 171 (24), 169 (14), 168 (41), 160 (32), 158 (12), 157 (26), 146 (16), 132 (97), 128 (88), 117 (18), 116 (19), 105 (13), 104 (78), 103 (21), 102 (16), 101 (32), 91 (36), 77 (58), 68 (20), 53 (16).



m/z 199 (100%)
m/z 227 (37%)

5 R′ = Me *m/z* 200 (93%)
6 R′ = Pr *m/z* 228 (76%)

m/z 185 (24%, 100%)

Scheme 5

In the 2D HSQC spectrum, cross-peaks between proton and carbon signals enable to assign the *N*-Bu carbon signals (11.3, 20.1, 28.7 and 49.7 ppm) and both Et groups (12.7, 13.8, 44.4 and 45 ppm). In the ^{1}H and ^{13}C NMR spectra of compounds **5** and **6**, the signals of the phenyl and cyano groups virtually coincide.

The chromatomass investigation of mixture **5** + **6** clearly shows distinct peaks of two individual compounds with retention times 15.6 (**5**) and 16.7 min (**6**). In their electron ionization mass spectra, the intense peaks of molecular ions are present: $[M]^{+\cdot}$ 200 (93%) and 228 (76%), with the same fragmentation patterns. The main fragmentation ions are due to elimination of substituents from α-C atom in $[M]^{+\cdot}$ to generate ammonium ions that is typical of the amine fragmentation (Scheme 5).[9]

In conclusion, water-promoted nonconventional vinylation of trialkylamines *via* the C–N bond cleavage has been first observed for acyl- and cyanoacetylenes. In the case of triethylamine/3-phenylprop-2-ynenitrile, a Stevens/Sommelet type rearrangement to furnish *N*-butyl-*N*-ethylamino derivative occurs. Despite the modest yields of the vinylation products, the reaction appreciably contributes to the toolkit for the synthesis of functionalized *N*-vinylamines as well as to the fundamental chemistry of acetylenes.

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