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SHORT COMMUNICATIONS

Synthesis of Mixed Secondary and Tertiary Amines

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Abstract—A one-stage and facile method of synthesis of expensive methyl- and ethyl(allyl)amines, methyl- and ethyl(prop-2-ynyl)amines, and methyl- and ethyl(allyl)(3-phenylprop-2-ynyl)amines is developed. The synthesized amines present practical interest, because some (prop-2-ynyl)amines are used in the therapy cancer.

Keywords: halides, mixed secondary amines, methylallyl(3-phenylprop-2-ynyl)amines, ethylallyl(3-phenylprop-2-ynyl)amines

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Methyl(allyl)- and methyl(prop-2-ynyl)amines are synthesized by multistage procedures, which require a long time, a large amount of electricity, and hardly accessible starting materials [1–4].

By reacting 40% aqueous methyl or ethylamine with allyl chloride (amine–chloride molar ratio 4 : 1) we obtained the methyl- (**1a**) and ethyl(allyl)amines (**1b**) in yields of 57 and 49%, respectively. Under similar conditions, using prop-2-ynyl bromide instead of allyl chloride, we obtained methyl- (**1c**) and ethyl(prop-2-ynyl)amines (**1d**).

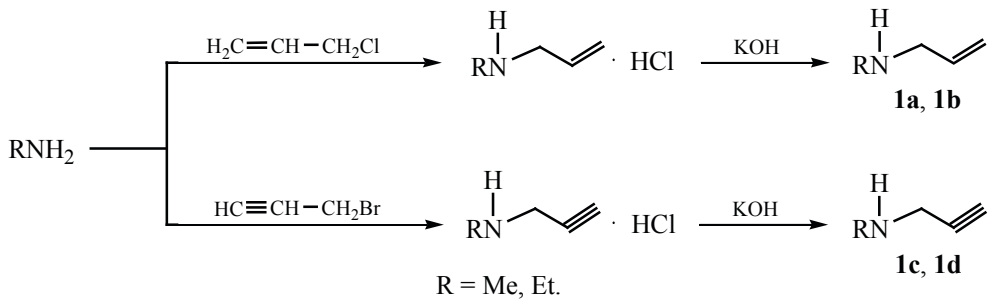
It should be noted that the synthesis of amines **1b** and **1d** gave, along with the target secondary amines, ethyl(diallyl)- and ethyldi(prop-ynyl)amines. According to ^{1}H NMR, the contents of the tertiary amines in the mixtures were 30 and 40%, respectively. In the case of amine **1c**, a mixture of methyl(prop-2-ynyl)amine with a vinylamine was obtained. According to ^{1}H NMR, the mixture contained 70% of methyl(prop-2-ynyl)amine (Scheme 1). All attempts to isolate the tertiary amines from the mixtures were unsuccessful.

The structure of the synthesized amines was established by ^{1}H and ^{13}C NMR spectroscopy.

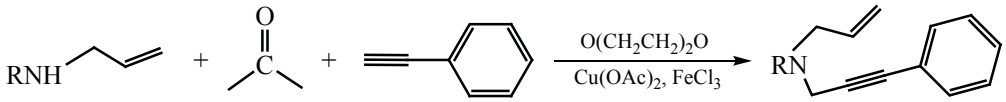
Alkylation of secondary amines with various halides leads to mixed tertiary amines. By the Mannich reaction, from methyl- and ethyl(allyl) amines **1a** and **1b** we synthesized methyl- (**2a**) and ethyl(allyl)(3-phenylprop-2-ynyl)amines (**2b**) in yields of 71 and 65%, respectively (Scheme 2).

According to the results of toxicity testing on rats, methyl(allyl)amine caused muscle weakness, ataxia, and changes in the structure and functions of the salivary glands [5]. Methyl(allyl) amine is also used in the production of *N*-allyl-α,α-dichloro-*N*-methylacetamide and as a functional monomer for coordination with Cd(II)/Zn(II) ions in the production of poly(methyl methacrylate–butyl methacrylate–*N*-allylmethylamine

Scheme 1.



Scheme 2.



1a, **1b** **2a**, **2b**

R = Me, Et.

films (PMBA) used as building blocks in the manufacture of photocatalytic cells [6].

Allyl(methyl)amine (1a) and methyl(prop-2-ynyl)amine (1b) (*general procedure*). Allyl chloride or propargyl bromide in a 4 : 1 molar ratio, respectively, was added in portions from a dropping funnel to a 40% aqueous solution of methylamine at room temperature under constant stirring. The solution was stirred at room temperature for 3–4 h and then carefully acidified with HCl. The mixture was then treated with ether to extract unreacted halide. The amine hydrochloride solution was concentrated under reduced pressure and then transferred to a Favorsky flask equipped with a Liebig condenser and a receiver cooled by ice. A highly concentrated KOH solution was slowly added through a dropping funnel to a heated reaction mixture. The fractions boiling at 40–70°C (**1a**) and 45–92°C (**1b**) were collected, dried over $MgSO_4$, and placed into a refrigerator. A day after, the amine layer was decanted, dried over $MgSO_4$, and distilled from a Favorsky flask.

Allyl(methyl)amine (1a). Yield 6 g (65%), bp 64–66°C (760 mmHg), n_D^{20} 1.4110, mp (picrate) 106–108°C; the physicochemical constants are consistent with published data [1, 4]. ^{1}H NMR spectrum (300.077 MHz, DMSO-d_6 + CCl_4), δ, ppm: 1.28 br.s (1H, NH), 2.32 s (3H, CH_3), 3.11 dt (2H, CH_2, *J* 5.8, 1.5 Hz), 5.01 d.d.t (1H, =CH_2, *J* 10.2, 2.0, 1.5 Hz), 5.11 d.d.t (1H, =CH_2, *J* 17.2, 2.0, 1.5 Hz), 5.81 d.d.t (1H, =CH, *J* 17.2, 10.2, 5.8 Hz). ^{13}C NMR spectrum (75.465 MHz, DMSO-d_6 + CCl_4), δ, ppm: 35.2 (CH_3), 53.7 (CH_2), 114.6 (=CH_2), 136.8 (=CH). Found, %: C 67.34; H 12.61; N 19.52. C_4H_9N. Calculated, %: C 67.55; H 12.75; N 19.69.

Methyl(prop-2-ynyl)amine (1c). Yield 11.16 g (55%), bp 82–85°C, n_D^{20} 1.4303, mp 141°C (oxalate); the physicochemical constants are consistent with published data [3]. ^{1}H NMR spectrum (300.077 MHz, DMSO-d_6 + CCl_4), δ, ppm: 2.36 s (3H, CH_3), 2.39 t (1H, ≡CH, *J* 2.4 Hz), 2.47 br s (1H, NH), 3.26 d (2H, CH_2, *J* 2.4 Hz). ^{13}C (75.465 MHz, DMSO-d_6 + CCl_4), δ, ppm: 40.4 (CH_3), 43.7 (CH_2), 73.6 (≡CH), 78.2 (≡C). Found, %: C 69.37; H 10.05; N 20.13. C_4H_7N. Calculated, %: C 69.52; H 10.21; N 20.27.

A mixture comprising methyl(prop-2-ynyl)amine and an amine with a vinyl group was also obtained [3.7 g; bp 30°C (17–18 mmHg); n_D^{20} 1.4620]. According to ^{1}H NMR, the mixture contained 70% of methyl(prop-2-ynyl)amine.

Allyl(ethyl)amine (1b) and ethyl(prop-2-ynyl)-amine (1d) (*general procedure*). The synthesis was performed as described above, except that unreacted ethylamine was collected in an absorption coil cooled with ice. The fractions boiling at 64–78°C (**1b**) and 45–92°C (**1d**) were collected and dried over $MgSO_4$. A day after, the amine layer was decanted, dried over $MgSO_4$, and distilled from a Favorsky flask.

Allyl(ethyl)amine (1b). Yield 20.6 g (62%), bp 74–75°C, n_D^{20} 1.4196, mp 145–147°C (hydrochloride), does not form picrate. ^{1}H NMR spectrum (300.077 MHz, DMSO-d_6 + CCl_4), δ, ppm: 1.05 t (3H, CH_3, *J* 7.1 Hz), 2.17 br s (1H, NH), 2.56 q (2H, C$\underline{H}_2$CH$_3$, *J* 7.1 Hz), 3.15 dt (2H, C$\underline{H}_2$CH=CH$_2$, *J* 5.8, 1.5 Hz), 4.99 d.d.t (1H, =CH_2, *J* 10.2, 2.0, 1.5 Hz), 5.09 d.d.t (1H, =CH_2, *J* 17.2, 2.0, 1.5 Hz), 5.81 d.d.t (1H, =CH, *J* 17.2, 10.2, 5.8 Hz). ^{13}C NMR spectrum (75.465 MHz, DMSO-d_6 + CCl_4), δ, ppm: 14.8 (CH_3), 42.8 ($\underline{C}H_2CH_3$), 51.7 ($\underline{C}H_2CH=CH_2$), 114.5 (=CH_2), 137.1 (=CH). Found, %: C 70.41; H 12.88; N 16.31. $C_5H_{11}N$. Calculated, %: C 70.53; H 13.02; N 16.45.

A mixture comprising, according to ^{1}H NMR, 70% of allyl(ethyl)amine and 30% of dially(ethyl) amine was also obtained (2 g; bp 75–78°C; n_D^{20} 1.4334).

Ethyl(prop-2-ynyl)amine (1d). Yield 6.8 g (48%), bp 80–83°C, n_D^{20} 1.4300, mp 165–168°C (hydrochloride), does not form picrate. ^{1}H NMR spectrum (300.077 MHz, DMSO-d_6 + CCl_4), δ, ppm: 1.04 t (3H, CH_3, *J* 7.1 Hz), 2.36 t (1H, ≡CH, *J* 2.4 Hz), 2.63 q (2H, C$\underline{H}_2$CH$_3$, *J* 7.1 Hz), 2.50 br.s (1H, NH), 3.29 d (2H, C$\underline{H}_2$C=CH, *J* 2.4 Hz). ^{13}C NMR spectrum (75.465 MHz, DMSO-d_6 + CCl_4), δ, ppm: 14.4 (CH_3), 37.2 (CH_2), 42.0 (CH_2), 71.5 (≡CH), 82.3 (≡C). Found, %: C 72.11; H 10.77; N 16.73. C_5H_9N. Calculated, %: C 72.24; H 10.91; N 16.85.

A mixture comprising, according to ^{1}H NMR, 60 % of ethyl(prop-2-ynyl)amine and 40% of ethyldi(prop-2-ynyl)amine was also obtained [1.5 g; 70–73°C (60 mmHg); n_D^{20} 1.4836].

Attempted isolation of diallyl(ethyl)amine and methyl- and ethyldi(prop-ynyl)amines failed.

Allyl(methyl)(3-phenylprop-2-ynyl)amine (2a) and allyl(ethyl)(3-phenylprop-2-ynyl)amine (2b) (*general procedure*). A mixture of 8 g (80 mmol) of phenylacetylene, 2.4 g (80 mmol) of Paraform, 50 mL of dioxane, 5.8 g (80 mmol) of allyl(methyl)amine, 0.2 g of $FeCl_3$, and 0.2 g of $(CH_3COO)_2Cu$ was placed in a metal cylinder, heated at 90–95°C for 60–65 h, and then acidified with 25% HCl. The solvent was removed by distillation. The reaction mixture and distillate were treated with ether to extract unreacted phenylacetylene (about 5–10% was recovered in all cases). The reaction mixture was made alkaline and extracted with ether (3 × 100 mL). The extract was washed with water, dried over $MgSO_4$, the solvent was removed by distillation, and the residue was distilled in a vacuum to obtain **allyl(methyl)-(3-phenylprop-2-ynyl)amine (2a)**. Yield 10.8 g (71%), bp 112–115°C (1.5–2.0 mmHg), n_D^{20} 1.5450. ^{1}H NMR spectrum (300.077 MHz, DMSO-d_6 + CCl_4), δ, ppm: 2.30 s (3H, CH_3), 3.07 d.t (2H, C$\underline{H}_2$CH=CH_2, *J* 6.4, 1.3 Hz), 3.48 s (2H, C$\underline{H}_2$C=CPh), 5.13 d.d.t (1H, =CH_2, *J* 10.1, 2.0, 1.3 Hz), 5.22 d.d.t (1H, =CH_2, *J* 17.2, 2.0, 1.3 Hz), 5.81 d.d.t (1H. =CH, *J* 17.2, 10.1, 6.4 Hz), 7.26–7.31 m (3H), 7.34–7.40 m (2H, C_6H_5). ^{13}C NMR spectrum (75.465 MHz, DMSO-d_6 + CCl_4), δ, ppm: 40.9 (CH_3), 45.2 (CH_2), 58.3 (CH_2), 84.1 ($\underline{C}$≡C), 84.8 (C≡$\underline{C}$), 116.9 (=CH_2), 122.7, 127.3 (CH), 127.7 (2CH), 131.0 (2CH), 135.2 (=CH). Found, %: C 84.15; H 8.03; N 7.42. $C_{13}H_{15}N$. Calculated, %: C 84.28; H 8.16; N 7.56.

Allyl(ethyl)(3-phenylprop-2-ynyl)amine (2b) was prepared by the same procedure from 8.16 g (80 mmol) of phenylacetylene, 2.4 g (80 mmol) of Paraform, 50 mL of dioxane, 7 g (80 mmol) of allyl(ethyl)amine, 0.2 g of $FeCl_3$, and 0.3 g of $(CH_3COO)_2Cu$. Yield 10.4 g (65%), bp 100–101°C (0–1 mmHg), n_D^{20} 1.5388. ^{1}H NMR spectrum (300.077 MHz, DMSO-d_6 + CCl_4), δ, ppm 1.09 t (3H, CH_3, *J* 7.1 Hz), 2.57 q (2H, C$\underline{H}_2$$CH_3$, *J* 7.1 Hz), 3.13 d.t (2H, C$\underline{H}_2$CH=CH_2, *J* 6.4, 1.3 Hz), 3.54 s (2H, C$\underline{H}_2$C=CPh), 5.12 d.d.t (1H, =CH_2, *J* 10.1, 2.1, 1.3 Hz), 5.23 d.d.t (1H, =CH_2, *J* 17.2, 2.1, 1.3 Hz), 5.81 d.d.t (1H, =CH, *J* 17.2, 10.1, 6.4 Hz), 7.26–7.39 m (5H, C_6H_5). ^{13}C NMR spectrum (75.465 MHz, DMSO-d_6 + CCl_4), δ, ppm: 12.2 (CH_3), 41.0 ($\underline{C}$$H_2CH_3$), 46.4 ($\underline{C}$$H_2$C=C), 56.1 ($\underline{C}$$H_2$CH=$CH_2$), 84.0 and 84.6 (C≡C), 116.7 (=CH_2), 122.8 (C_{ipso}), 127.2(C_{para}), 127.6 and 131.0 (C_{ortho} and C_{meta}), 135.4 (=CH). Found, %: C 84.22; H 8.46; N 6.88. $C_{14}H_{17}N$. Calculated, %: C 84.37; H 8.6; N 7.03.

The ^{1}H and ^{13}C NMR spectra were recorded on a Varian Mercury 300 VX spectrometer (300 and 75 MHz, respectively) in DMSO-d_6–CCl_4 (1 : 3), internal reference TMS. The elemental analyses were obtained on an Elementar vario MICRO cube CHN analyzer. The melting points were measured on a Nagema melting point microscope.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

1. Grogoryan, D.V., Kazaryan, A.Ts., Martirosyan, G.T., and Babayan, A.T., *Zh. Org. Khim*., 1970, vol. 6, p. 1390.
2. Babayan, A.T., Martirosyan, G.T., Grogoryan, D.V., and Grigoryan, E.A., *Izv. Akad. Nauk Arn. SSR, Khim. N*., 1963, vol. 16, p. 449.
3. Paal, C. and Hermann, C., *Ber*., 1889, vol. 22, p. 3076. https://doi.org/10.1002/cber.188902202238
4. Morrison, A.L. and Rinderknecht, H., *J. Chem. Soc*., 1950, p. 1478. https://doi.org/10.1039/JR9500001478
5. https://chem.nlm.nih.gov/chemidplus/sid/0000627372
6. https://www.fishersci.com/shop/products/n-allylmethyl-amine-96/AAH2755103