Reduction of (*E*)-3-aryl-2-(thiazol-2-yl)acrylonitriles with lithium aluminum hydride*

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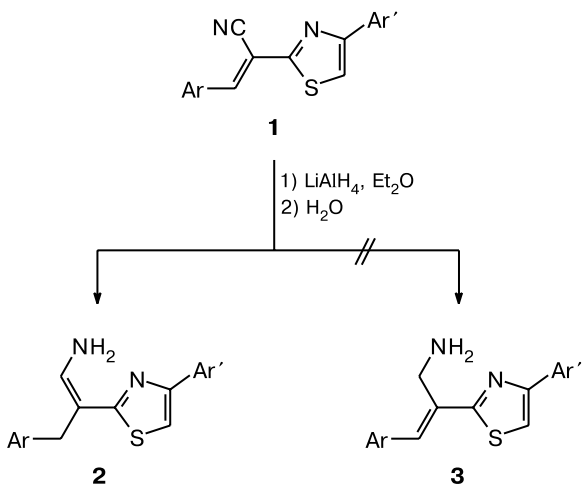
Reduction of (*E*)-3-aryl-2-(4-arylthiazol-2-yl)acrylonitriles with lithium aluminum hydride in dry ether afforded (*Z*)-1-amino-3-aryl-2-(thiazol-2-yl)prop-1-ene derivatives in 15 to 40% yields. The structure of (*Z*)-1-amino-3-(2-chlorophenyl)-2-[4-(4-methylphenyl)thiazol-2-yl]prop-1-ene was confirmed by X-ray diffraction analysis.

Key words: (*E*)-3-aryl-2-(thiazol-2-yl)acrylonitriles, reduction, lithium aluminum hydride, (*Z*)-1-amino-3-aryl-2-(thiazol-2-yl)prop-1-enes, enamines, X-ray diffraction analysis.

Being highly reactive and accessible, lithium aluminum hydride is widely used in synthetic practice.[1—3] It is known[1] that $LiAlH_4$ can partially or completely reduce multiple bonds in the α,β-position relative to a polar group. Earlier, we obtained 3-aryl-2-(4-arylthiazol-2-yl)acrylonitriles (**1**)[4] and proved that they exist as (*E*)-isomers (X-ray diffraction data).[5] In our further study of the reduction of hetarylnitriles with $LiAlH_4$ for creation of novel promising reagents for fine organic synthesis, we found that treatment of a suspension of compounds **1a**—**d** in dry ether with $LiAlH_4$ (2.3 equiv.) under mild conditions leads to (*Z*)-1-amino-3-aryl-2-(thiazol-2-yl)prop-1-enes (**2**) in 15 to 40% yields (Scheme 1). It should be noted that enamines **2** are highly labile and acids such as HCl are inefficient for separation of the product from aluminum hydroxide (resulting from hydrolysis of the reaction mixture); this, along with the high adsorptivity of $Al(OH)_3$, lowers the yields of the reaction products.

Scheme 1



1—3	Ar	Ar′
a	2-ClC_6H_4	Ph
b	2-ClC_6H_4	4-MeC_6H_4
c	4-ClC_6H_4	Ph
d	4-$EtOC_6H_4$	4-ClC_6H_4

Previously,[6] according to IR and ^1H NMR spectroscopic data, the product of the reaction of nitrile **1a** with $LiAlH_4$ was assigned the structure of 3-amino-1-aryl-2-(4-arylthiazol-2-yl)prop-1-ene (**3a**). However, more thorough reexamination of the spectroscopic data inclined us in favor of structure **2a**. For instance, the narrow singlet at δ 3.82 does not relate to the methylene protons $C\underline{H}_2NH_2$ (in this case, a more complex signal should be expected to appear in the spectrum), while the doublet of doublets at δ 6.59 (1 H) resolved as a pseudotriplet belongs to the proton of the aminomethylene group $=C\underline{H}—NH_2$. The

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signal of the amino group cannot be detected because of an overlap with a complex multiplet for the aromatic protons. An analogous pattern was observed in the spectra of enamines **2b—d**.

To identify the products obtained, the structure of compound **2b** was examined by X-ray diffraction analysis (Fig. 1). The five-membered ring S(1)N(1)C(1)C(2)C(3) is planar: the deviations of the atoms from the mean-square plane do not exceed 0.004 Å. The benzene ring C(13)—C(18) is virtually coplanar with this plane (the dihedral angle is 3.9°), while the benzene ring C(7)—C(12) is orthogonal to it (the respective dihedral angle is 85.7°). As the result of the conjugation between the π systems of the five-membered ring S(1)N(1)C(1)C(2)C(3) and the C(4)=C(5) bond, the C(1)—C(4) bond (1.435(8) Å) is noticeably shorter than the standard value for a purely single C_{sp^2}—C_{sp^2} bond (1.48 Å).[7] Analogously, the $n_{N(2)}$—$\pi_{C(4)=C(5)}$ interaction substantially shortens the N(2)—C(5) bond (1.358(7) Å) compared to the 1.43—1.45 Å range characteristic[7,8] of the single N_{sp^2}—C_{sp^2} bond. Compound **2b** is stabilized[9] by a very strong intramolecular N(2)—H...N(1) hydrogen bond (N(1)...N(2) 2.764(6) Å, N(2)—H 0.80(5) Å, N(1)...H 2.19(5) Å; the N(1)—H—N(2) angle is 129(4)°) that closes the six-membered N(1)C(1)C(4)C(5)N(2)H ring.

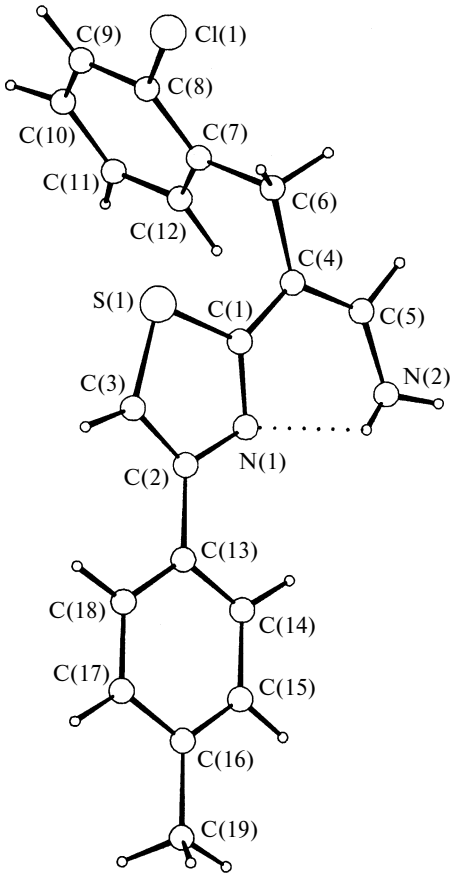

Fig. 1. General view of molecule **2b**. Selected bond lengths are S(1)—C(1) 1.745(8) Å, S(1)—C(3) 1.701(6) Å, N(1)—C(1) 1.329(6) Å, N(1)—C(2) 1.384(7) Å, N(2)—C(5) 1.358(7) Å, C(1)—C(4) 1.435(8) Å, C(2)—C(3) 1.362(7) Å, and C(4)—C(5) 1.349(8) Å. Selected bond angles are C(1)—S(1)—C(3) 90.0(3)°, C(1)—N(1)—C(2) 111.8(5)°, S(1)—C(1)—N(1) 112.7(5)°, N(1)—C(2)—C(3) 114.2(5)°, and S(1)—C(3)—C(2) 111.3(5)°.

Experimental

^{1}H NMR spectra were recorded on a Varian Gemini 200 instrument (200 MHz) in DMSO-d_6 with Me_4Si as the internal standard. IR spectra were recorded on an IKS-29 spectrophotometer (Nujol). Elemental analysis was performed on a Perkin—Elmer C,H,N-analyser instrument. The course of the reaction was monitored and the purity of the compounds obtained was checked by TLC on Silufol UV 254 plates in acetone—heptane (1 : 1); spots were visualized with the iodine vapor. Melting points were determined on a Kofler hot stage and are given uncorrected. (*E*)-3-Aryl-2-(thiazol-2-yl)acrylonitriles **1a—d** were prepared according to a general procedure.[4]

X-ray diffraction study of a single crystal (0.31×0.31×0.49 mm) of compound **2b** was carried out at room temperature on an Enraf—Nonius CAD4 automatic four-circle diffractometer (Cu-*K*α radiation, λ = 1.54178 Å, scan rate ratio $2\theta/\omega = 1.2$, $\theta_{max} = 70°$, sphere segment $0 \le h \le 18$, $0 \le k \le 6$, $-27 \le l \le 27$). The total number of reflections was 3773; the number of independent reflections was 3237 ($R_{int} = 0.031$). The crystals of compound **2b** are monoclinic, $a = 15.310(8)$ Å, $b = 5.043(3)$ Å, $c = 22.548(10)$ Å, $\beta = 100.11(4)°$, $V = 1713.8$ Å^3, $M = 339.9$, $Z = 4$, $d_{calc} = 1.32$ g cm^{-3}, $\mu = 31.03$ cm^{-1}, $F(000) = 716.1$, space group $P2_1/n$. The structure was solved by the direct method and refined by the least-squares method in the full-matrix anisotropic approximation with the CRYSTALS program package.[10] In the refinement, 1564 reflections with $I > 4\sigma(I)$ were used (the number of the parameters refined was 216; the number of reflections per parameter was 7.3). All hydrogen atoms were located from electron-density difference maps and refined with fixed coordinates and thermal parameters (only the H atoms at the N(2) atom were refined isotropically). The weighting scheme $w = 1/[0.01F_0^2 + 12\sigma(|F_0^2|) + 1$ was used. The final residuals are $R = 0.068$ and $R_w = 0.075$; GOOF = 0.883. The residual electron densities from the difference Fourier series were 0.29 and −0.29 e Å^{-3}. Absorption correction was applied by the azimuthal scanning method.[11] The complete array of X-ray diffraction data for compound **2b** has been deposited with the Cambridge Crystallographic Database.

(*Z*)-1-Amino-3-aryl-2-(thiazol-2-yl)prop-1-enes (2) (general procedure). A suspension of $LiAlH_4$ (0.35 g, 9.2 mmol) in ether (10 mL) was added in small portions for 5 to 7 min to a cooled suspension of (*E*)-3-aryl-2-(thiazol-2-yl)acrylonitrile **1a—d** (4 mmol) in dry ether (40 mL). The mixture was vigorously stirred in an ice bath for 6 h and kept in a refrigerator for 12 h. Water (2 mL) was carefully added dropwise to the stirred reaction mixture. The precipitate of $Al(OH)_3$ was filtered off and the ethereal filtrate was concentrated. Aluminum hydroxide was treated with boiling EtOH—acetone (1 : 1) for 15 min, the mixture was filtered, and the filtrate was concentrated. Solid residues were combined and recrystallized from an appropriate solvent.

(*Z*)-1-Amino-3-(2-chlorophenyl)-2-(4-phenylthiazol-2-yl)prop-1-ene (2a). The yield was 40%, m.p. 98—100 °C (from Et_2O) (*cf.* Ref. 6: m.p. 101—103 °C). Found (%): C, 66.92; H, 4.60; N, 8.60. $C_{18}H_{15}ClN_2S$. Calculated (%): C, 66.15; H, 4.63; N, 8.57. IR, ν/cm^{-1}: 3450 (ν(NH_2)). ^{1}H NMR, δ: 3.82 (s, 2 H, $\underline{H}_2$CAr); 6.59 (pseudot, 1 H, =C$\underline{H}$—NH_2); 7.15—7.43 (m, 10 H, Ar (7 H) + NH_2 + thiazolyl (1 H)); 7.91 (d, 2 H, Ar, ^3J = 7.8 Hz).

(*Z*)-1-Amino-3-(2-chlorophenyl)-2-[4-(4-methylphenyl)thiazol-2-yl]prop-1-ene (2b). The yield was 22%, m.p. 94—96 °C (from EtOH). Found (%): C, 67.41; H, 5.00; N, 8.30. $C_{19}H_{17}ClN_2S$. Calculated (%): C, 66.95; H, 5.03; N, 8.22. IR, ν/cm^{-1}: 3420 (ν(NH_2)). ^{1}H NMR, δ: 2.36 (s, 3 H, Me); 3.72 (s, 2 H, $\underline{H}_2$CAr); 6.58 (pseudot, 1 H, =C$\underline{H}$—NH_2); 7.16—7.39 (m, 9 H, Ar (6 H) + NH_2 + thiazolyl (1 H)); 7.77 (d, 2 H, Ar, ^3J = 8.1 Hz).

(*Z*)-1-Amino-3-(4-chlorophenyl)-2-(4-phenylthiazol-2-yl)prop-1-ene (2c). The yield was 15%, m.p. 115—118 °C (decomp., from EtOH). Found (%): C, 66.83; H, 4.66; N, 8.55. $C_{18}H_{15}ClN_2S$. Calculated (%): C, 66.15; H, 4.63; N, 8.57. IR, ν/cm^{-1}: 3490 (ν(NH_2)); 1635 (δ(NH_2)). ^{1}H NMR, δ: 3.60 (s, 2 H, $\underline{H}_2$CAr); 6.72 (pseudot, 1 H, =C$\underline{H}$—NH_2); 7.21—7.47 (m, 10 H, Ar (7 H) + NH_2 + thiazolyl (1 H)); 7.87 (d, 2 H, Ar, ^3J = 7.9 Hz).

(*Z*)-1-Amino-2-[4-(4-chlorophenyl)thiazol-2-yl]-3-(4-ethoxyphenyl)prop-1-ene (2d). The yield was 29%, m.p. 126—128 °C (from EtOH—Me_2CO, 1 : 1). Found (%): C, 65.19; H, 5.18; N, 7.72. $C_{20}H_{19}ClN_2OS$. Calculated (%): C, 64.77; H, 5.16; N, 7.55. IR, ν/cm^{-1}: 3470 (ν(NH_2)). ^{1}H NMR, δ: 1.36 (t, 3 H, $OCH_2C\underline{H}_3$, ^3J = 7.0 Hz); 3.55 (s, 2 H, $ArC\underline{H}_2$); 3.96 (q, 2 H, $OCH_2C\underline{H}_3$, ^3J = 7.0 Hz); 6.65 (pseudot, 1 H, =C$\underline{H}$—NH_2); 6.75 (d, 2 H, 4-$EtOC_6H_4$, C(2)H and C(6)H, ^3J = 8.5 Hz); 7.16 (d, 2 H, 4-$EtOC_6H_4$, C(3)H and C(5)H, ^3J = 8.5 Hz); 7.33 (br.d, 2 H, NH_2); 7.39 (d, 2 H, 4-ClC_6H_4, C(3)H and C(5)H, ^3J = 8.5 Hz); 7.49 (s, 1 H, thiazolyl); 7.90 (d, 2 H, 4-ClC_6H_4, C(2)H and C(6)H, ^3J = 8.5 Hz).

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