Chemistry of Heterocyclic Compounds, Vol. 41, No. 2, 2005

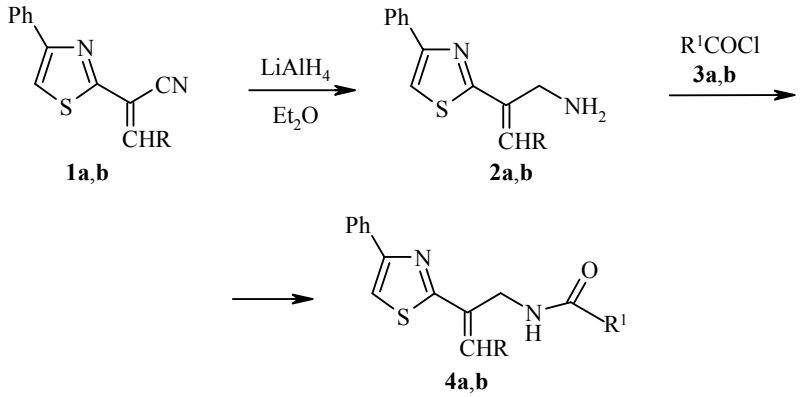
REDUCTION OF DERIVATIVES OF α-ARYLIDENE-α-(2-THIAZOLYL)ACETONITRILE WITH LITHIUM ALUMINUM HYDRIDE

A. A. Zubarev, V. K. Zav'yalova, and V. P. Litvinov

The action of lithium aluminum hydride on derivatives of α-arylidene-α-(2-thiazolyl)acetonitrile in absolute ether leads to reduction of the nitrile group without affecting the double bond conjugated with it. The reaction products are the corresponding substituted allylamines.

Keywords: α-arylidene-α-(2-thiazolyl)acetonitriles, β-arylidene-β-(2-thiazolyl)ethylamines, lithium aluminum hydride, reduction.

Lithium aluminum hydride is widely used in synthetic practice for the reduction of the nitrile group. In the case of α,β-unsaturated nitriles the direction of the reaction depends strongly on the structure of the compound and the conditions of conducting the synthesis [1]. In many cases hydrogenation of only the double bond occurs without affecting the nitrile group [2] or simultaneous reduction of both functions occurs [3]. Esters of arylidenecyanoacetic acid are reduced with lithium aluminum hydride even in the cold to the corresponding 2-(arylmethyl)-3-aminopropanols [4]. Only the double bond is reduced in substituted esters of 2-cyanocrotonic and 2-cyanoacrylic acids, and the nitrile and carbalkoxy groups are not affected [5]. The behavior of certain compounds of the stilbene series is of interest. For example, α,β-diphenyl-β-methoxyacrylonitrile undergoes reduction of the double bond with fission of the methoxy group with the formation of α-cyano-α,β-diphenylethane [6].



1a, 2a, 4a,b R = 2-ClC_6H_4; **1b**, **2b** R = 2-furyl, **3**, **4**, **a** R^1 = 2-Me-3-$O_2NC_6H_3$; **b** R^1 = 4-ClC_6H_4

N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, Moscow 119991; e-mail: vpl@ioc.ac.ru. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 2, pp. 221-224, February, 2005. Original article submitted July 10, 2002.

The reduction of α,α'-dicyano-4,4'-dimethoxystilbene with lithium aluminum hydride in THF solution leads to 2,3-di(4-methoxyphenyl)propylamine [7]. There is therefore significant interest in the study of the reduction of derivatives of α-arylidene-α-(2-thiazolyl)acetonitrile having a structure similar to the structure of the stilbenes mentioned above.

We have studied the interaction of $LiAlH_4$ with derivatives of α-arylidene-α-(2-thiazolyl)acetonitrile, the reduction products of which may be of interest both as new biologically active compounds and as synthons in organic synthesis.

It was found that on reduction of derivatives of α-arylidene-α-(2-thiazolyl)-acetonitrile **1a,b** with $LiAlH_4$ in ether with subsequent treatment with water the corresponding β-arylidene-β-(2-thiazolyl)ethylamines **2a,b** were formed in 55-70% yield (see Scheme). The structure of amines **2a,b**, which form crystals of a bright yellow color with sharp melting points, was confirmed by data of IR, ^1H NMR, and mass spectra. The signal of the CN group (2200 cm^{-1}) was absent in the IR spectra, there were absorption bands for an NH_2 group (3450-3470 cm^{-1}) and an intense absorption band for the C=C group (1630 cm^{-1}). In the ^1H NMR spectra of amines **2a,b** a singlet was observed for the methylene group at 3.6-3.8 and for the alkene fragment at 6.5-6.7 ppm.

Amine **2a** is readily acylated by carboxylic acid chlorides **3a,b** in the presence of an equimolar amount of triethylamine in acetonitrile with the formation of amides **4a,b**. An intense absorption band was present in their IR spectra for the C=O group (1680 cm^{-1}), and in the ^1H NMR spectra a doublet was observed for the NH group at 12.6-12.75 ppm (Table 2).

EXPERIMENTAL

Melting points were determined on a Kofler block. The IR spectra were recorded on a Specord M 80 spectrophotometer in KBr disks, and ^1H NMR spectra on a Bruker WM 250 (250 MHz) spectrometer in DMSO-d_6, internal standard was the signal of the solvent (δ_H = 2.50 ppm). Elemental analysis was carried out on a Perkin-Elmer 2400 instrument.

β-Arylidene-β-(2-thiazolyl)ethylamines (2a,b). A solution of thiazole **1a,b** (3 mmol) in abs. Et_2O (50 ml) was added dropwise with stirring during 20 min to a suspension of $LiAlH_4$ (6 mmol) in abs. Et_2O (50 ml). The suspension was stirred for 1 h at the boiling point, cooled, and water (100 ml) was added dropwise. The organic layer was separated, and the aqueous phase with the solid was extracted with Et_2O (2 × 25 ml). The combined organic phase was dried over $MgSO_4$, and evaporated. The residue was recrystallized from hexane.

TABLE 1. Characteristics of Compounds **2a,b** and **4a,b**

Compound	Empirical formula	Found, % / Calculated, %					mp, °C (solvent)	Yield, %
		C	H	Cl	N	S		
2a	$C_{18}H_{15}ClN_2S$	66.03 / 66.15	4.69 / 4.63	10.59 / 10.85	8.73 / 8.57	9.96 / 9.81	101-103 (C_6H_{14})	69
2b	$C_{16}H_{14}N_2OS$	68.31 / 68.06	4.87 / 5.00	—	9.81 / 9.92	11.55 / 11.36	80-82 (C_6H_{14})	55
4a	$C_{26}H_{20}ClN_3O_3S$	63.45 / 63.73	4.20 / 4.11	7.11 / 7.24	8.47 / 8.58	6.72 / 6.54	86-87 (AcOEt)	26
4b	$C_{25}H_{18}Cl_2N_2OS$	64.69 / 64.52	3.84 / 3.90	15.05 / 15.24	5.89 / 6.02	7.07 / 6.89	162-163 (AcOEt)	62

TABLE 2. Spectral Characteristics of Compounds **2a,b** and **4a,b**

Compound	IR spectrum, ν, cm^{-1}	Mass spectrum, *m/z* (*I*, %)	^1H NMR spectrum, δ, ppm (*J*, Hz)
2a	3456 (NH_2), 3112 (CH=C), 1632 (C=C)	326 $[M]^+$ (87), 309 (13), 291 (100), 274 (27), 215 (18), 155 (31), 145 (32), 134 (99), 102 (34), 89 (77), 77 (34)	3.82 (2H, s, CH_2); 6.47 (3H, m, C=CH, NH_2); 7.17 (3H, m, H_{Ph}-3,4,5); 7.32 (2H, m, 2-ClC_6H_4 (H-4,5)); 7.41 (3H, m, 2-ClC_6H_4 (H-3,6), thyazole); 7.87 (2H, d, *J* = 7.9, H_{Ph}-2,6)
2b	3464 (NH_2), 3112 (CH=C), 1628 (C=C)	—	3.62 (2H, s, CH_2); 6.12 (1H, m, (H-4) furan); 6.34 (1H, d, *J* = 3.7, (H-3) furan); 6.75 (1H, s, CH=C); 7.3-7.5 (4H, m, H_{Ph}-3,4,5, (H-5 furan)); 7.66 (1H, s, thyazole); 7.9 (2H, d, *J* = 7.9, H_{Ph}-2,6)
4a	3440 (NH), 3072 (CH=C), 1680 (C=O), 1632 (C=C)	489 $[M]^+$ (42), 327 (25), 325 (49), 289 (56), 262 (23), 187 (18), 164 (97), 134 (58), 125 (21), 118 (64), 90 (100)	2.65 (3H, s, CH_3); 4.01 (2H, br. s, CH_2); 7.24 (1H, m, 2-ClC_6H_4 (H-5)); 7.26-7.30 (4H, m, H_{Ph}-3,4,5, 2-ClC_6H_4 (H-4)); 7.32-7.37 (2H, m, 2-ClC_6H_4 (H-3), CH=C); 7.4 (1H, s, thyazole); 7.46 (2H, m, 2-ClC_6H_4 (H-6), 2-CH_3-3-$NO_2C_6H_3$ (H-5)); 7.58 (2H, d, *J* = 7.9, H_{Ph}-2,6); 7.88 (1H, d, *J* = 7.7, 2-CH_3-3-$NO_2C_6H_3$ (H-6)); 7.98 (1H, d, *J* = 8.2, 2-CH_3-3-$NO_2C_6H_3$ (H-4)); 12.75 (1H, d, *J* = 5.6, NH)
4b	3464 (NH), 3064 (CH=C), 1680 (C=O), 1636 (C=C)	464 $[M]^+$ (16), 429 (5), 325 (22), 289 (18), 139 (100), 125 (6), 111 (46), 102 (8), 91 (26), 75 (19), 51 (6)	4.01 (2H, br. s, CH_2); 7.22-7.35 (6H, m, C=CH, *o*-ClC_6H_4 (H-4,5), H_{Ph}-3,4,5); 7.4 (1H, m, *o*-ClC_6H_4 (H-3)); 7.49 (2H, m, *n*-ClC_6H_4CO (H-3,5)); 7.61 (2-H, m, H_{Ph}-2,6); 7.69 (2H, m, *n*-ClC_6H_4CO (H-2,6)); 7.78 (1H, d, *J* = 7.6, *o*-ClC_6H_4 (H-6)); 7.9 (1H, s, thyazole); 12.58 (1H, d, *J* = 5.6, CONH)

Amides of β-Methylidene-β-(2-thiazolyl)ethylamines (4a,b). Triethylamine (1 mmol) and carboxylic acid chlorides **3a,b** were added to a suspension of amine **2a** (1 mmol) in MeCN (5 ml). The mixture obtained was heated to boiling, cooled, and left for 24 h at 20°C. The reaction mixture was diluted with water (30 ml), acidified with aqueous 3% HCl solution, and extracted with chloroform (3 × 15 ml). The organic phase was dried over $MgSO_4$, and evaporated. The residue was recrystallized from ethyl acetate.

The work was carried out with the financial support of the Russian Fund for Fundamental Investigations (Project No. 02-03-32063).

REFERENCES

1. A. Khaiosh, *Complex Hydrides in Organic Chemistry* [in Russian], Khimiya, Leningrad (1971), 624 pp.
2. M. Mousseron, R. Jacquier, M. Mousseron-Canet, and R. Zagdoun, *Bull. Soc. Chim. France*, 1042 (1952).
3. E. A. Braude and O. H. Wheeler, *J. Chem. Soc.*, 327 (1955).
4. A. Dornow, G. Messwarb, and H. H. Frey, *Chem. Ber.*, **83**, 445 (1950).
5. H. Le Moal, R. Carrie, and M. Bargain, *C. R. Acad. Sci.*, **251**, 2541 (1960).
6. J. Matti and P. Reynaud, *Bull. Soc. Chim. France*, 410 (1954).
7. H. Bretschneider and R. Lutz, *Monatsh.*, **84**, 573 (1953).