ISSN 1070-4280, Russian Journal of Organic Chemistry, 2006, Vol. 42, No. 8, pp. 1248–1249. © Pleiades Publishing, Inc. 2006.
Original Russian Text © V.V. Ganzha, A.D. Kotov, V.G. Sokolov, V.Yu. Orlov, 2006, published in Zhurnal Organicheskoi Khimii, 2006, Vol. 42, No. 8, pp. 1263–1264.

SHORT COMMUNICATIONS

Direct Amination of 5-Halo-3-phenyl-2,1-benzisoxazoles

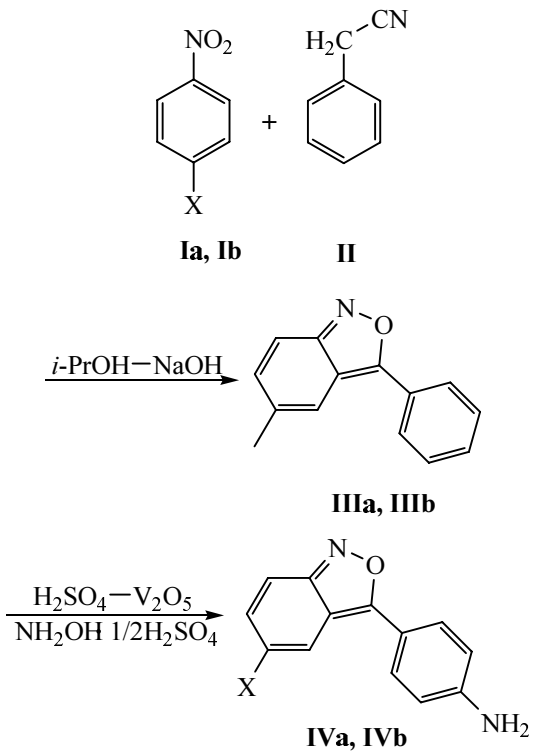
V.V. Ganzha, A.D. Kotov, V.G. Sokolov, and V.Yu. Orlov

Demidov Yaroslavskii State University, Yaroslavl, 150000 Russia
e-mail: kot@bio.uniyar.ac.ru

Received February 1, 2006

DOI: 10.1134/S107042800608029X

2,1-Benzisoxazoles are multipurpose synthons [1], therefore their functionalization, in particular, an introduction of an amino group, extends the bank of initial compounds for the combinatorial chemistry. A convenient procedure for preparation of 5-R-3-aryl-2,1-benzisoxazoles consists in the reaction of 4-substituted arenas with arylacetonitriles in alcohol in the presence of excess alkali [2]. The attempts to build up the target structures from initial compounds containing an amino group meet some difficulties. A direct amination of alkylbenzenes and aryl halides conjugate with sulfonation occurs in a system hydroxylamine sulfate–concn. H_2SO_4–vanadium(V) oxide (catalyst) [3]. We established that under these conditions 5-halo-3-phenyl-2,1-benzisoxazoles **IIIa** and **IIIb** obtained from 4-halonitrobenzenes **Ia** and **Ib** and a phenylacetonitrile (**II**) were converted into 3-(4-aminophenyl)-5-halo-2,1-benzisoxazoles **IVa** and **IVb**.



X = Cl (**a**), Br (**b**).

The method we developed for the synthesis of 5-R-3-aryl-2,1-benzisoxazoles amino derivatives is advantageous compared to the other procedures for it is a simple preparative process giving a high yield of the target product.

3-(4-Aminophenyl)-5-chloro-2,1-benzisoxazole (IVa). To a solution of 5 mg (0.026 mmol) of vanadium(V) oxide in 20 ml of hot concn. H_2SO_4 was aded 0.4 g (4.35 mmol) of hydroxylamine sulfate, the mixture was heated to 120°C, then 1 g (4.35 mmol) of compound **IIIa** was added thereto. The reaction mixture was heated for 6 h at 120°C, then cooled and poured into 300 ml of water. The separated precipitate was filtered off, dried, and recrystallized from 50 ml of a mixture 2-propanol–benzene, 3:1. Yield 0.9 g (85%), brown lustrous plates, mp >310°C. IR spectrum, cm^{-1}: 3504, 3376 (NH_2). ^1H NMR spectrum, δ, ppm: 8.15 d (1H, H^4), 7.92 d (2H, $H^{2'}$, $H^{6'}$), 7.74 d (1H, H^7), 7.38 d.d (1H, H^6), 6.94 d (2H, $H^{3'}$, $H^{5'}$), 6.3 br.s (2H, NH_2). Mass spectrum, *m/z* (I_{rel}, %): 244 $[M]^+$ (100), 209 $[M - Cl]^+$ (97), 181 (58), 154 (20), 92 (27), 77 (19), 65 (72). Found, %: C 63.57; H 3.35; N 11.14. $C_{13}H_9ClN_2O$. Calculated, %: C 63.82; H 3.71; N 11.45. *M* 244.67.

3-(4-Aminophenyl)-5-bromo-2,1-benzisoxazole (IVb) was prepared similarly to compound **IVa**. Yield 81%, mp >310°C. ^1H NMR spectrum, δ, ppm: 8.29 d (1H, H^4), 7.86 d (2H, $H^{2'}$, $H^{6'}$), 7.61 d (1H, H^7), 7.46 d.d (1H, H^6), 6.83 d (2H, $H^{3'}$, $H^{5'}$), 5.3 br.s (2H, NH_2). Mass spectrum, *m/z* (I_{rel}, %): 288 $[M]^+$ (54), 209 $[M - Br]^+$ (95), 181 (63), 166 (65), 154 (31), 92 (49), 77 (100),

65 (82). Found, %: C 53.79; H 3.15; N 9.54. $C_{13}H_9BrN_2O$. Calculated, %: C 54.01; H 3.14; N 9.69. *M* 289.12. ^{1}H NMR spectra were registered on a spectrometer Bruker AC-300 (300.13 MHz) from solutions in DMSO-d_6, internal reference TMS. IR spectra were recorded on a Specord M-80 from mulls in mineral oil. Elemental analysis was carried out on a CHN-1 analyzer (Czechia). Mass spectra were obtained on a device MKh-1310, ionizing electrons energy 70 eV.

The study was carried out under a financial support of the grant MK-2573.2005.3 from the President of the Russian Federation.

REFERENCES

1. Granik, V.G., Pechenina, V.M., and Mukhina, N.A., *Khim.-Farm. Zh.*, 1991, no. 1, p. 57.
2. Davis, R.B. and Pizzini, L.C., *J. Am. Chem. Soc.,* 1960, vol. 25, p. 1884.