

SHORT COMMUNICATIONS

Interrelation between the Structure and Cyclization Direction of *o*-Alkynylbenzenediazonium Salts

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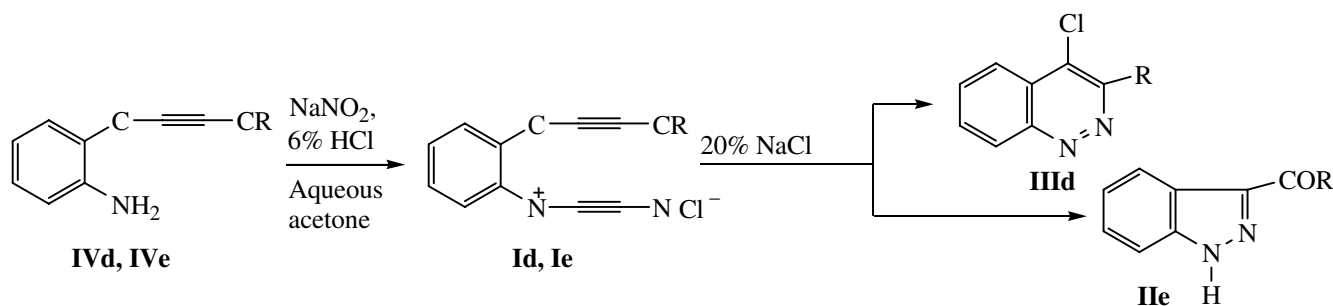
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Until recently the cyclization of *o*-alkynylbenzenediazonium salts discovered by Richter [1], was regarded as a method for preparation of cinnoline derivatives [2, 3]. However in the study of cyclization of diazonium salts *o*-(RC≡C)C₆H₄N≡N⁺Cl[−] (**I**), where R = *p*-CH₃OC₆H₄ (**Ia**) and *p*-(CH₃)₂NC₆H₄ (**Ib**) we established [4] that in contrast to findings from [3] a closure occurred not of a six-membered pyridazine ring but of a five-membered pyrazole ring with indazole derivatives formation. This fact shows that the behavior of *o*-alkynylbenzenediazonium salts in cyclization reactions is not sufficiently understood and requires additional investigation. We suggested that the substituents in direct conjugation with both reaction sites (−C≡C− and [−N≡N]⁺) were capable to significantly affect the direction of the ring closure, and therewith strong donor substituents of the +C-character favored the formation of a five-membered ring, and substituents of −C- or neutral character, of a six-membered ring [4]. In all likelihood, the most suitable

parameter for forecasting the probable cyclization direction would be the electrophilic constant of the substituents σ_p^+ . See for comparison: σ_p^+ of substituents OCH₃ and N(CH₃)₂ equal respectively −0.78 and −1.70, and σ_p^+ of NO₂ group, +0.79 [5]. The suggested relation as we believe provides an opportunity of selective cyclization into five-membered or six-membered rings. One was of this control may consist in the influence of protective groups attached to the functions involved into the conjugation chain of the alkynyl substituent. In this report we present the results of testing this opportunity by an example of the hydroxy function in *o*-(4-hydroxyphenylethynyl)-benzenediazonium chloride (**Ic**) which is unstable under the conditions of Richter reaction. As already mentioned [4], the diazonium salt of its methyl ether **Ia** underwent cyclization to give a pyrazole ring of 3-(4-methoxybenzoyl)indazole (**IIa**). It was presumable that the diazonium salt of the acetate of this phenol **Id** would undergo cyclization in another fashion. The strong

Scheme.



R = *p*-C₆H₄OCOCH₃ (**d**), *p*-C₆H₄NHCOCH₃ (**e**).

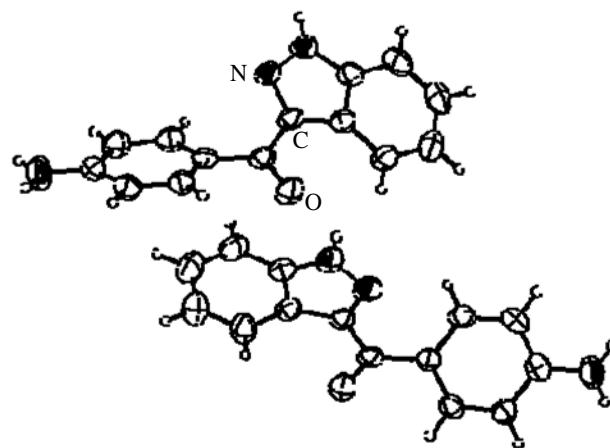
acceptor group COCH_3 possessing $-\text{C}$ -character should considerably decrease the donor ability of the phenol oxygen. This suggestion is supported by the low value of the electrophilic constant of the OCOCH_3 group equal to -0.19 [6]. It was established that the cyclization of compound **Id** under conditions analogous to those applied in cyclization of diazonium salt **Ia** a six-membered ring formed giving 4-chloro-3-(4-acetoxyphenyl)cinnoline (**IIId**) (see the scheme).

The structure of compound **IIId** was established from analytical and spectral data. In the light of the results obtained especially interesting was the study of cyclization of *o*-(4-acetylaminophenylethynyl)benzenediazonium chloride (**Ie**). In this compound the donor properties of nitrogen linked to the COCH_3 group remain still sufficiently high (σ_p^+ of substituent HNAC is -0.60 [5]). Therefore it was expected that diazonium salt **Ie** would undergo cyclization into a five-membered ring. It was actually established that the cyclization of compound **Ie** occurred with a closure of a pyrazole ring and the formation of 3-(4-acetylaminobenzoyl)indazole (**IIf**) (see the scheme). After deprotection 3-(4-aminobenzoyl)indazole (**IIIf**) is an interesting semiproduct capable to be involved into further transformations at the NH_2 group. Besides compound **IIIf** unlike the other indazoles that we had prepared before formed good crystals fit for the X-ray diffraction study. The X-ray analysis gave additional proof of five-membered ring formation in the cyclization of *o*-alkynylbenzenediazonium chlorides (see the figure). 3-(4-Aminophenyl)-4-hydroxycinnoline, isomer of indazole **IIIf**, can be obtained by Richter cyclization of *o*-(4-nitrophenylethynyl)aniline with subsequent reduction of the nitro group into NH_2 .

Thus the discovered relation of the cyclization direction to the structure of the alkynyl substituent in the diazonium salts **I** opens an opportunity of prediction and in some cases of governing the formation either of indazoles or cinnolines. Both classes of compounds are essentially interesting from the viewpoint of potential biological action.

3-(4-Acetoxyphenyl)-4-chlorocinnoline (**IIId**).

Into a solution of 0.80 g (3.2 mmol) of aniline **IVd** in 10 ml of acetone was added at stirring 5 ml of 18% HCl , the mixture was cooled to -15°C , and 0.44 g (6.4 mmol) of NaNO_2 in 3 ml of H_2O was added. After 5 min the solution of the formed diazonium salt **Id** was diluted with 200 ml of 20% solution of NaCl , the mixture was stirred for 5 h, the reaction products were extracted into chloroform, the extract was washed with water, dried, the solvent was distilled off in a vacuum, and the residue



General view of crystallographically nonequivalent molecules in the structure **IIIf**.

was recrystallized from a mixture toluene–hexane, $1:1$. Yield 0.67 g (70%), mp 158 – 159°C (toluene–hexane, $1:1$). ^1H NMR spectrum (CDCl_3), δ , ppm: 2.35 s (3H , CH_3), 7.30 d (2H , C_6H_4 , J 8.0 Hz), 7.80 – 8.00 m (4H , $\text{C}_6\text{H}_4 + \text{H}^{6,7}$), 8.20 – 8.30 m (1H , $\text{H}^{5(8)}$), 8.55 – 8.70 m (1H , $\text{H}^{8(5)}$). Found, %: C 64.42 ; H 3.45 ; Cl 11.61 . $\text{C}_{16}\text{H}_{11}\text{ClN}_2\text{O}_2$. Calculated, %: C 64.33 ; H 3.71 ; Cl 11.87 .

3-(4-Acetylaminobenzoyl)indazole (IIf**).** A solution of diazonium salt **Ie** prepared from 1.0 g (4.0 mmol) of aniline **Ive** similarly to salt **Id** was diluted with 250 ml 20% solution of NaCl . After 5 min the separated precipitate was filtered off, washed with water, and dried. Yield of the chromatographically pure compound **IIf** 0.95 g (85%), mp 286 – 287°C (acetone). ^1H NMR spectrum [$(\text{CD}_3)_2\text{CO}$], δ , ppm: 2.15 s (3H , NCOCH_3), 7.37 t (1H , $\text{H}^{5(6)}$, J 7.5 Hz), 7.50 t (1H , $\text{H}^{6(5)}$, J 7.5 Hz), 7.75 d (1H , H^7 , J 7.5 Hz), 7.79 d (2H , $\text{H}^{3',5'}$, J 8.8 Hz), 8.44 m (3H , $\text{H}^4 + \text{H}^{2',6'}$), 9.50 br.s (1H , NHCO), 13.0 br.s (1H , H_{Ht}). Mass spectrum, m/z (I_{rel} , %): 279 [M] $^+$ (19.3), 280 [$M + 1$] $^+$ (3.7), 236 (7.7), 145 (6.2), 120 (22.9), 119 (3.7), 92 (10.4), 91 (7.4), 43 (100), 42 (9.2). Found, %: C 68.55 ; H 4.59 ; N 14.87 . $\text{C}_{16}\text{H}_{13}\text{N}_3\text{O}_2$. Calculated, %: C 68.81 ; H 4.69 ; N 15.05 .

3-(4-Aminobenzoyl)indazole (IIIf**).** To a solution of 0.30 g (1.1 mmol) of indazole **IIf** in 20 ml of dioxane was added 10 ml of 62% H_2SO_4 , the mixture was stirred at 94°C for 30 min and cooled. The separated precipitate was filtered off and charged into 20 ml of 5% Na_2CO_3 solution, it was stirred for 30 min and again filtered off, washed with water, and dried. Yield of the chromatographically pure compound **IIIf** 0.19 g (72%), mp 194 – 195°C (ethanol). ^1H NMR spectrum [$(\text{CD}_3)_2\text{CO}$], δ , ppm: 5.55 br.s (2H , NH_2), 6.77 d (2H , $\text{H}^{3',5'}$, J 8.4 Hz), 7.32 t

(1H, $H^{5(6)}$, J 7.5 Hz), 7.47 t (1H, $H^{6(5)}$, J 7.5 Hz), 7.72 d (1H, $H^{4(7)}$, J 7.5 Hz), 8.25–8.55 m (3H, $H^{7(4)} + H^{2',6'}$, J 8.4 Hz), 12.85 br.s (1H, H_{Ht}). Found, %: C 70.80; H 4.90. $\text{C}_{14}\text{H}_{11}\text{N}_3\text{O}$. Calculated, %: C 70.86; H 4.67.

The reaction progress was monitored by TLC on Silufol UV-254 plates (eluent chloroform–acetone, 10:1). ^1H NMR spectra were registered on a spectrometer Bruker DPX-200 in CDCl_3 or $(\text{CD}_3)_2\text{CO}$, internal reference TMS. Mass spectrum was measured on Finnigan MATinstrument. X-ray diffraction study of indazoleamine **III**: $\text{C}_{14}\text{H}_{11}\text{N}_3\text{O}$, automatic diffractometer Bruker-NoniusApex CCD, λMoK_α , rhombic crystals, at 20°C a 14.2761(5), b 7.1139(4), c 22.8889(9) Å, space group $Pca2_1$, Z 8, C_{calc} 1.356 g/cm³, R_1 0.0403 for 2208 reflections with $F_{hkl} \geq 4\sigma(F)$. The extinction was accounted for empirically by SADABS program [7]. The structure was solved by the direct method and refined in the full-matrix least-squares method in the anisotropic approximation for nonhydrogen atoms using software package SHELX-97 [8]. Hydrogen atoms were refined

in the rigid body approximation. The atomic coordinates, anisotropic thermal parameters, complete tables of bond distances and bond angles are deposited in the Cambridge Structural Database and can be obtained from the authors.

REFERENCES

1. Richter, V., *Ber.*, 1883, vol. 16, p. 677.
2. *Comprehensive Organic Chemistry*, Barton, D. and Ollis, W.D., Eds., Oxford: Pergamon, 1979, vol. 4, p. 122.
3. Vasilevsky, S.F. and Tretyakov, E.V., *Lieb. Ann.*, 1995, p. 775.
4. Fedenok, L.G. and Zolnikova, N.A., *Tetrahedron Lett.*, 2003, vol. 44, p. 5453.
5. Brown, H.C. and Okamoto, Y., *J. Am. Chem. Soc.*, 1958, p. 80, p. 4979.
6. Taylor, R., *J. Chem. Soc., Perkin Trans. 2*, 1978, p. 755.
7. Sheldrick, G.M., *SADABS. Program for Empirical X-ray Absorption Correction*, Bruker-Nonius, 1990–2004.
8. Sheldrick, G.M., *SHELX-97, Release 97-2*, University of Goettingen, Germany, 1998.