Chemistry of Heterocyclic Compounds, Vol. 42, No. 6, 2006

4',4"(5")-DIBENZO-18-CROWN-6-DIARYL-ACETOHYDROXAMIC ACIDS

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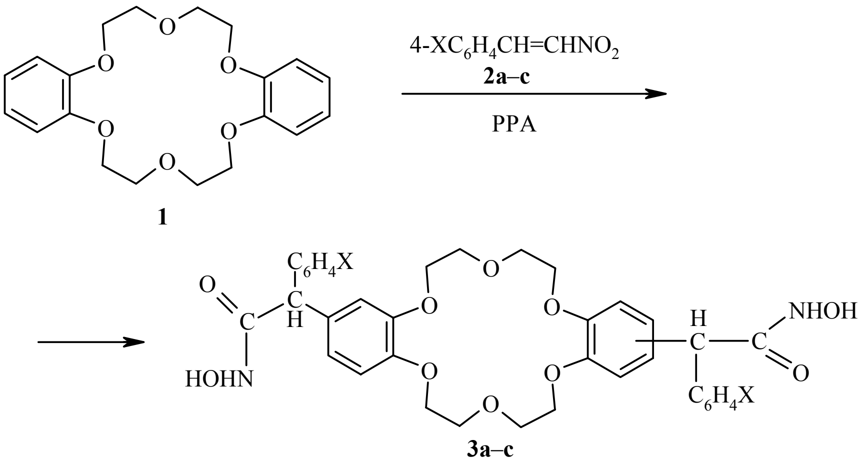
4',4"(5")-(Dibenzo-18-crown-6)diarylacetohydroxamic acids were obtained by the reaction of DB18C-6 with β-nitrostyrenes under the influence of polyphosphoric acid.

Keywords: 4',4"(5")-(dibenzo-18-crown-6)diarylacetohydroxamic acids, 4-β-dinitrostyrene, 4-methoxy-β-nitrostyrene, β-nitrostyrene, polyphosphoric acid.

It is well known that synthetic and natural compounds containing a hydroxamic acid fragment have antibiotic, anticancer, fungicidal, anti-inflammatory, antileukemic, and other forms of biological activity [1-4].

While continuing our investigations into reactions involving β-nitrostyrenes [5, 6] and making use of the known ability of these compounds to alkylate aromatic compounds [5-8], we realized for the first time the reaction of dibenzo-18-crown-6 ether (DB18C-6) (**1**) with a twice the amount of β-nitrostyrenes **2a-c** in the presence of polyphosphoric acid (PPA) in a **1**–PPA ratio of 1:20.



a X = H, **b** X = OMe, **c** X = NO_2

The reaction mostly took place at room temperature with spontaneous heating and with the formation of 4',4"(5")-(dibenzo-18-crown-6)diarylacetohydroxamic acids **3a-c** with yields between 37 (for **3c**) and 97-100% (for **3a**,**b**). The structure of the compounds was proved by their reprecipitation from an alkaline solution with CO_2, by a qualitative reaction with ferric chloride, and by means of the IR and ^1H NMR spectra.

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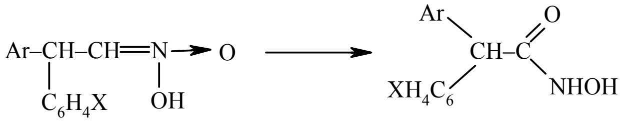
The fact that a hydroxamic acid is formed preferentially in the reaction of an aromatic compound with β-nitrostyrenes was established for the first time. Such a reaction path is probably determined by the specific characteristics of PPA as catalyst. All the reactions take place through a nitronic acid, which determines the structure of the product, depending on the nature of the catalyst, the conditions, and the structure of the radical. One of the directions in the transformation of the nitronic acid is its conversion into the hydroxamic acid.



EXPERIMENTAL

The ^{1}H NMR spectra were obtained in DMSO on a Varian XL-100 spectrometer (100 MHz) with HMDS as internal standard (δ 0.05 ppm). The IR spectra were obtained in tablets with potassium bromide on a Perkin-Elmer System 2000 IR Fourier spectrometer. Aluminum oxide "for chromatography" was used for TLC.

The initial β-nitrostyrenes were obtained by the previously described methods by condensation of the respective benzaldehydes with nitromethane [9]: Compound **2a**, mp 57-58°C (57-58°C [9]); compound **2b**, mp 86°C (86-87°C [10]); compound **2c**, mp 199-201°C (206-207°C [11]). The PPA was prepared by heating a mixture of orthophosphoric acid (*d* 1.7) with phosphoric anhydride at 110-115°C.

4',4"(5")-(Dibenzo-18-crown-6)diphenylacetohydroxamic Acid (3a). A mixture of the ether **1** (0.4 g, 1.1 mmol) and styrene **2a** (0.33 g, 2.2 mmol) was rubbed in a mortar and added to PPA (8.06 g) with vigorous stirring. The solution became crimson in color and heated slightly. After 2 h a test by TLC (1:2 acetone–hexane) showed the absence of the initial substances. The reaction mixture was decomposed with ice. The light-brown precipitate was filtered off, washed to a neutral reaction with water, and dried. (The substance exhibited thermochromic characteristics and on heating acquired a crimson color that disappeared on cooling.) The substance was dissolved in an aqueous (5%) solution of sodium hydroxide and filtered, and carbon dioxide was passed through the filtrate. The gelatinous precipitate was filtered off, dried, and recrystallized from 2-propanol; mp 163-167°C. An alcohol solution gave a positive reaction for hydroxamic acid with $FeCl_3$ (a red-violet color). Yield 97%. IR spectrum, ν, cm^{-1}: 3236, 3062 (OH, NH); 2920, 2880 (OCH_2 of macrocycle); 1668 (amide I); 1599 (amide II); 1557 (ArH). ^{1}H NMR spectrum, δ, ppm: 7.24 (10H, m, C_6H_5); 6.87 (6H, m, ArH DB18C6); 4.58 (2H, s, CH); 3.02-4.03 (16H, m, OCH_2).

4',4"(5")-(Dibenzo-18-crown-6)di-4-methoxyphenylacetohydroxamic Acid (3b). A mixture of the ether **1** (0.30 g, 0.8 mmol) and the styrene **2b** (0.29 g, 1.6 mmol) was rubbed in a mortar and added to PPA (6.18 g) with vigorous stirring. The solution became crimson in color. After 1 h the crimson glassy complex was decomposed with cold water. The obtained pinkish powder was dissolved in 5% sodium hydroxide. Carbon dioxide was passed into the solution, and the precipitate was dried in air; mp 66-69°C (2-propanol). Yield 100%. A solution of the dry product in chloroform gave a dark-crimson color with $FeCl_3$. IR spectrum, ν, cm^{-1}: 3393, 3065 (OH, NH); 2933, 2881 (OCH_2 of macrocycle); 1610 (amide I); 1596 (amide II). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.26 (4H, d, $J = 8.0$, C_6H_4); 6.95 (4H, d, $J = 4.0$, C_6H_4); 6.80 (6H, m, ArH, DB18C6); 4.62 (2H, s, CH); 3.67-4.11 (16H, m, OCH_2); 3.62 (6H, s, OCH_3).

4',4"(5")-(Dibenzo-18-crown-6)di-4-nitrophenylacetohydroxamic Acid (3c). A rubbed mixture of DB18C6 (0.27 g, 0.7 mmol) and the styrene **2c** (0.27 g, 1.4 mmol) was added with stirring to PPA (5.48 g). The solution gradually became green in color and heated to 35-40°C. The course of the reaction was monitored by TLC. After 2 h 30 min the initial crown ether was present in the mixture, and the reaction mixture was therefore heated at 50-60°C for 3 h 30 min. The reaction mass was decomposed with ice (the dark-blue solution became crimson in color), and the crimson precipitate was washed to a neutral reaction with water. The precipitate was treated with an aqueous solution of sodium hydroxide (5%), the undissolved impurity was filtered off, and the alkaline solution was neutralized with CO_2. We obtained 0.18 g of a red powder. Yield 37%; mp 161-164°C (acetonitrile). ^1H NMR spectrum, δ, ppm (J, Hz): 8.15 (4H, d, J = 7.5, C_6H_4); 7.50 (4H, d, J = 6.5, C_6H_4); 6.85 (6H, m, ArH DB18C6); 4.79 (2H, s, CH); 3.62-4.25 (16H, m, OCH_2 of macrocycle). IR spectrum, ν, cm^{-1}: 3395 (OH, NH); 2934 (OCH_2 of macrocycle); 1597 (amide I); 1557 (amide II); 1517, 1347 (NO_2).

REFERENCES

1. L. Bayer and O. Exner, *Angew. Chem.*, **86**, 419 (1974).
2. A. T. Pilipenko and O. S. Zul'fagirov, *Hydroxamic Acids* [in Russian], Nauka, Moscow (1989), 267 pp.
3. J. B. Neiland, *Science*, **156**, 1443 (1967).
4. Takase Munzaki and Okuyama Masao, Jpn. Patent Appl. 55-62050; *Ref. Zh. Khim.*, 17047 (1981).
5. A. D. Grebenyuk, M. Kholmatov, and I. P. Tsukervanik, *Zh. Obshch. Khim.*, **32**, 2654 (1962).
6. A. D. Grebenyuk N. Zaitseva, and T. Logunova, *Zh. Org. Khim.*, **1**, 691 (1965).
7. Ch. P. Hurd, May E. Nilson, and P. M. Wikholm, *J. Am. Chem. Soc.*, **72**,4697 (1950).
8. J. Ohvada, J. Ohta, and K. Studo, *Tetrahedron*, **43**, 297 (1987).
9. *Synthesis of Organic Preparations* [Russian translation], Izd. Inostr. Lit., Moscow (1949), Coll. 1, p. 308.
10. H. Kondo and S. Ishiwata, *Zbl.*, **11**, 55 (1928).
11. A. C. Huitric and W. D. Kumber, *J. Am. Chem. Soc.*, **78**, 614 (1956).