Chemistry of Heterocyclic Compounds, Vol. 35, No. 11, 1999

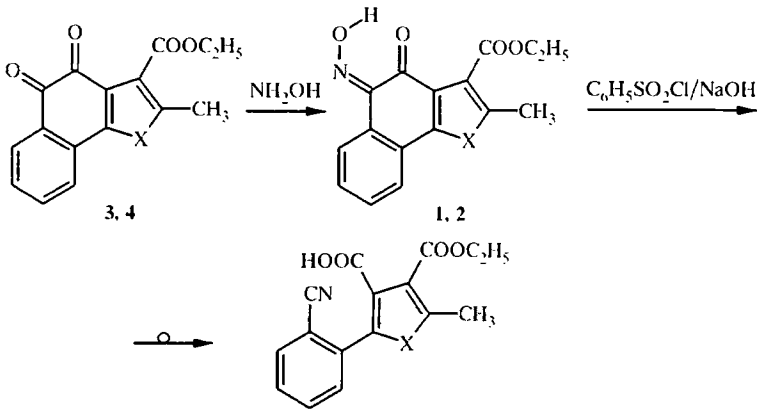
REARRANGEMENT OF 3-ETHOXYCARBONYL-5-HYDROXYIMINO-2-METHYL-4-OXONAPHTHO[1,2-*b*]FURAN AND 3-ETHOXYCARBONYL-5-HYDROXYIMINO-2-METHYL-4-OXO-1-PHENYLBENZO[*g*]INDOLE BY THE ACTION OF BENZENESULFONYL CHLORIDE IN AN ALKALINE MEDIUM

A. P. Stankyavichus, L. M. M. Stankyavichene, and P. B. Terent'ev

The treatment of 3-ethoxycarbonyl-2-methyl-4,5-dioxonaphtho[1,2-b]furan 5-monoximes and also the similarly substituted benzo[g]indole with benzenesulfonyl chloride in an alkaline medium give 5-(2-cyanophenyl)-3-ethoxycarbonyl-2-methylfuran-4-carboxylic and pyrrole-4-carboxylic acids with high yields as a result of a second-order Beckmann rearrangement. The structures of the initial and final compounds were confirmed by analysis of their mass spectra.

Earlier we showed that the monoximes of naphthoquinone [1], quinoline-3,4-quinone [2], isatin, and other heterocycles [3, 4] undergo fragmentation under the influence of arenesulfonyl chlorides in an alkaline medium with ring cleavage by a second-order Beckmann rearrangement and form *ortho*-cyanocinnamic or *ortho*-cyanoheteroarylcarboxylic acids. While continuing these investigations, we used the 5-monoximes of 3-ethoxycarbonyl-2-methylnaphtho[2,3-*b*]furan-4,5-quinone (**1**) and 3-ethoxycarbonyl-2-methylbenzo[g]indole-4,5-quinone (**2**), which we obtained with yields of 57-59% (Scheme 1) by the action of hydroxylamine on the corresponding quinones **3**, **4**, synthesized by the known methods [5].

Scheme 1



3, 4 **1, 2** **5, 6**

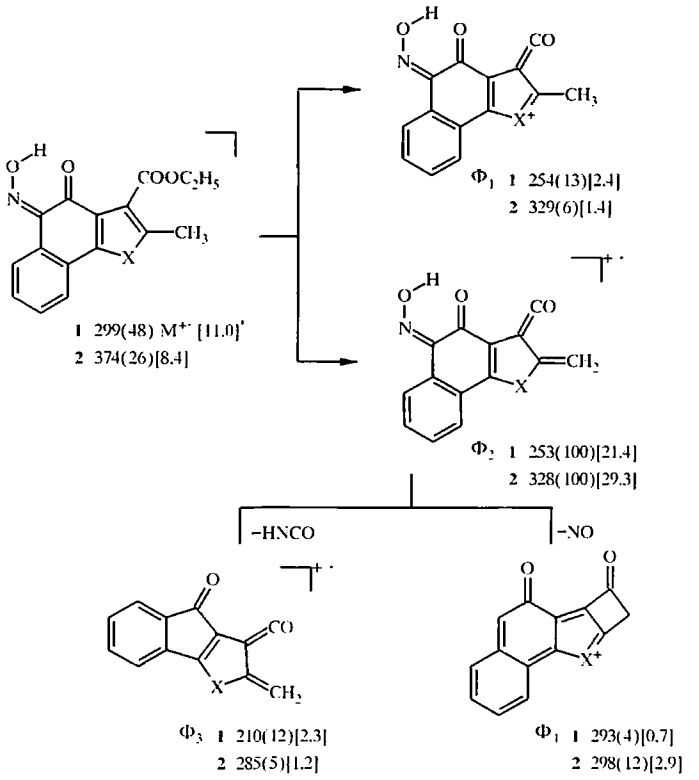
1, 3, 5 X = O; **2, 4, 6** X = N–C_6H_5

Institute of Cardiology, Kaunas Medical Academy, Kaunas 233007, Lithuania. M. V. Lomonosov Moscow State University, Moscow 119899, Russia; e-mail: petr@ms-bioorg.chem.msu.ru. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 11, pp. 1462-1465, November, 1999. Original article submitted June 17, 1998.

 0009-3122/99/3511-1272$22.00

The molecular ions of compounds **1** and **2** formed during electron impact eject an ethoxy group (ion Φ_1) at the first stage of dissociation (Scheme 2) but mainly eliminate an ethanol molecule (the ortho effect, ion Φ_2), after which they lose a molecule of HNCO (ion Φ_3) or even NO (ion Φ_4). The initial ejection of a carbon monoxide molecule, so characteristic of the mass-spectral behavior of the initial quinones (see Experimental) does not occur in this case.

Scheme 2



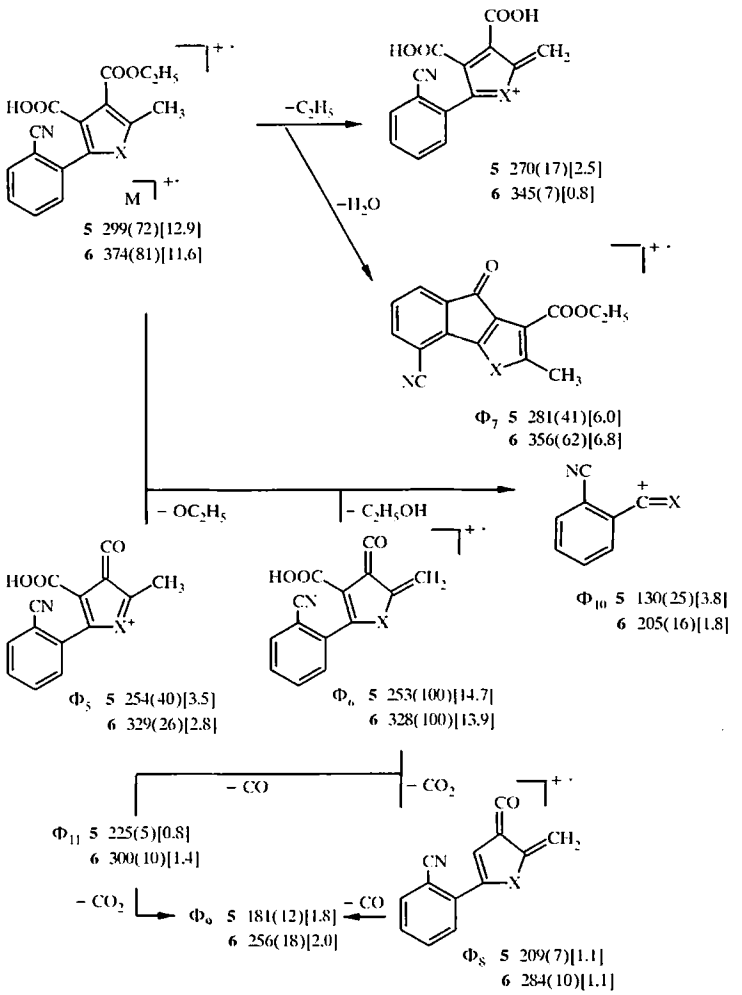
When a dilute solution of sodium hydroxide was added to an equimolar mixture of the respective oxime with benzenesulfonyl chloride, exothermic rearrangement was observed with the formation of the cyanophenyl-substituted heterocycles **5**, **6**, isobaric with the original monoximes, with yields of 80% or more after only 20-25 min (Scheme 1).

Their mass spectra contain peaks for highly stable molecular ions, which together with the strong elimination of the ethoxy group or ethanol molecule (ions Φ_5 and Φ_6, Scheme 3) effectively lose water, which is typical of *ortho*-arylpyrrolecarboxylic and furancarboxylic acids (ion Φ_7) [6]. The ions Φ_6 then eject successively CO_2 and CO molecules (ions Φ_8 and Φ_9) which confirms the presence of the carboxyl groups in the molecules of compounds **5** and **6**. On the other hand, the fragmentation of the molecular ions of these compounds is characterized by cleavage of the five-membered ring with the formation of the fragment ion Φ_{10}, and this demonstrates unambiguously the position of the cyanoaryl group in the molecules of compounds **1** and **2**. The single-stage nature of such dissociation of the M^+ ions with the formation of the ion Φ_{10} is confirmed by the presence of the peaks for metastable ions with apparent masses of 56.3 (calc. 56.5) and 112.5 (calc. 112.3) for compounds **5** and **6** respectively in the mass spectra.

---

* Here and subsequently: *m/z* (relative intensity, %), [intensity, $\%\Sigma_i$].

Scheme 3



It is interesting to note that whereas the $(M - C_2H_5)^+$ ions, typical of 3-ethoxycarbonyl-2-methylpyrroles [7], are almost completely absent in the mass spectra of the monoximes **1** and **2**, such ions have appreciable intensity in the mass spectra of the rearrangement products (both **5** and **6**).

EXPERIMENTAL

The purity of the compounds and the course of the reactions were monitored by TLC on Silufol with a 4:1 mixture of isopropyl alcohol and 10% aqueous ammonia as eluant for the oximes and acids and with iodine vapor as developer. The UV spectra were recorded on a Specord UV-Vis spectrometer in ethanol. The mass spectra were obtained on LKB-2091 and MX-1320 instruments at 70 eV with direct injection of the sample into the ion source.

The quinones **3** and **4** were synthesized by the previously described methods [8]. Mass spectrum of compound (**3**)[M^+ and the ten strongest peaks; *m/z* (relative intensity, %) (formation path)]: 284 (71) M^+, 256 (10) (M - CO) (ion A), 239 (11) (M - C_2H_5O), 238 (28) (M - C_2H_5OH) (ion B), 210 (100) (B - CO), 183 (13) (A - $CO_2C_2H_5$), 182 (99) (B - 2CO), 155 (7) (A - $CO_2C_2H_5$ - CO), 154 (5) (B - 3CO), 127 (17) (A - $CO_2C_2H_5$ - 2CO) 126 (14) (B - 4CO). Mass spectrum of compound **4**: 359 (100) (M^+), 331 (10) (M - CO), 330 (68) (M - CO - H)A, 314 (18) (M - C_2H_5O), 313 (12) (M - C_2H_5OH), 302 (53) (A - CO), 285 (75) (M - CO - C_2H_5OH), 257 (57) (B - CO), 256 (80) (B - CO - H), 230 (20) (B - CO - HCN), 228 (24) (B - H - 2CO).

3-Ethoxycarbonyl-5-hydroxyimino-2-methyl-4-oxonaphtho[1,2-*b*]furan (1). To a boiling solution of 2.84 g (10 mmol) of the quinone **3** in 35 ml of ethanol over 20 min we added dropwise a solution of 0.7 g (10 mmol) of hydroxylamine hydrochloride in 8 ml of water. The mixture was left overnight, and the precipitate was separated, washed with the smallest amount of water, and recrystallized from propanol. Yield 1.7 g (57%); mp 130-134°C (decomp.), R_f 0.64. Found %: C 64.02; H 4.39; N 4.90. $C_{16}H_{13}NO_5$ Calculated %: C 64.21; H 4.35; N 4.68

3-Ethoxycarbonyl-5-hydroxyimino-2-methyl-4-oxo-1-phenylbenzo[g]indole (2). The compound was obtained by analogy with compound **1** from 7.2 g (20 mmol) of the quinone **4** and 1.4 g (20 mmol) of hydroxylamine hydrochloride. Yield 4.4 g (59%); mp 190°C (decomp.) (propanol), R_f 0.54. Found %: C 70.23; H 4.65; N 7.37. $C_{22}H_{18}O_5N_2$. Calculated %: C 70.58; H 4.81; N 7.49.

5-(2-Cyanophenyl)-3-ethoxycarbonyl-2-methylfuran-4-carboxylic Acid (5). To a boiling solution of 1.5 g (5 mmol) of the oxime **1** and 0.8 ml (5 mmol) of benzenesulfonyl chloride in 50 ml of acetone while stirring we added 8 ml of a 10% solution of sodium hydroxide in such a way that the mixture boiled uniformly. It was then boiled for a further 20 min, 20 ml of a 5% solution of sodium bicarbonate was added, and the acetone was evaporated. The remaining aqueous solution was boiled with active charcoal and filtered. The filtrate was acidified with dilute hydrochloric acid (Congo red). The precipitate was separated, purified again with active charcoal, and dried. Yield 1.2 g (80%); mp 126°C (decomp.) (carbon tetrachloride), R_f 0.69. UV spectrum, λ_{max} (log ε), nm): 284 (4.09). Found %: C 64.38; H 4.19; N 4.70. $C_{16}H_{13}NO_5$. Calculated %: C 65.21; H 4.35; N 4.68.

5-(2-Cyanophenyl)-3-ethoxycarbonyl-2-methyl-1-phenylpyrrole-4-carboxylic Acid (6). The compound was obtained by analogy with compound **5** from 1.6 g (5 mmol) of the oxime **2** in 50 ml of dioxane. Yield of the chromatographically pure acid 1.4 g (87%); mp 128-130°C, R_f 0.55. Found %: C 70.19; H 4.94; N 7.32. $C_{16}H_{13}NO_5$. Calculated %: C 70.58; H 4.81; N 7.49. UV spectrum, λ_{max} (log ε, nm): 282 (4.48). When the product was boiled with a water–alcohol solution of alkali and then acidified 3,4-dicarboxy-5-(2-carboxyphenyl)-2-methyl-1-phenylpyrrole was obtained; mp 229-231°C. Published data: mp 230-233°C [8].

REFERENCES

1. A. N. Kost and A. P. Stankyavichus, *Zh. Org. Khim.*, **6**, 1022 (1970).
2. P. B. Terent'ev, L. Mazhilis, A. G. Kalandarishvili, and A. P. Stankyavichus, *Khim. Geterotsikl. Soedin.*, No. 8, 1052 (1986).
3. A. P. Stankyavichus, P. B. Terent'ev, and O. A. Solov'ev, *Khim. Geterotsikl. Soedin.*, No. 9, 1243 (1989).
4. A. N. Kost, A. P. Stankyavichus, L. N. Zhukauskaite, and I. M. Shulyakene, *Khim. Geterotsikl. Soedin.*, No. 4, 509 (1971).
5. A. N. Grinev, Hun Shii Tsun, and A. P. Terent'ev, *Zh. Obshch. Khim.*, **32**, 1951 (1962).
6. P. B. Terent'ev and A. P. Stankyavichus, *Mass Spectrometry of Biologically Active Nitrogen Compounds* [Russian translation], Mokslas, Vilnius (1987).
7. H. Budzikiewicz, C. Djerassi, and D. Williams, *Mass Spectrometry of Organic Compounds*, Holden-Day, San Francisco, London, Cambridge, Amsterdam (1967), p. 605.
8. A. N. Grinev, Hun Shii Tsun, and A. P. Terent'ev, *Zh. Obshch. Khim.*, **30**, 3668 (1960).