Reductive Acetylation of Some Naphthoquinones

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9-Acetylaminonaphtho[1,2-*b*:4,3-*b'*]bis[1,4]oxathiin-2,7-dione and 4,9-diacetoxy-8-acetylamino-2,3-dihydronaphtho[2,3-*b*]furan-2-one were synthesized by reductive acetylation reaction of the newly prepared compounds. 2-Methyl-8-nitro-2,3-dihydronaphtho[2,3-*b*]furan-3,4,9-trione was prepared *via* reaction of *O*-(5-nitro-1,4-naphthoquinon-2-yl)glycolic acid with polyphosphoric acid.

Many reactions of 1,4-naphthoquinones have been studied [1—4]. An important class of reactions is the 1,4-addition of nucleophilic reagents [5—10]. In this communication we report on some addition-oxidation reactions of the 5-nitro-1,4-naphthoquinone derivative (*I*) with some sulfur and oxygen nucleophiles. Additionally, the reductive acetylation was applied onto the produced new quinonoid structures with a view to synthesize new interesting heterocyclic ring systems.

Reaction of 5-nitro-1,4-naphthoquinone (*I*) with thioglycolic acid in ethanol gave 2,3-bis(2-carboxymethylthio)-5-nitro-1,4-naphthoquinone (*II*) (Scheme 1). The mechanistic pathway for the formation of this product involves the addition of thioglycolic acid to the α,β-unsaturated carbonyl compound (*I*) followed by oxidation of the resulting intermediate to the corresponding final isolable product *II*. The oxidizing agent is, most probably, the starting naphthoquinone molecule itself. The IR and ^{1}H NMR spectral data were found to be in complete agreement with the assigned structure. Refluxing compound *II* with a mixture of zinc, glacial acetic acid, and acetic anhydride afforded 9-acetylaminonaphtho[1,2-*b*:4,3-*b'*]bis[1,4]oxathiin-2,7-dione (*III*) as an unusual product. The pathway for this product was assumed to occur through the usual reductive acetylation process, followed by an intramolecular cyclodehydration reactions. The structure of *III* was assigned on the basis of its spectral data.

In an attempt to prepare analogous heterocyclic systems, compound *I* was allowed to react with glycolic acid in ethanol at the reflux temperature. The structure of the produced compound (*IVa*) was deduced on the basis of analytical and spectral data. The preferable formation of the bis product *II* may be due to the relatively higher nucleophilicity of thioglycolic acid with respect to its oxygen analogue. Reaction of *IVa* with zinc, glacial acetic acid, and acetic anhydride under similar reaction conditions gave the hitherto unknown 4,9-diacetoxy-8-acetylamino-2,3-dihydronaphtho[2,3-*b*]furan-2-one (*V*). Structure of this product was confirmed on the basis of ^{1}H NMR and IR spectral data (*cf.* Experimental). The formation of furan derivative (*V*) instead of the expected compound *VI* might be ascribed to the prior intramolecular cyclodehydration followed by reductive acetylation.

In continuation of this work, lactic acid was reacted with compound *I* in ethanol. Attempts for cyclization of the produced compound *IVb*, using the same reaction condition that was used for preparation of *V*, were unsuccessful. Conversion of this alkyloxy derivative *IVb* to the corresponding furan derivative (*V*) was affected successfully by treatment with polyphosphoric acid at 100 °C. Structural assignment of *VII* was based on its spectral analysis.

EXPERIMENTAL

Melting points are uncorrected. IR spectra were recorded on a Perkin—Elmer 157 infracord (KBr). ^{1}H NMR spectra were run on a 90 MHz Perkin—Elmer R-32 instrument using TMS as an internal standard. Chemical shifts are given in δ. Microanalytical data are measured at Microanalytical unit, Cairo University, Egypt.

2,3-Bis(2-carboxymethylthio)-5-nitro-1,4-naphthoquinone (*II*)

Thioglycolic acid (0.9 g; 0.01 mol) was added to a solution of *I* (2.0 g; 0.01 mol) in absolute ethanol (50 cm^3) and the reaction mixture was stirred for 6 h. Concentration of the resulting brown coloured solution afforded a sticky brownish yellow mass. Crystallization of the so formed product from benzene yielded orange crystals of m.p. = 190 °C, yield = 63 %. IR spectrum, $\tilde{\nu}$/cm^{-1}: 3460, 2900, 1680, 1535, and 1290. ^{1}H NMR spectrum, δ: 2.98, 3.11 (s, s, 2 × 2H, CH_2 protons), 12.52, 12.61 (s, s, 2 × 1H, COOH, exchangeable with D_2O), 7.91—8.31 (m, 3H, H_{arom}). For $C_{14}H_9NO_8S_2$ (M_r =

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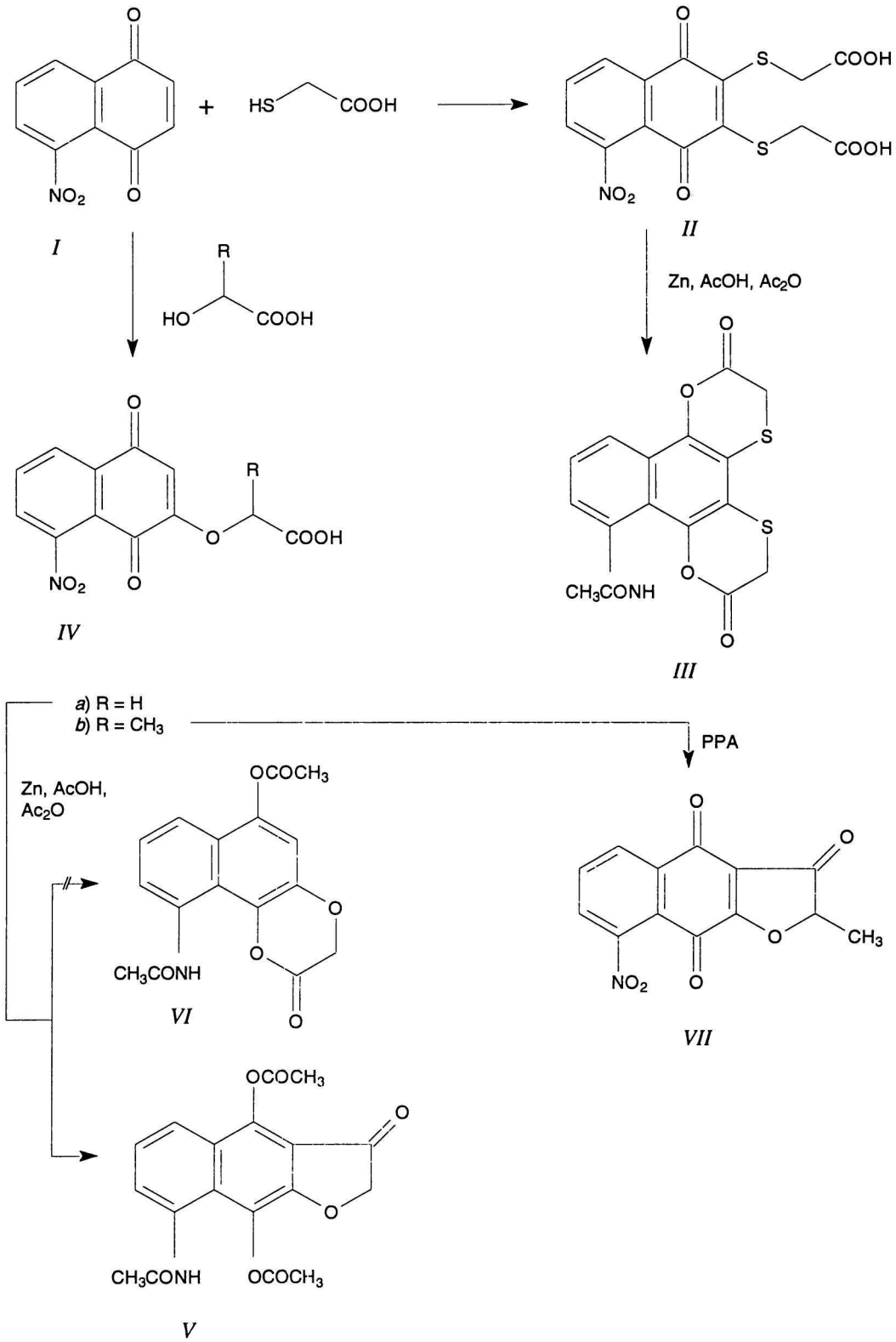

Scheme 1

383.36) w_i(calc.): 43.85 % C, 2.37 % H, 3.65 % N; w_i(found): 43.73 % C, 2.51 % H, 3.55 % N.

9-Acetylaminonaphtho[1,2-*b*:4,3-*b'*]bis[1,4]oxathiin-2,7-dione (*III*)

To a solution of *II* (3.8 g; 0.01 mol) in excess of glacial acetic acid, acetic anhydride (10 cm^3) and zinc dust (0.01 mol) were added and the reaction mixture was refluxed for about 5 h and concentrated. Addition of diethyl ether afforded a brown solid precipitate which was filtered off and recrystallized from chloroform/hexane mixture as brown crystals of m.p. = 270 °C, yield = 45 %. IR spectrum, $\tilde{\nu}/cm^{-1}$: 3300, 2850, 1770, 1710, and 1210. ^{1}H NMR spectrum ($CDCl_3$), δ: 2.13 (s, 3H, $COC\underline{H}_3$), 3.31, 3.52 (s, s, 4H, 2 × $C\underline{H}_2$ at C-3 and C-6), 7.63—7.96 (m, 3H, H_{arom}), 9.11 (s, 1H, N$\underline{H}$CO). For $C_{16}H_{11}O_5S_2N$ (M_r = 361.39) w_i(calc.): 53.17 % C, 3.07 % H, 3.88 % N; w_i(found): 53.41 % C, 3.39 % H, 3.72 % N.

O-(5-Nitro-1,4-naphthoquinon-2-yl)glycolic (*IVa*) and -lactic acid (*IVb*)

Compound *I* (0.01 mol) in absolute ethanol (30 cm^3) was treated with the corresponding hydroxy acid (0.01 mol in each case) and the reaction mixture was refluxed for 3 h where brilliant orange crystals were separated out. Recrystallization from benzene afforded the product as orange crystals.

IVa: M.p. = 210 °C, yield = 60 %. IR spectrum, $\tilde{\nu}/cm^{-1}$: 3450, 2860, 1700, 1680, 1500, and 1220. ^{1}H NMR spectrum ($CDCl_3$), δ: 12.81 (s, 1H, COO$\underline{H}$, exchangeable with D_2O), 3.42 (s, 2H, CH_2), 6.71 (s, 1H, C$\underline{H}$=C), 7.63—7.91 (m, 3H, H_{arom}). For $C_{12}H_7O_7N$ (M_r = 277.19) w_i(calc.): 51.99 % C, 2.55 % H, 5.05 % N; w_i(found): 52.09 % C, 2.46 % H, 5.13 % N.

IVb: M.p. = 230 °C, yield = 50 %. IR spectrum, $\tilde{\nu}/cm^{-1}$: 3410, 2900, 1690, 1680, and 1530. ^{1}H NMR spectrum (DMSO), δ: 1.46 (d, 3H, $C\underline{H}_3$), 12.91 (s, 1H, COO$\underline{H}$, exchangeable with D_2O), 3.21 (q, 1H, C$\underline{H}$), 6.42 (s, 1H, C$\underline{H}$=C), 7.61—7.92 (m, 3H, H_{arom}). For $C_{13}H_9O_7N$ (M_r = 291.21) w_i(calc.): 53.62 % C, 3.11 % H, 4.81 % N; w_i(found): 53.77 % C, 3.32 % H, 5.01 % N.

4,9-Diacetoxy-8-acetylamino-2,3-dihydronaphtho[2,3-*b*]furan-2-one (*V*)

This product was prepared adopting the same procedure that was used in preparation of compound *III* starting from *IVa*. The pure product (m.p. = 180 °C) was obtained in 70 % yield. IR spectrum, $\tilde{\nu}/cm^{-1}$: 3210, 1695, 1690, 1685, and 1510. ^{1}H NMR spectrum (DMSO), δ: 1.82 (s, 3H, NCOC$\underline{H}_3$), 2.31, 2.49 (s, s, 6H, 2 × OCOC$\underline{H}_3$), 4.11 (s, 2H, C$\underline{H}_2$), 7.63—7.89 (m, 3H, H_{arom}). For $C_{18}H_{15}O_7N$ (M_r = 357.31) w_i(calc.): 60.50 % C, 4.23 % H, 3.91 % N; w_i(found): 60.69 % C, 4.34 % H, 4.01 % N.

2-Methyl-8-nitro-2,3-dihydronaphtho[2,3-*b*]furan-3,4,9-trione (*VII*)

To compound *IVb* (0.2 g) excess polyphosphoric acid (20 g) was added and the mixture was stirred on an oil bath at 170 °C for 2 h and cooled. The reaction mixture was poured on ice-cold water and the precipitated brown product was filtered off and recrystallized from ethanol in 80 % yield of m.p. = 220 °C; IR spectrum, $\tilde{\nu}/cm^{-1}$: 2700, 1690, 1680, 1530, and 1220. ^{1}H NMR spectrum ($CDCl_3$), δ: 1.46 (d, 3H, $C\underline{H}_3$), 4.56 (q,1H, C$\underline{H}$), 7.98—8.21 (m, 3H, H_{arom}). For $C_{13}H_7O_6N$ (M_r = 273.19) w_i(calc.): 57.15 % C, 2.58 % H, 5.13 % N; w_i(found): 57.41 % C, 2.63 % H, 5.32 % N.

REFERENCES

1. Smell, J. M. and Weissberger, A., *J. Am. Chem. Soc. 61*, 450 (1939).
2. Thomson, R. H., *J. Org. Chem. 16*, 1802 (1951).
3. Blackhall, A. and Thomson, R. H., *J. Chem. Soc. 1953*, 1138.
4. Fieser, L. E. and Turner, R. B., *J. Am. Chem. Soc. 69*, 2335 (1947).
5. Crosby, A. H. and Lutz, R. E., *J. Am. Chem. Soc. 78*, 337 (1956).
6. Dodgson, J. W., *J. Chem. Soc. 1930*, 2498.
7. Huisgen, R., *Angew. Chem. 75*, 604 (1963).
8. Huisgen, R., *J. Org. Chem. 41*, 403 (1976).
9. Eistert, B. and Bock, G., *Chem. Ber. 92*, 1274 (1959).
10. Inove, A., Nomura, Y., Kuroki, N., and Konishi, Y., *Gaei Kagaki Shi 16*, 536 (1958).