Thermal and base-induced rearrangements of furoxanylketones phenylhydrazones

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The thermal recyclization of 3-methyl-4-acetyl(benzoyl)furoxans [3-methyl-4-acetyl(benzoyl)-1,2,5-oxadiazole 2-oxides] phenyl-hydrazones to oximes of 5-acetyl-4-phenyl(methyl)-2-phenyl-2*H*-1,2,3-triazole 1-oxide and the base-induced mononuclear hetero-cyclic rearrangement of the above phenylhydrazones to 4-phenyl(methyl)-5-(1-nitroethyl)-2-phenyl-2*H*-1,2,3-triazoles were found.

Mononuclear heterocyclic rearrangements in the series of azoles have been studied rather extensively.[1–6] These rearrangements involve a nucleophilic attack on a nitrogen atom of the azole followed by the rupture of an adjacent bond to form a new heterocycle. As a rule, they are initiated thermally or in the presence of bases; in a number of cases, these reactions are reversible. Similar rearrangements in the series of furoxanes were examined by the case of benzofuroxans[7–9] (the Boulton–Katritzky rearrangement). However, of noncondensed furoxan derivatives, only oximes[10–13] have been shown to undergo mono-nuclear heterocyclic rearrangements. In particular, the base-catalysed rearrangement of the *Z*-isomer of 4-benzoyl-3-methyl-furoxan oxime to 3-(1-nitroethyl)-4-phenylfurazan was de-scribed[10,11] (Scheme 1). Recently,[14] the thermal recyclization of the diazenofuroxanyl fragment in 4,4′-bis(acetamido)-3,3′-azofuroxan derivatives to the 4-nitro-1,2,3-triazole unit was found. This reaction involves two consecutive mononuclear hete-rocyclic rearrangements (Scheme 1). Thus, mononuclear hetero-cyclic rearrangements of furoxans can be convenient for pre-paring other heterocyclic systems.
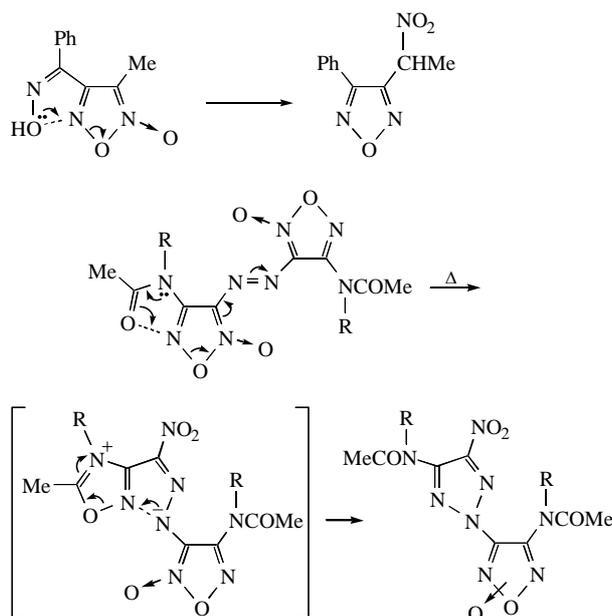
Scheme 1

In this work, we used 4-benzoyl- and 4-acetyl-3-methyl-furoxan hydrazones[15,16] **1a,b** as starting compounds. The reac-tions were initiated either thermally or in the presence of vari-ous bases. The thermal rearrangement was performed by boiling solutions of **1a,b** in *o*-xylene; only the *Z*-isomers of parent compounds **1a,b** entered into the reaction. However, in both cases, oximes of 5-acetyl-4-phenyl(methyl)-2-phenyl-2*H*-1,2,3-triazole 1-oxide **3a,b**† (Scheme 2) were obtained in place of expected 4-phenyl(methyl)-5-(1-nitroethyl)-2-phenyl-2*H*-1,2,3-triazoles **2a,b**. It is likely that the reaction began with the rupture of the O(1)–N(2) bond in a furoxan ring rather than with the attack of the NH group of a hydrazone on the N(5) atom of

a furoxan, as would be expected in the case of classical mono-nuclear heterocyclic rearrangements. This bond rupture resulted in the formation of dinitrosoethylene intermediates **4a,b** fol-lowed by the reaction of one nitroso group with a phenyl-hydrazone moiety to form 1,2,3-triazole-1-oxide and the trans-formation of the other nitroso group into an oxime group. The thermal ring-opening of a furoxan ring to dinitrosoethylene was

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*5-(1-Nitroethyl)-2,4-diphenyl-2*H-*1,2,3-triazole* **2a**: yield 40%, mp 90–91 °C (hexane), R_f 0.71 (eluent: CHCl₃). ^{1}H NMR (CDCl₃) δ: 2.1 (d, 3H, Me, [3]J 8 Hz), 5.92 (q, 1H, CH, [3]J 8 Hz), 7.5 (m, 6H, Ph), 7.75 (m, 2H, Ph), 8.15 (m, 2H, Ph). ^{13}C NMR (CDCl₃) δ: 18.7 (Me), 77.76 (CH–NO₂), 119.0, 128.1, 128.2, 129.1, 129.25, 129.34, 139.4 (Ph), 140.6 (C-5 in triazole ring), 147.9 (C-4 in triazole ring). IR (ν/cm⁻¹): 660, 690, 740 (triazole ring), 1360, 1390, 1505, 1570 (NO₂), 1600 (Ph), 2910, 2950 (CH). MS, *m/z*: 294 (M⁺).

*5-(1-Nitroethyl)-4-methyl-2-phenyl-2*H-*1,2,3-triazole* **2b**: yield 15%; mp 43-4 4 °C (hexane), R_f 0.78 (eluent: CHCl₃). ^{1}H NMR (CDCl₃) δ: 2.05 (d, 3H, Me, [3]J 7.5 Hz), 2.45 (s, 3H, Me), 5.8 (q, 1H, CH, [3]J 7.5 Hz), 7.4 (m, 3H, Ph), 8.05 (m, 2H, Ph). IR (ν/cm⁻¹): 670, 690, 760 (triazole ring), 1280, 1300, 1520, 1560 (NO₂), 1600 (Ph), 2940, 2960 (CH). MS, *m/z*: 232 (M⁺).

*5-(1-Hydroximinoethyl)-2,4-diphenyl-2*H-*1,2,3-triazole 1-oxide* **3a**: yield 67%, mp 186–18 7 °C (benzene), R_f 0.65 (eluent: Pr^{i}OH–CHCl₃, 1:25). ^{1}H NMR ([²H₆]DMSO) δ: 2.25 (s, 3H, Me), 7.7 (m, 10H, 2Ph), 11.9 (s, 1H, =NOH). ^{13}C NMR (CDCl₃) δ: 12.5 (q, Me, [1]J 130.2 Hz), 122.35, 124.5, 126.3, 127.45, 128.0, 128.4, 129.15, 129.5, 130.1, 130.4 (2Ph), 134.2 (C-5 in triazole ring), 142.7 (C=NOH), 143.9 (C-4 in triazole ring). IR (ν/cm⁻¹): 680, 700, 730 (triazole ring), 1310, 1320 (N→O), 1440, 1480, 1495, 1510 (Ph), 1590 (C=N), 3200 (OH). MS, *m/z*: 294 (M⁺).

*5-(1-Hydroximinoethyl)-4-methyl-2-phenyl-2*H-*1,2,3-triazole 1-oxide* **3b**: yield 48%, mp 124–125 °C (benzene), R_f 0.46 (eluent: Pr^{i}OH–CHCl₃, 1:25). ^{1}H NMR ([²H₆]DMSO) δ: 2.2 (s, 3H, Me), 3.25 (s, 3H, Me), 7.55 (m, 3H, Ph), 7.8 (m, 2H, Ph), 11.75 (s, 1H, =NOH). IR (ν/cm⁻¹): 620, 660, 700 (triazole ring), 1300 (N→O), 1510 (Ph), 1590 (C=N), 3060 (CH), 3190 (=NOH). MS, *m/z*: 232 (M⁺).

*5-Acetyl-2,4-diphenyl-2*H-*1,2,3-triazole 1-oxide* **5a**: yield 95%, mp 72–73 °C, R_f 0.64 (eluent: CHCl₃). ^{1}H NMR ([²H₆]acetone) δ: 2.7 (s, 3H, Me), 7.5 (m, 3H, Ph), 7.65 (m, 3H, Ph), 7.8 (m, 2H, Ph), 8.05 (m, 2H, Ph). ^{13}C NMR ([²H₆]acetone) δ: 20.65 (Me), 124.6, 128.9, 129.9, 130.06, 130.54, 130.7 (Ph), 135.5 (C-5 in triazole ring), 146.4 (C-4 in triazole ring), 189.25 (C=O). [14]N NMR ([²H₆]acetone) δ: –7 6.5 (N→O). IR (ν/cm⁻¹): 640, 700 (triazole ring), 1310 (N→O), 1432, 1464, 1472, 1496 (Ph), 1680 (C=O), 2960 (CH). MS, *m/z*: 279 (M⁺).

*5-Acetyl-4-methyl-2-phenyl-2*H-*1,2,3-triazole 1-oxide* **5b**: yield 95%, mp 52-5 4 °C, R_f 0.68 (eluent: CHCl₃). ^{1}H NMR ([²H₆]DMSO) δ: 2.45 (s, 3H, Me), 2.6 (s, 3H, Me), 7.6 (m, 3H, Ph), 7.85 (m, 2H, Ph). [14]N NMR ([²H₆]acetone) δ: –7 6 (N→O). IR (ν/cm⁻¹): 600, 650, 690, 730 (triazole ring), 1305 (N→O), 1480, 1520, 1590 (Ph), 1680 (C=O), 2960 (CH). MS, *m/z*: 217 (M⁺).

*5-Acetyl-2,4-diphenyl-2*H-*1,2,3-triazole* **6a**: yield 25%, mp 61-6 2 °C (MeOH), R_f 0.60 (eluent: CHCl₃). ^{1}H NMR (CDCl₃) δ: 2.78 (s, 3H, Me), 7.5 (m, 6H, Ph), 8.05 (m, 2H, Ph), 8.2 (m, 2H, Ph). IR (ν/cm⁻¹): 670, 700, 740, 760 (triazole ring), 1500, 1600 (Ph), 1690 (C=O), 2950, 3030 (CH). MS, *m/z*: 263 (M⁺).

postulated in a number of reactions.[17] With the use of benzo-furoxans as an example, both of the nitroso groups in a dinitroso-benzene intermediate were trapped by appropriate traps.[18] How-ever, such a reaction of both of the nitroso groups derived from a noncondensed furoxan derivative is reported for the first time.
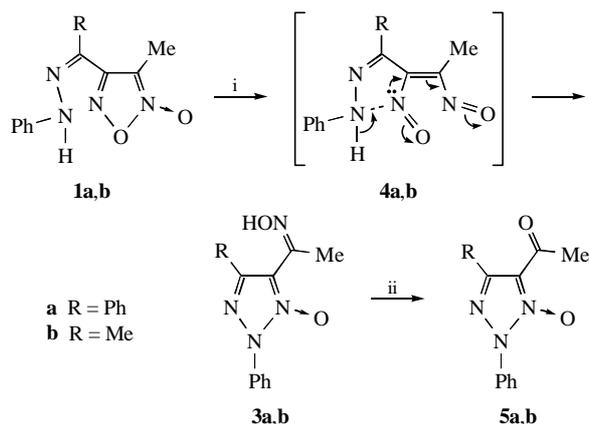
Scheme 2 *Reagents and conditions*: i, *o*-xylene, 150 °C (reflux), 24 h; ii, 20% HCl, steam distillation.

The structures of compounds **3a,b** and **5a,b** were confirmed by elemental analysis, IR spectroscopy, ¹H, ¹³C and ¹⁴N NMR spectroscopy and mass spectrometry. The spectroscopic charac-teristics correspond to literature data.[19,20] In the ¹⁴N NMR spec-trum, a signal of the *N*-oxide nitrogen atom was detected only after the hydrolysis of oxime groups to ketone groups with the formation of acetyl derivatives **5a,b** (Scheme 2).

Classical mononuclear heterocyclic rearrangements of parent phenylhydrazones **1a,b** were performed only in the presence of bases at different temperatures. In all cases the reaction mixture was acidified in order to isolate target compounds. Of the bases examined [aqueous NaOH solutions, sodium ethoxide, sodium methylsulfinyl carbanion[21] (demsil sodium) and Bu^{t}OK], a solu-tion of Bu^{t}OK in DMF at 10 °C was found to be most efficient, although a small amount of target product **2a** was separated by preparative TLC on silica gel after the reaction between com-pound **1a** with sodium ethoxide. In this case, the major portion of parent **1a** underwent decomposition under reaction conditions. This is likely due to the well-known sensitivity of acylfuroxans to bases.[22(a),(b)] In the case of Bu^{t}OK the decomposition of parent compounds was also observed, which was more pronounced with **1b**. In this connection, a higher yield was attained for **2a**† (Scheme 3).
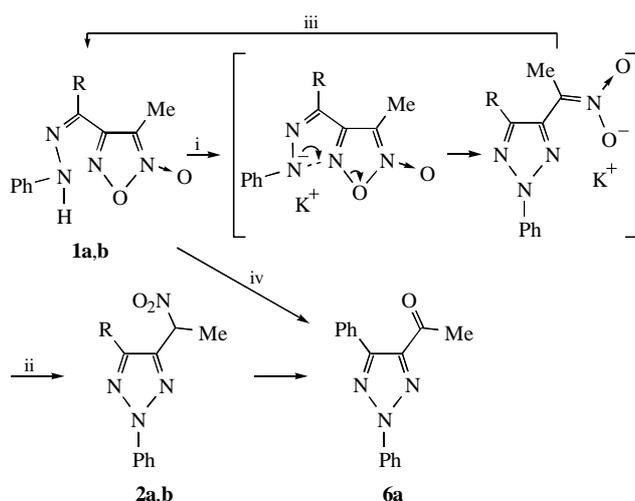
Scheme 3 *Reagents and conditions*: i, Bu^{t}OK, DMF, 10 °C, 8–10 h; ii, 5% HCl; isolation by preparative TLC, SiO₂ (eluent: CHCl₃); iii, R = Ph, H₂O, 20 °C, 20 min; iv, R = Ph, Bu^{t}OK, DMF, 120–140 °C, 2 h, then H₂O, isolation by preparative TLC, SiO₂ (eluent: CHCl₃).

An attempt to isolate **2a** by slowly adding water drop by drop to reaction mixture (without acidification) resulted in parent phenylhydrazone **1a**. It is evident that a reverse mononuclear heterocyclic rearrangement of product **2a** (as *aci*-form) into parent furoxan phenylhydrazone **1a** was observed in an aqueous alkaline medium. In this case, an oxygene atom of the *aci*-nitro group anion could attack nitrogen atom of 1,2,3-triazole ring (Scheme 3). The rearrangement of **1a** in the presence of Bu^{t}OK on heating resulted in 3-acetyl-2,4-diphenyl-2*H*-1,2,3-triazole **6a**† (Scheme 3). The formation of compound **6a** can be explained by the participation in a Nef-type reaction[23] of 5-(1-nitroethyl)-triazole **2a** formed at the first stage. The formation of ketone **6a** in insignificant amounts was also observed when the reaction was performed at 10 °C (TLC monitoring).

Thus, we found the following two new rearrangements in the series of noncondensed furoxan derivatives: a base-induced clas-sical mononuclear heterocyclic rearrangement of 3-methyl-4-benzoyl(acetyl)furoxans phenylhydrazones **1a,b** to 4-phenyl-(methyl)-5-(1-nitroethyl)-2-phenyl-2*H*-1,2,3-triazoles **2a,b**, which was found to be reversible, and a thermal recyclization of phenylhydrazones **1a,b** to oximes of 5-acetyl-4-phenyl(methyl)-2-phenyl-2*H*-1,2,3-triazole-1-oxides **3a,b**.

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