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Benzohydroxamic acid addition to propiolate esters—a reinvestigation

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Abstract

Addition of benzohydroxamic acid to propiolate esters gives 1,4,2-diozaxoles which originate, by base-catalysed ring opening with NaH, the isomeric *O*-vinyl hydroxamic acids. These compounds on thermolysis afford 1,3-oxazoles. © 2000 Elsevier Science Ltd. All rights reserved.

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As part of our program to explore the utility of enehydroxylamines in 3,3′-sigmatropic rearrangements,[1,2] it was decided to study the base catalysed ring opening of *N*-acyloxaziridines[3,4] of type **1** (cf. Scheme 1). That prompted us to prepare **1** (R = Ph, R′ = Me) by a recently reported general method,[5] i.e. a Michael addition of benzohydroxamic acid to methyl propiolate catalysed by *N*-methyl morpholine in CH_3CN at rt. The product obtained as a colourless oil[6] (yield >90%) possessed a ^1H NMR spectrum identical to that reported.[7] However it failed to release iodine from an iodide solution in acid,[3,8] and was thermally stable (110°C/3 h), a behaviour which is inconsistent with the proposed oxaziridine structure[8] **1**. Its molecular formula ($C_{11}H_{11}NO_4$), and mass spectrum suggested that the product could be the thermodynamically more stable isomeric 1,4,2-dioxazole **2a**[9] (Scheme 1) formed by ring closure of the initially generated *O*-vinylcarbomethoxy benzohydroxamic acid **3b**/**4b**.

A careful literature search revealed that the ethyl ester **2b** had in fact been obtained via a similar Michael addition of benzohydroxamic acid to ethyl propiolate in DMSO containing $NaCH_2SOCH_3$.[10] Compound **2b**, thus secured, was found to be *identical* in all respects (^1H, ^{13}C NMR, IR, TLC) with the product derived from *the same reaction partners and N-methyl morpholine in CH_3CN at rt*.

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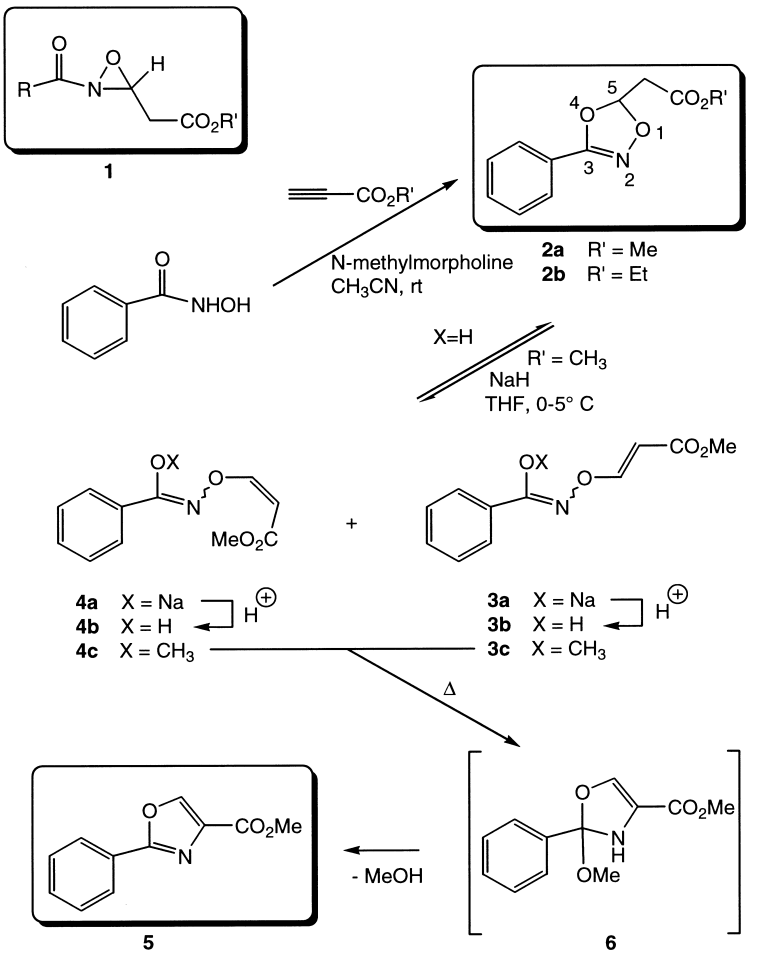

Scheme 1.

Methyl α-(3-phenyl-1,4,2-dioxazol-5-yl)-propionate (**2a**) in THF at 0–5°C, on treatment with NaH, led to a 5.5:1 mixture of sodium salts **3a** and **4a**, which on careful acidification afforded **3b** and **4b**.[11] These tended to revert slowly to **2a** either on standing at room temperature or during silica gel chromatography. The methyl ethers **3c** and **4c**,[12] obtained almost quantitatively by methylation of **3b** and **4b** with CH_2N_2, on thermolysis (220°C; 15 min) yielded the 1,3-oxazole[13] **5** in ca. 20% yield.[14] Similar thermal and photochemical[15,16] fragmentation reactions have been described and found to be of synthetic value.[2]

In conclusion, Michael addition of benzohydroxamic acid to propiolate esters *does not afford*, *as claimed*, *oxaziridines*, but instead leads to the isomeric 1,4,2-dioxazoles. These in turn, under aprotic basic conditions, suffer ring opening to the corresponding *O*-vinyl hydroxamic acid derivatives.

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6. Experimental selected data: **2a**, colourless oil, bp 104–106°C/0.1 mmHg (Ref. 9: 134–136°C/0.6 mmHg); IR 1739 (C=O), 1625 (C=N); ^{1}H NMR ($CDCl_3$, TMS, 400 MHz): δ 7.78 (2H, d, *J* 7.3 Hz, *ortho*-ArH), 7.49 (1H, t, *J* 7.3 Hz, *para*-ArH), 7.42 (2H, t, *J* 7.3 Hz, *meta*-ArH), 6.49 (1H, t, *J* 5.2 Hz, O–CH–O), 3.76 (3H, s, OMe), 2.95 (2H, d, *J* 5.2 Hz, CH_2); ^{13}C NMR 168.4 (C=O), 158.7 (C=N), 105.7 (O–CH–O), 52.1 (OCH_3), 39.1 (CH_2); *m*/*z* 221 (M^+), 205, 148, 121, 120, 119, 105, 104, 103, 77 (100%); HRMS found 221.0684, calc. 221.0688.
7. The δ value of the O–CH–O proton is incorrectly reported in Ref. 5 and it coincides with the value reported here; Professor E. K. Ryu, private communication.
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11. **3b**: IR (film) 3500 (OH), 1714 (C=O), 1635 (C=N); ^{1}H NMR ($CDCl_3$): δ 10.6 (1H, bs, OH exchanges with D_2O), 7.81 (2H, d, *J* 7.5 Hz, *ortho*-ArH), 7.65 (1H, d, *J* 12.3 Hz, O–CH=C), 7.52 (1H, t, *J* 7.2 Hz, *para*-ArH), 7.41 (2H, t, *J* 7.5 Hz, *meta*-ArH), 5.62 (1H, d, *J* 12.3 Hz, O–C=CH), 3.67 (3H, s, OCH_3); ^{13}C NMR 167.5 (O=C–O), 162.1 (C=N), 97.9 (O=C–*C*H), 51.0 (O–CH_3); HRMS found 221.0684, calc. 221.0688. **4b**: IR ($CHCl_3$) 3364 (OH), 1700 (C=O), 1639 (C=N); ^{1}H NMR ($CDCl_3$): δ 10.9 (1H, bs, OH exchanges with D_2O), 7.86 (2H, d, *J* 7.5 Hz, *ortho*-ArH), 7.51–7.46 (1H, m, *para*-ArH), 7.45–7.39 (3H, m, 2×*meta*-ArH, O–CH=C), 5.01 (1H, d, *J* 7.4 Hz, O–C=CH), 3.71 (3H, s, OCH_3); ^{13}C NMR 166.6 (O=C–O), 160.7 (C=N), 94.6 (O=C–*C*H), 51.0 (O–CH_3); HRMS found 221.0678, calc. 221.0688.
12. HRMS found 235.0847, calc. 235.0845. **3c**: ^{1}H NMR ($CDCl_3$) 7.92 (1H, d, *J* 12.4 Hz, O–CH=C), 5.72 (1H, d, *J* 12.4 Hz, O–C=CH), 4.02 (3H, s, $NOCH_3$), 3.72 (3H, s, OCH_3). **4c**: ^{1}H NMR ($CDCl_3$) 7.25 (1H, d, *J* 7.4 Hz, O–CH=C), 4.92 (1H, d, *J* 7.4 Hz, O–C=CH), 4.30 (3H, s, $NOCH_3$), 3.71 (3H, s, OCH_3).
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14. **5**: mp 85–87°C (ether–*n*-hexane) (Ref. 13: mp 85–87°C), IR 1729 (C=O), 1605; ^{1}H NMR 8.25 (1H, s, C=CH), 3.91 (3H, s, OCH_3); ^{13}C NMR 162.6 (O=C–O), 161.8 (C=N).
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