Intramolecular Electron Transfer in the Novel Photoreaction of some β,γ-Unsaturated Oxime–Boron Trifluoride Complexes. A New Synthetic Path to Dihydroisoxazoles

Diego Armesto,[a]* John C. Barnes,[b] William M. Horspool,[b]* and Fernando Langa[b]

[a] *Departamento de Química Orgánica, Facultad de Ciencias Químicas, Universidad Complutense, 28040-Madrid, Spain*

[b] *Department of Chemistry, The University, Dundee DD1 4HN, Scotland*

β,γ-Unsaturated oximes are photochemically reactive in benzene solution when irradiated in the presence of boron trifluoride–diethyl ether; typically 2,2-dimethyl-4,4-diphenylbut-3-enal oxime affords a low yield of 2,2-diphenyl-3,3-dimethylcyclopropanecarboxaldehyde by the aza-di-π-methane rearrangement, and a principal product (48%) identified by *X*-ray diffraction analysis as 4,4-dimethyl-5-(diphenylhydroxymethyl)-4,5-dihydroisoxazole.

Our study of the photochemical reactivity of β,γ-unsaturated imines has resulted in the discovery of the acyclic aza-di-π-methane (ADPM) reaction.[1—3] Reactivity of this type appears to be dependent upon the ionization potential of the nitrogen lone pair and the oxime (**1a**) with a relatively low ionization potential is unreactive by this mode,[2] as is the β,γ-unsaturated oxime ether (**2**).[4] The ionization potential can be raised by the introduction of an electron withdrawing group as in the oxime acetate (**3**) which is reactive in the ADPM rearrangement yielding the cyclopropyl oxime acetate (**4a**) (Scheme 1).[5] A similar effect has been observed for the related *N*-aryl-[3] and *N*-benzyl-imines (**5**).[6] It is conceivable that alternative methods of inhibiting electron transfer from the nitrogen could be used. This note describes the influence of boron trifluoride–diethyl ether on the photochemical reactivity of the oximes (**1**).

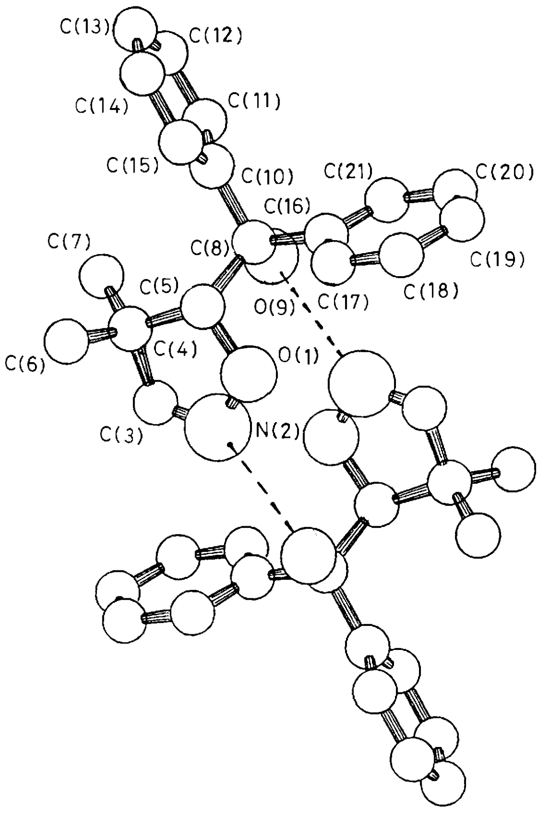
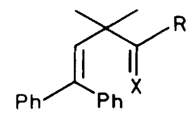
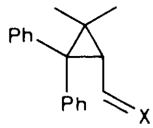


Figure 1. Molecular structure of (**8a**) as hydrogen bonded dimer showing crystallographic numbering scheme. Bond lengths in the heterocycle, are O(1)–N(2) 1.409(5), N(2)–C(3) 1.263(6), C(3)–C(4) 1.497(7), C(4)–C(5) 1.560, and C(5)–O(1) 1.448(5) Å.

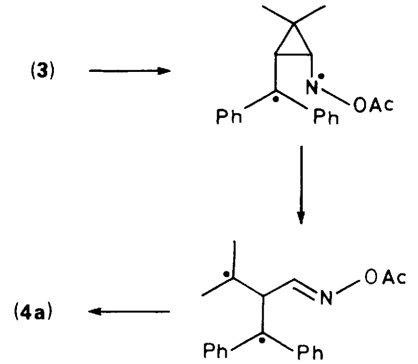
The oxime [(**1a**) 2.8 mmol], along with a stoicheiometric amount of boron trifluoride–diethyl ether in benzene (380 ml), was purged with oxygen-free nitrogen and irradiated through Pyrex for 4 h. Regular monitoring of the mixture showed the disappearance of starting material and the formation of other products. Work-up in a conventional manner† afforded a mixture of the aldehyde [(**6**) 5%], by hydrolysis of the starting material, the cyclopropyl aldehyde [(**7**) 3%], by hydrolysis of the corresponding oxime (**4b**), starting material [(**1a**) 19%], and an unknown product (48%) which was not isomeric with starting material.‡ The identification of this compound which apparently had incorporated an



(1) **a**; X = NOH, R = H
b; X = NOH, R = Ph
c; X = NOH, R = Me
(2) X = NOMe, R = H
(3) X = NOCOMe, R = H
(5) X = NAr or NCH Ar, R = H
(6) X = O, R = H



(4) **a**; X = NOCOMe
b; X = NOH
(7) X = O



Scheme 1

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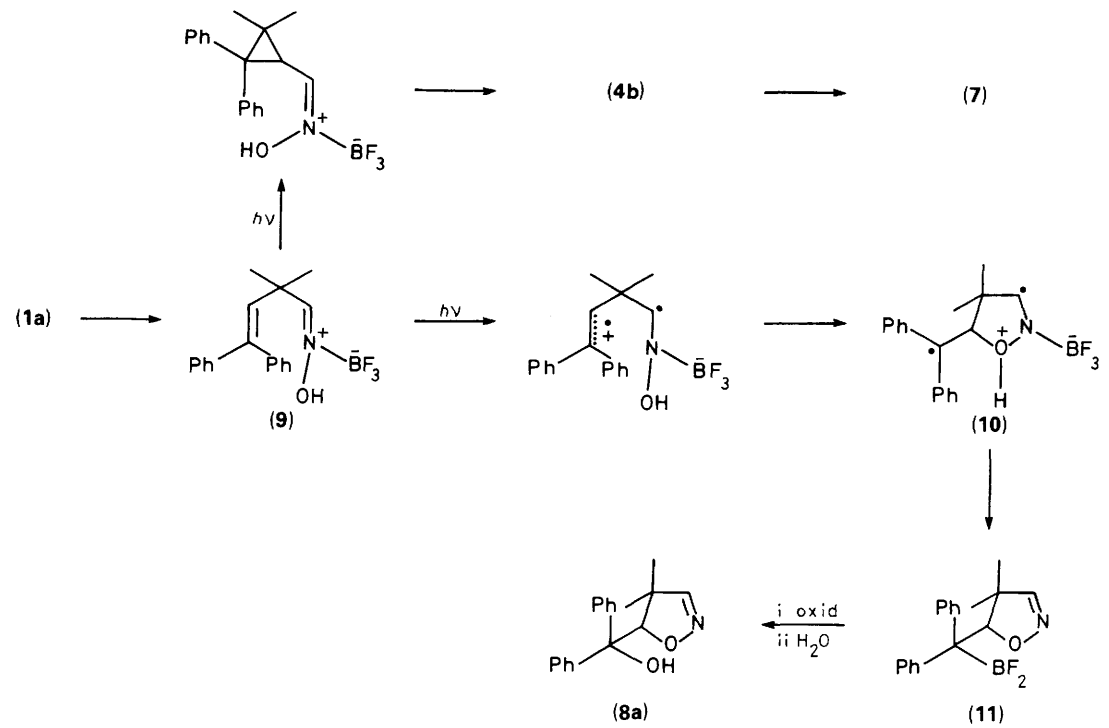
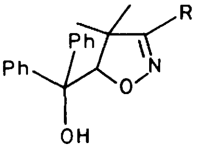
† After irradiation the reaction mixture is poured into water and separated. The organic layer is washed with water, dried, filtered, and evaporated to dryness. The residue was flash chromatographed on silica gel.

‡ *Selected data*: m.p. 192—194 °C; IR $\nu_{max.}$ (KBr) 3240, 1620 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 1.03 (s, 6H), 2.95 (br. s, 1H), 5.18 (s, 1H), 6.83 (s, 1H), 7.1—7.7 (m, 10H); ^{13}C NMR (CDCl$_3$) δ 157.92, 147.02, 142.52, 128.20, 127.92, 126.89, 125.90, 125.39, 89.01; *m/z* 281 (M^+, 1%), 183 (100), 165 (4), 152 (4), 105 (90), 77 (53), 51 (12). Satisfactory elemental analyses were obtained.



Scheme 2



(8) **a**; R = H
b; R = Ph
c; R = Me

additional oxygen atom was not readily achieved. Thus, the highly crystalline material was subjected to *X*-ray diffraction analysis whereby the structure was shown to be (**8a**) and is illustrated in Figure 1.§ The other oximes (**1b, c**) were cyclised successfully under similar conditions to yield the dihydroisoxazoles [(**8b**) 35%] and [(**8c**) 30%], respectively. The yields of product have not been optimised.

An intermolecular hydrogen bond O(9) · · · N(2) [2.833(6) Å] links the molecules into dimers about the centre of inversion at (0.5, 1, 0). The torsion angle O(1)–C(5)–C(8)–C(9) is 64.8(2)°. The phenyl rings are placed to minimise contacts, giving torsion angles O(9)–C(8)–C(10)–C(15) as −6.2(2)° and O(9)–C(8)–C(16)–C(17) as −142.3(3)°.

The formation of the dihydroisoxazoles (**8**) from the oximes (**1**) was surprising. The reaction of oxime (**1a**) was studied in more detail and was shown to be photochemical since dark control reactions fail to yield the dihydroisoxazole (**8a**).¶ The source of the additional oxygen incorporated during the reaction could come from either water or oxygen. Various experiments showed that water was not involved and oxygen in large quantities totally suppresses the reaction. Furthermore (**8a**) is formed with the same efficiency under argon as it is under deoxygenated nitrogen. Thus it seems likely that the oxidation step occurs after the photochemical rearrangement and during work up. The preferred route to the product is shown in Scheme 2. Here it is envisaged that the complex of the oxime and BF_3 (**9**) is photochemically excited and undergoes electron transfer from the diphenyl alkene moiety to the iminium salt, a process with ample precedence.[9] The successful cyclisation of (**1b**) is in support of this proposal since the phenyl substituted oxime moiety will be a better electron acceptor than the aldoxime in (**1a**). Indeed the cyclisation of (**1b**) seems to be more efficient and requires only 1 h irradiation to achieve a reasonable yield of product. The resultant radical cation/radical anion reacts intramolecularly to afford the dihydroisoxazole system (**10**). We propose that (**10**) is converted into the borane (**11**), although thus far we have been unable to detect the presence of the borane spectroscopically. The involvement of a borane is speculative but it is well known that difluoroalkylboranes undergo facile oxidation.[8] A possible path to the formation of the borane (**11**) could involve a boron trifluoride transfer, within (**10**), and elimination of HF. We propose that the conversion of (**11**) to the final product (**8a**) occurs during isolation.

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§ *Crystal data* for (**8a**) ($C_{18}H_{19}NO_2$, M = 281.3) at 298 K: triclinic, space group $P\bar{1}$, a = 6.128(5), b = 9.521(6), c = 13.514(7) Å, α = 94.93(5), β = 96.23(5), γ = 106.41(5)°, U = 746.2 Å^3, Z = 2, D_c = 1.25 g cm^{-3}. From 2786 unique, observed, reflexions, 1651 with $|F| > 2\sigma(F)$ were used in refinement to convergence at R = 0.088, R_w = 0.111. Anisotropic temperature parameters were used for all non-hydrogen atoms. The phenyl rings were refined as rigid groups. The hydroxy hydrogen atom was located on a difference map and refined. All other hydrogen atoms were included in the final stages of refinement on calculated positions with isotropic temperature parameters refined for each group. Atomic co-ordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Notice to Authors, Issue No. 1.

¶ Oxime (**1a**) and a stoicheiometric amount of boron trifluoride etherate in benzene were left under nitrogen in the dark at room temperature for 9 days. After work up, only starting material and its hydrolysis product [(**6**) 18%] were obtained.

The formation of the cyclopropyl derivative (**4b**), albeit in low yield, demonstrates that oxime (**1a**) can be made to undergo the ADPM rearrangement if the electron transfer from the nitrogen is suppressed.[||] Thus the use of boron trifluoride for this purpose has allowed the substantiation of our original proposal. However, it is obvious that the ADPM rearrangement is not efficient and competes very poorly with the alternative process, that of electron transfer from the 1,1-diphenyl moiety to the iminium salt. Furthermore the boron must play an important part in the reaction since the rearrangement of (**1a**) into (**8a**) does not occur when the irradiation is carried out using perchloric acid to protonate the oxime nitrogen. The reaction described above provides a new route to the synthesis of dihydroisoxazoles. Unlike the present method the more common synthetic paths to molecules of this type usually afford dihydroisoxazoles with substituents at C(3).[9] Currently we are studying this novel cyclization process in more detail with a view to establishing the mechanism and scope.

We thank the British Council and The Ministerio de Educación y Ciencia of Spain for a Fleming Fellowship to one of us (F. L.), the Comisión Asesora de Investigación Científica y Técnica (Grant no. PB85/0040), and NATO (Grant no. 0734/87) for financial assistance. Sincere thanks are expressed to Dr. Alan Howie (Aberdeen University, Aberdeen, U.K.) for the crystal data collection.

Received, 13th April 1989; Com. 9/01533G

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[||] At this stage the formation of the ADPM product is presumed to be formed *via* a conventional vinyl–vinyl bonding route. However, the possibility exists for the ADPM product (**4b**) to be formed by the electron transfer path. Thus the electron transfer process shown in Scheme 2 could also yield the ADPM product if it is assumed that the electron density in the diphenylalkene part of the radical cation/radical anion is partitioned between the two extreme representations $Ph_2\overset{+}{C}\text{–}\dot{C}H\text{–}$ and $Ph_2\dot{C}\text{–}\overset{+}{C}H\text{–}$. The former could lead to the ADPM product (**4b**) *via* bridging and the latter to (**8a**). However, this is speculative at this time.