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# The Aza-di-π-Methane Rearrangement of β,γ-Unsaturated Oximes.

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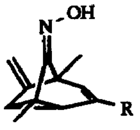
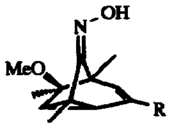
***Abstract:*** *Although previous studies have shown that acyclic β,γ-unsaturated oximes and oxime ethers do not undergo the aza-di-π-methane (ADPM) rearrangement, the 2-methyl-4,4-diphenyl-2-vinylbut-3-enal oxime* ***5a****, its methyl ether* ***5b*** *and the 2,2,4,4-tetraphenylbut-3-enal oxime* ***14*** *give the corresponding cyclopropyl derivatives* ***8a, 8b*** *and* ***15*** *by the ADPM path, in a reaction that is controlled by the stability of the intermediate 1,3-biradical.*

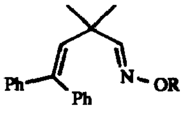
Several years ago two examples of the photochemical aza-di-π-methane (ADPM) rearrangement of tricyclic β,γ-unsaturated oximes **1** and **2** were reported.[1] However, all attempts to observe similar reactivity in acyclic systems such as **3** have been unsuccessful.[2, 3] Our reasoning regarding this failure was that the ionization potential of the lone pair electrons on the oxime nitrogen was sufficiently low to become involved in an adverse single electron transfer (SET) step that deactivated the triplet excited state before bridging, the initial step of the rearrangement, could occur.[4] Studies carried out by us[2] on the photochemistry of oxime **3a** and by others[3] on the photochemical reactivity of β,γ-unsaturated oxime ethers **3b** and **4** have shown that these compounds are unreactive in the ADPM rearrangement. Only in the case of compound **4** photochemical *syn,anti*-isomerization of the C-N double bond was observed on direct or sensitized irradiation. Subsequent studies reported here illustrate that the outcome of sensitized irradiation of such oximes is dependent on the type of substituent on the central carbon of the β,γ-unsaturated oxime under investigation.



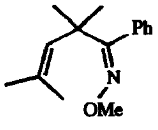
**1**: R = H or Me



**2**: R = H or Me



**3a**: R = H
**3b**: R = Me



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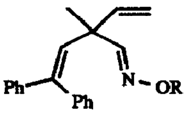
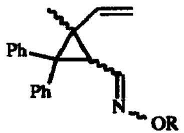
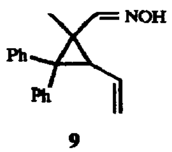


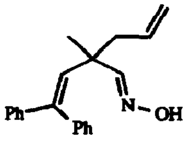
**5a**: R = H
**5b**: R = Me



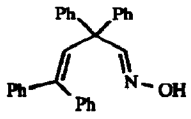
**8a**: R = H
**8b**: R = Me



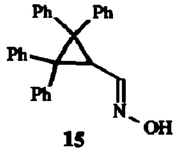
**9**



**13**

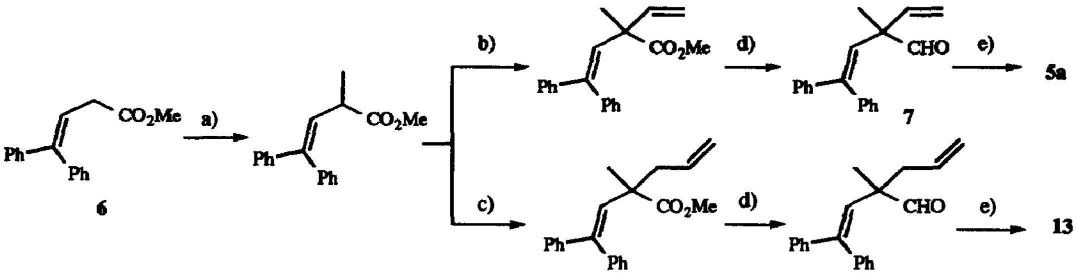


**14**



**15**

Our results arise from attempts to demonstrate that both the ADPM and the di-π-methane (DPM) rearrangements could be brought about within the same substrate. One of the compounds selected for this study was the oxime **5a**. The synthesis of **5a** was achieved by conversion of the known ester **6**[5] into the aldehyde **7**, by the route outlined in Scheme 1, followed by oximation.[6]



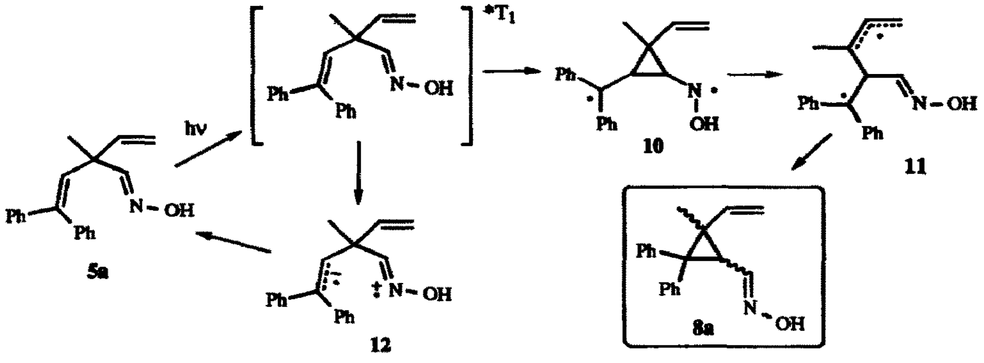
(a) NaH, MeI; (b) 1) KBu$^t$O, PhSOCH=CH$_2$, 2) Δ; (c) NaH, CH$_2$=CHCH$_2$Br; (d) 1) LiAlH$_4$, 2) PCC; (e) NH$_2$OH.HCl

**Scheme 1**

It was considered certain that irradiation of the oxime **5a** should follow the DPM reaction pathway since earlier studies by Zimmerman *et al.* showed that 1,4-diene moieties such as that in **5a** undergo this rearrangement albeit with a low quantum yield.[7] Thus it was no surprise that direct irradiation for 5 h and sensitized irradiation for 20 min brought about conversion to a cyclopropane derivative in 21% and 30% yield respectively.[8, 9] However, detailed $^1$H NMR analysis of the product, using NOE experiments, showed it to have the structure illustrated in **8a**, and is present as a 26:35:17:22 mixture of the four possible stereoisomers (*Z*)-*RR,SS*: (*Z*)-*RS,SR*: (*E*)-*RR,SS*: (*E*)-*RS,SR* respectively.[10] The usual spectroscopic and analytical techniques have also confirmed the assignment of the structure. This product can arise only by the ADPM rearrangement as shown in Scheme 2. A careful examination of the reaction mixture showed that the other regioisomer **9**, that would have resulted from the alternative DPM path, was not formed. The involvement of an oxime derivative in an ADPM rearrangement was **extremely surprising and completely unexpected** in view of the failures reported earlier. This report is the first example of the ADPM reaction of an acyclic β,γ-unsaturated oxime.

The question of why such a rearrangement should occur in compound **5a** when it was not observed in the irradiations of **3** and **4** had to be answered. As mentioned earlier we were able to overcome the failure of oximes to rearrange by the ADPM path by their conversion to oxime acetates[4] and other derivatives[11] where an electron withdrawing group was attached to the oxime nitrogen. With these derivatives it was argued that the increase in the ionization potential of the nitrogen lone pair minimized the electron transfer and thus the ADPM reaction became operative and efficient with quantum yields of up to 0.82 and almost quantitative chemical yields in some cases. If this argument is to be used in explanation of the photoreactivity of the oxime **5a** then a method by which the ionization potential of the oxime nitrogen lone pair can be increased must be available to the molecule. One possibility considered was that the hydroxyl group of the oxime could form a hydrogen bond with the 2-vinyl-substituent. That this is inoperative was shown by the experiment using the ether **5b**. Sensitized irradiation of this for 20 min also brought about its conversion into a mixture of isomers of the cyclopropane **8b**, in 53% yield, that can only arise from the ADPM process. Again this is surprising in view of earlier studies that demonstrated the failure of the oxime ethers **3b** and **4** to rearrange.

A possible explanation for the successful ADPM rearrangement of the compounds **5a** and **5b** might be related to differences between the energy barriers for the various processes open to the excited state of the molecule in question. The principal processes of concern are the conversion of the excited state *via* the bridging biradical **10** to the biradical **11** or SET to the zwitterionic biradical **12**, the presumed energy wasting step. This line of argument is outlined in Scheme 2.



**Scheme 2**

Thus if the energy barrier for conversion of the excited state to the 1,3-biradical and thence to the ADPM product is lower than that for the SET process ultimately leading back to starting material, then the ADPM process dominates. In the opposite situation SET will dominate and no rearrangement reaction will be observed. It is likely that subtle changes in substitution would be sufficient to change the balance in reactivity. Thus for the examples **5a** and **5b** the additional stability given to the 1,3-biradical by the vinyl substituent is sufficiently important to bring about the ADPM rearrangement and the SET process either does not occur or is comparatively unimportant as an energy wasting step. The converse must hold for the 1,3-biradical that would be formed by rearrangement of the oxime **3a** and its ether **3b**. In this situation the SET process is less energetic and is preferred to the ring opening of the 1,4-bridged biradical. Thus the oxime **3a** and the ether **3b** fail to undergo the ADPM process. If the rearrangement of oximes is to be a general process then the biradical **11** has to be sufficiently stable so that the SET, the energy wasting step, is unfavoured. As a test of this the sensitized irradiation of the oxime **13**, synthesized by the route shown in Scheme 1, was carried out. However, this failed to yield a product from the ADPM process and a complex inseparable mixture was obtained. This result supports the suggestion that the stability of the 1,3-biradical is crucial for the success of the ADPM process with oximes. Indeed the 1,3-biradical from oxime **13** is of the same stability as that from oxime **3a** or its methyl ether **3b** both of which fail to react. The failure of the oxime **13** to rearrange also removes the possibility that a complex between the 2-vinyl group and the oxime group in **5a** or between the oxime group and the 2-propenyl substituent in **13** would be a controlling feature in the ADPM rearrangement of such systems. The concept of the need to have a stable 1,3-biradical was tested further using the oxime **14**.[4b] Here again the reaction was rapid in qualitative terms and chemically efficient and yields the ADPM product **15**, in 74% yield, after triplet sensitized irradiation for 30 min.

The new reaction described by us has considerable interest since it demonstrates that acyclic β,γ-unsaturated oximes, that were previously considered to be photochemically inert towards the ADPM rearrangement, can undergo this reaction provided that the intermediate 1,3-biradical is sufficiently stabilized. This study has increased the knowledge of the factors that control the ADPM reaction and has allowed the extension of the rearrangement to novel C-N double bond stable derivatives. Currently a study is in hand to establish the versatility of the process.

**Acknowledgments:** We are grateful to Dr. William M. Horspool, University of Dundee (Scotland) for fruitful discussions. We also thank the Direccion General de Investigacion Cientifica y Tecnica (Grant No. PB91-0396) and NATO (Grant 870734/92) for financial assistance.

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6. Selected data for oxime **5a**: mp 102-104°C (hexane); $\delta_H(CDCl_3)$ 1.3 (3H, s, Me), 4.95 (1H, dd, *J* 10.5, 0.9 Hz, CH=C*H*$_2$), 4.98 (1H, dd, *J* 17.3, 0.9 Hz, CH=C*H*$_2$), 5.8 (1H, dd, *J* 17.3, 10.5 Hz, C*H*=CH$_2$), 5.9 (1H, s, CH=CPh$_2$), 6.9 (1H, s, imine H), 7.0-7.2 (10H, m, aryl H) and 7.3 (1H, br s, OH); $\delta_C(CDCl_3)$ 25.0 (Me), 45.5 (quaternary C), 113.3 (vinyl C), 127.0-142.7 (aryl and vinyl C) and 155.3 (C=N); $\nu_{max}$ (KBr)/cm$^{-1}$ 3250 (OH) and 1630 (C=N); $\lambda_{max}$ (CH$_2$Cl$_2$)/nm 250 ($\varepsilon$ 14 900 dm$^3$ mol$^{-1}$ cm$^{-1}$); *m/z* 277 (M$^+$, 7%), 260 (100), 233 (40), 165 (37), 91 (66) and 77 (32) (Found: C, 82.0; H, 6.9; N, 4.9. $C_{19}H_{19}NO$ requires C, 82.27; H, 6.90; N, 5.04%).
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8. Satisfactory microanalytical data were obtained for all new solid compounds and accurate mass spectra for oils. The irradiations were carried out in methylene dichloride in an immersion well apparatus with a Pyrex filter and a 400 W medium pressure Hg arc lamp. Acetophenone was used as sensitizer.
9. Triplet quenching experiments using cyclooctadiene show that the reaction is taking place *via* the triplet excited state.
10. Selected data for the mixture of stereoisomers of cyclopropyloxime **8a**: Isomer (*E*) (*RS,SR:RR,SS*) (3:2): $\delta_H(CDCl_3)$ 1.09 (9/5H, s, Me × 3/5), 1.28 (6/5H, s, Me × 2/5), 2.50 (3/5H, d, *J* 10.2 Hz, cyclopropyl H × 3/5), 2.56 (2/5H, d, *J* 9.5 Hz, cyclopropyl H × 2/5), 4.8-5.3 (2H, m, CH=C*H*$_2$), 5.6 (1H, dd, *J* 17.1, 10.8 Hz, C*H*=CH$_2$) and 7.0-7.4 (11H, m, aryl and imine H).

    Isomer (*Z*) (*RS,SR:RR,SS*) (3:2): $\delta_H(CDCl_3)$ 1,12 (9/5H, s, Me × 3/5), 1.31 (6/5H, s, Me × 2/5), 3.08 (3/5H, d, *J* 8.1 Hz, cyclopropyl H × 3/5), 3.15 (2/5H, d, *J* 8.1 Hz, cyclopropyl H × 2/5), 4.8-5.3 (2H, m, CH=C*H*$_2$), 5.7 (1H, dd, *J* 17.1, 10.8 Hz, C*H*=CH$_2$), 6.44 (2/5H, d, *J* 8.1 Hz, imine H × 2/5) , 6.49 (3/5H, d, *J* 8.1 Hz, imine H × 3/5) and 7.1-7.4 (10H, m, aryl H).

    $\delta_C(CDCl_3)$ 15.7, 19.82, 19.88 (Me), 30.3, 31.9 (CH), 33.60, 33.62 (quaternary C), 33.64 (CH), 33.8, 34.5 (quaternary C), 35.8 (CH), 47.7, 48.2, 48.6, 49.2 (quaternary C), 112.0, 112.07, 113.5, 113.6 (vinyl C), 126.3-143.8 (aryl and vinyl C) and 149.3, 149.8, 150.9, 151.3 (C=N); $\nu_{max}$ (KBr)/cm$^{-1}$ 3220 (OH) and 1635 (C=N).
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