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The Oxa-di-π-methane Rearrangement of β,γ-Unsaturated Aldehydes

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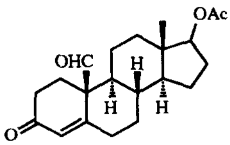
Abstract: *As far as we are aware, there are only two examples of oxa-di-π-methane (ODPM) rearrangement with β,γ-unsaturated aldehydes. However, we have discovered four other cases of this reaction, taking place with 1-methyl-3-phenyl-2-cyclohexene-1-carbaldehyde, 1-methyl-3-phenyl-2-cyclopentene-1-carbaldehyde, 2,2-dimethyl-4-phenyl-3-butenal and 2,2-dimethyl-4,4-diphenyl-3-butenal. All of these undergo very efficient ODMP rearrangement affording the corresponding cyclopropyl derivatives in high yield.*

The photochemical reactivity of β,γ-unsaturated carbonyl compounds has been the subject of extensive studies.[1] The results obtained show that, in simple terms, direct irradiation of β,γ-unsaturated ketones yields the corresponding 1,3-acyl migration product. The triplet photochemical reactivity of these compounds brings about the formation of the corresponding cyclopropyl ketones by an ODPM rearrangement. However, there are exceptions to this general rule and many β,γ-unsaturated carbonyl compounds do not undergo the rearrangement.[1] β,γ-Unsaturated aldehydes are the most typical example of carbonyl compounds that do not undergo either the 1,3-formyl migration or the ODPM reaction.[1] The normal photochemical reactivity of such compounds, both on direct or sensitized irradiations, is decarbonylation to the corresponding alkene.[1] There are only two examples of aldehydes that do not follow this general rule. The first example of an ODPM rearrangement in a β,γ-unsaturated aldehyde was reported by Schaffner *et al.* in the direct irradiation of the steroidal aldehyde **1** that gives the ODPM product **2** in 30% yield in addition with two other compounds derived from 1,3-formyl migration and decarbonylation respectively.[2] Many years later Zimmerman and Cassel[3] reported the ODPM reactivity of the sterically hindered aldehyde **3** that yields the cyclopropyl aldehyde **4** on acetophenone-sensitized irradiation.



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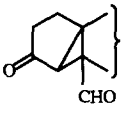

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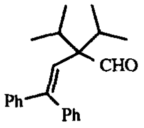

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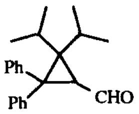

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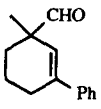
However, apart from these two cases, all the studies carried out on the photochemical reactivity of β,γ-unsaturated aldehydes failed to detect the ODPM rearrangement and decarbonylation to the corresponding alkenes was the only reaction observed.[4] On the basis of these precedents it was accepted that β,γ-unsaturated aldehydes do not generally undergo the ODPM rearrangement. We wish to report here four additional examples of aldehydes that undergo the ODPM rearrangement very efficiently on triplet sensitized irradiation.

Our interest in the aza-di-π-methane rearrangement (ADPM) has led us to a study of its application to the synthesis of bicyclo[n.1.0]alkanes.[5] An extension of such a study was aimed at identifying ring contraction processes. To this end the known aldehyde **5**,[6] that could be transformed into different imine derivatives, was selected as the target molecule. Since the photochemistry of the aldehyde **5** was not described, it was of importance to establish the photochemical behaviour of this compound to compare its reactivity with that of the corresponding nitrogen derivatives. Brief (10 min) direct irradiation[7] of **5** afforded, after work-up, a mixture of starting material (20%) and a new product. The usual spectroscopic techniques[8] identified the photoproduct as the cyclohexene (**6**,[9] 54%) resulting from decarbonylation of aldehyde **5**. This result was not a surprise since, as mentioned above, it has been established that decarbonylation is the main photochemical reactivity of β,γ-unsaturated aldehydes. However, acetophenone-sensitized irradiation of **5** for 20 min brought about different reactions and afforded the 1,3-migration product (**7**, 25%), the ODPM product (**8a**, 25%) and starting material (11%). The identity of aldehyde **7** was established by IR and MS evidence, showing that this compound was isomeric with starting material. The ^{1}H- and ^{13}C-NMR resonances also agree with the structure proposed for **7**.[10] The structure of the bicyclic aldehyde **8a** was unequivocally established by reduction, using LAH, to the known alcohol **8b**.[6] By this method it was also possible to assign the stereochemistry of the photoproduct **8a** as the *endo*-isomer exclusively.[11] The stereoselectivity observed in this reaction is similar to that reported by Mariano and Ko in the sensitized irradiation of the 1,4-diene **9** that yields the *endo*-isomer of the corresponding di-π-methane product **10** exclusively.[6] The formation of the 1,3-migration product **7** under sensitized conditions involving the T_2 excited state is the normal behaviour reported for many β,γ-unsaturated ketones.[1b] However, it is extremely rare to observe such a reaction with aldehydes and even more surprising is the formation of the ODPM product **8a**. As mentioned previously, there are only two examples of β,γ-unsaturated aldehydes that behave in a similar manner.[2,3]



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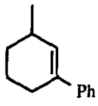

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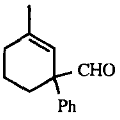

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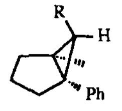
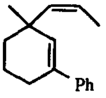


8a: R = CHO
8b: R = CH$_2$OH



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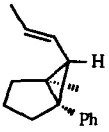

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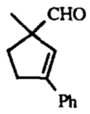
Compound **11** was synthesized to determine whether this unexpected reactivity could be extended to other related aldehydes. The synthesis of **11** was achieved by the one-pot conversion of 3-phenyl-2-cyclopentenone,[12] according to the method described by Martin *et al.* for similar compounds.[13] Acetophenone-sensitized irradiation (5 min) of **11** afforded, after conventional work-up, the ODPM product **12a** in 90% isolated yield. In this instance, a careful study of the ^{1}H- and ^{13}C-NMR spectra of the crude photolysate demonstrated that the 1,3-formyl migration product is not formed. The identity of **12a** was established by comparison of the ^{1}H-NMR resonances recorded for this compound[11] with those reported by Schaffner *et al.* for the analogous ketone **12b**.[14] This comparison also allowed us to assign the *endo*-configuration to **12a**. The result obtained in the irradiation of **11** shows that the ODPM reactivity observed for **5** can be extended to other cyclic β,γ-unsaturated aldehydes. However, it is still unclear why **15** does not undergo the 1,3-formyl migration and only yields the ODPM product.

From the foregoing it is clear that there are structural features in the compounds **5** and **11** that are critical for the success of the ODPM process. This is evident, not only from the fact that compounds **7** and **15** undergo rearrangements that have seldom been seen in related compounds, but also because of the very high efficiency of the rearrangement. The most likely controlling features are the stabilizing influence of the phenyl group on the bridging 1,4-biradical reaction intermediate and the absence of the free rotor effect on the vinyl component. In order to determine whether the suppression of the free rotor effect was essential for the success of the rearrangement the study was extended to the aldehyde **13**. When **13**[15] was irradiated (15 min) under similar conditions to those used for **5** and **11**, the cyclopropyl aldehyde **14a**, resulting from an ODPM rearrangement, was obtained in 90% isolated yield. The identity of **14a** was easily determined by comparison of the ^{1}H- and ^{13}C-NMR resonances[11] recorded for **14a** with those previously reported by us for the corresponding oxime acetate **14b**.[16] In this case the reaction is stereospecific yielding the *trans*-isomer exclusively. This result demonstrated clearly that the ODPM reactivity of β,γ-unsaturated aldehydes is not restricted to cyclic compounds, such as **5** and **11**, but can also be extended to acyclic derivatives. Therefore, the suppression of the free rotor effect is not essential for the success of the rearrangement.



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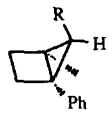
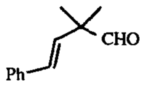


12a: R = CHO
12b: R = COMe



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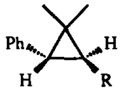
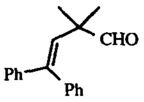


14a: R = CHO
14b: R = CH=NOAc



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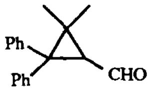

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The efficient ODPM reactivity of **13** was extremely surprising considering that Pratt[4e] had reported in an early study the absence of such rearrangement in the direct and sensitized irradiation of the closely related diphenyl substituted aldehyde **15**. The reactivity observed for **15** was decarbonylation on direct irradiation and what the author described as ambigous results, on acetophenone sensitization. No evidence for the formation of the corresponding ODPM product was obtained. Therefore, a logical extension of our study was to re investigate the photoreactivity of the aldehyde **15**. Surprisingly, *m*-methoxyacetophenone-sensitized irradiation of **15** (2 h) brought about the formation of the previously described cyclopropyl aldehyde **16**,[17] resulting from an ODPM rearrangement, in 57% isolated yield and starting material (30%). It is worth to note that the corresponding methyl ketone (3,3-dimethyl-5,5-diphenyl-4-penten-2-one) does not undergo the ODPM reaction.[4e]

The results obtained in our study show that β,γ-unsaturated aldehydes can undergo the ODPM rearrangement very efficiently. Particularly, the reactivity observed in simple compounds such as **13** and **15** demonstrate that the ODPM reactivity of aldehydes is not restricted to molecules with special structural features as in the cases previously reported. At the present moment it is unclear which factors control the ODPM reactivity of β,γ-unsaturated aldehydes. However, from our results it seems logical to predict that it would be possible to observe this type of reaction in many other aldehydes. The present study opens the possibility of extending the synthetic applications of the ODPM rearrangement to a new type of carbonyl compounds that were previously considered of little synthetic utility from a photochemical point of view. Further studies are in hand to investigate the scope and the structural effects of these reactions.

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7. 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 or *m*-methoxyacetophenonewere used as sensitizers.
8. *Selected spectroscopic data* for **6**: ν_{max}(liq. film)/cm^{-1} 1620; δ_H(300 MHz, $CDCl_3$) 1.1 (3H, d, *J* 6.8 Hz), 1.2-2.4 (7H, m), 5.9 (1H, br. s), 7.2-7.4 (5H, m); δ_C(75 MHz, $CDCl_3$). A small amount of another photoproduct was obtained in the irradiation of **5**. This was tentatively identified as the isomeric alkene (1-methyl-3-phenylcyclohexene) also resulting from decarbonylation of **5**.
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10. *Selected spectroscopic data* for **7**: ν_{max}(liq. film)/cm^{-1} 1695; δ_H(300 MHz, $CDCl_3$) 1.8 (3H, s), 1.4-2.4 (6H, m), 5.5 (1H, s), 7.1-7.4 (5H, m), 9.4 (1H, s); δ_C(75 MHz, $CDCl_3$) 18.9, 24.3, 29.8, 30.5, 37.3, 117.9, 124.8-130.1, 135.7, 141.3, 199.3.
11. *Selected spectroscopic data* for ODPM photoproducts **8a**, **12a** and **14a**: **8a**, ν_{max}(liq. film)/cm^{-1} 1690; δ_H(300 MHz, $CDCl_3$) 0.9 (3H, s), 1.8 (1H, d, *J* 6.3 Hz), 1.5-2.4 (6H, m), 7.1-7.5 (5H, m), 9.7 (1H, d, *J* 6.3 Hz). **12a**, ν_{max}(liq. film)/cm^{-1} 1700; δ_H(300 MHz, $CDCl_3$) 1.3 (3H, s), 1.9 (1H, d, *J* 6.0 Hz), 1.4-2.6 (4H, m), 7.1-7.3 (5H, m), 9.9 (1H, d, *J* 6.0 Hz). **14a**, δ_H(300 MHz, $CDCl_3$) 0.9 (3H, s), 1.4 (3H, s), 2.2 (1H, dd, J_a 5.5, J_b 5.0 Hz), 2.9 (1H, d, *J* 5.5 Hz), 7.1-7.4 (5H, m), 9.6 (1H, d, *J* 5.0 Hz).
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