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Novel Oxa-di-π-methane and Norrish Type I Reactions in the S_2 (π,π^*) Excited State of a Series of β,γ-Unsaturated Ketones

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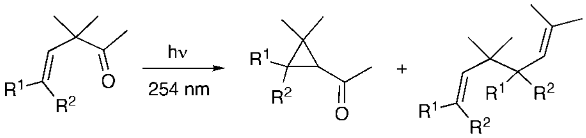
ABSTRACT



R^1 = CN, CO_2Me , C_6H_5, 4-CNC_6H_4; R^2 = H, Me, CN or CO_2Me

β,γ-Unsaturated methyl ketones with electron-withdrawing groups at the γ-position of the ene moiety undergo ODPM rearrangements and Norrish type I reactions on direct irradiation at 254 nm. The results are consistent with the involvement of alkene S_2 (π,π^*) as reactive excited states in these processes.

The oxa-di-π-methane (ODPM) photochemical rearrangement reaction has been the subject of numerous studies carried out for more than 35 years. The results of these efforts show that this process usually occurs from the lowest excited triplet state T_1 (π,π^*) of the ketone moiety.[1] There are very few exceptions to this general rule. Rogers et al. reported in 1984 that enones **1a**, **1b**, and **2** undergo ODPM rearrangements to yield **3a**, **3b**, and **4**, respectively, on triplet sensitized irradiation from the T_1 (π,π^*) excited states and also on direct irradiation from the T_2 (n,π^*) state or, less likely, from S_1 (n,π^*) states.[2] Four years later Cerfontain and Koppes described the direct irradiation reactions of enones **5a** and **5b**. They showed that direct irradiation of these substances using Pyrex-filtered light leads to formation of the respective ODPM products **6a** and **6b**. They suggested that these reactions occur via the alkene S_2 (π,π^*) excited state.[3] However, the conclusions drawn by Cerfontain and Koppes deserve reevaluation since it is difficult to explain how the S_2 (π,π^*) excited state of compounds **5** could be populated under these photochemical reaction conditions. Another example of T_2 (n,π^*) or S_1 (n,π^*) ODPM reactivity, uncovered by Dalton, is referred to as unpublished results in Roger's and Cerfontain's papers but apparently has never been published. As far as we are aware, these are the only exceptions to the rule mentioned above. In this publication we report the results of studies that demonstrate that electron-withdrawing groups at the γ-position of β,γ-unsaturated ketones promote ODPM rearrangements and Norrish type I reactions via the S_2 (π,π^*) excited state of the ene moieties.

As part of our studies exploring the photoreactivity of 1,4-unsaturated compounds promoted by electron-donor sensitiz-

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[1] For reviews, see: (a) Hixson, S. S.; Mariano, P. S.; Zimmerman, H. E. *Chem. Rev.* **1973**, *73*, 531−551. (b) Dauben, G. W.; Lodder, G.; Ipaktschi, J. *Top. Curr. Chem.* **1975**, *54*, 73−114. (c) Houk, K. N. *Chem. Rev.* **1976**, *76*, 1−74. (d) Schuster, D. I. In *Rearrangements in Ground and Excited States*; DeMayo, P., Ed.; Academic Press: New York, 1980; Vol. 3, pp 167−279. (e) Demuth, M. In *Organic Photochemistry*; Padwa, A., Ed.; Marcel Dekker: New York, 1991; Vol. 11, pp 37−109. (f) Demuth, M. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming. I., Paquette, L. A., Eds.; Pergamon Press: Oxford, 1991; Vol. 5, pp 215−237. (g) Zimmerman, H. E.; Armesto, D. *Chem. Rev.* **1996**, *96*, 3065−3112.

[2] Eckersley, E. J.; Parker, S. D.; Rogers, N. A. J. *Tetrahedron* **1984**, *40*, 3749−3758.

[3] Koppes, M. J. C. M.; Cerfontain, H. *Recl. Trav. Chim. Pays-Bas* **1988**, *107*, 549−562.

10.1021/ol050846d CCC: $30.25

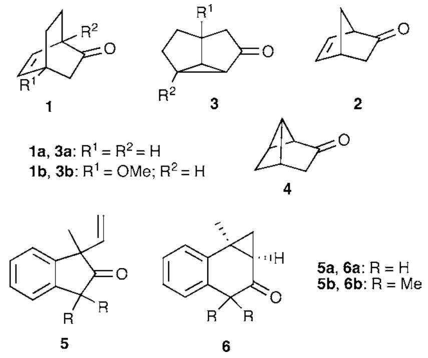


Figure 1.

ers, we investigated the reactivity of radical anions derived from β,γ-unsaturated ketones that contain electron-withdrawing groups on the alkene unit. Our goal was to determine whether radical anions centered on the C−C double bond could be generated selectively on irradiation using *N*,*N*-dimethylaniline (DMA) as electron-donor sensitizer. For this purpose, methyl ketone **7a** was synthesized and irradiated in an acetonitrile solution containg *N*,*N*-dimethylaniline. As anticipated, this reaction resulted in exclusive formation of the reduced product **8**, arising from the alkene-centered radical anion **9**. However, since the excited-state reactivity profile of **7a** was unknown, it was necessary to evaluate its photobehavior under direct and triplet-sensitized irradiation conditions. Prolonged direct or acetophenone-sensitized irradiations of **7a**, using a Pyrex filtered light, led to complete recovery of starting material. However, direct irradiation of **7a** through quartz produces the ODPM product **10a** (16%) and the 1,5-diene **11** (12%) (Scheme 1).

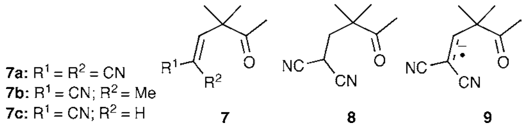
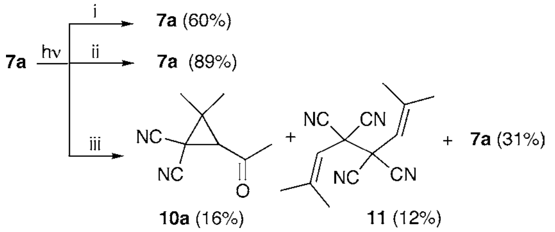


Figure 2.

Scheme 1 [a]



[a] Conditions: (i) acetophenone, 14 h; (ii) direct, Pyrex, 24 h; (iii) direct, quartz, 254 nm.

The formation of the ODPM product **10a** under the above conditions is surprising. The fact that the ODPM rearrangement of **7a** does not proceed upon triplet photosensitization rules out a reactive T_1 (π,π^*) triplet state as responsible for the reaction. On the other hand, the lack of reactivity of **7a** on direct irradiation using Pyrex filtered light discounts the involvement in the rearrangement of S_1 (n,π^*) and T_2 (n,π^*) excited states of the ketone moiety. The formation of **10a** in the direct irradiation reaction of **7a**, using 254 nm light, suggests that the ODPM rearrangement of **7a** proceeds from the higher energy singlet excited state S_2 (π,π^*) of the alkene. As mentioned above, an ODPM reaction of a β,γ-unsaturated enone that occurs from a state other than T_1 (π,π^*) is very uncommon and rarely found in the literature.

Another interesting observation is that the diene **11**, resulting from decarbonylation (a typical Norrish type I reaction) is formed when **7a** is irradiated at 254 nm. This compound is not obtained on direct irradiation using Pyrex-filtered light. Previous studies of Norrish type I reactions of β,γ-unsaturated enones have established that these reactions occur from S_1 (n,π^*) or T_2 (n,π^*) excited states. In addition, we have recently reported the first examples of decarbonylation and 1,3-formyl migration processes in excited-state reactions of β,γ-unsaturated aldehydes that take place via the T_1 (π,π^*).[4] Thus, the formation of Norrish type I products on 254 nm direct irradiation of **7a** represents the first example of Norrish type I reactions that occurs in an S_2 (π,π^*) excited state. The reason for this unusual reactivity might derive from the fact that the S_2 (π,π^*) excited state of **7a** possesses sufficient energy to promote homolytic bond fission at the allylic position. As a result decarbonylation competes with the ODPM rearrangement.

To determine if other β,γ-unsaturated ketones related to **7a** also display this unusual reactivity profile, the photochemistry of enones **7b** and **7c** was explored. Acetone-sensitized irradiation of (*E*)-**7b** affords recovered starting material as a 2:3 mixture of *E*/*Z* diastereoisomers. However, direct irradiation using Pyrex-filtered light yielded the 1,3-acyl shift product **12** and dienes **13** and (*E*)-**14**, resulting from decarbonylation of **7b** (Scheme 2).

Thus, the replacement of a cyano group in **7a** by a methyl group restores the normal Norrish type I reactivity of the carbonyl. Irradiation of (*E*)-**7b** at 254 nm affords the Norrish type I photoproducts **12**, **13**, **14**, and cyclopropane **10b** resulting from ODPM rearrangement (Scheme 2). The formation of **10b** under these conditions shows that monocyano substitution at the γ-position of the enone also allows ODPM rearrangement to take place via the S_2 (π,π^*) excited state. In this instance the Norrish type I photoproducts **12**, **13**, and **14** are formed by excitation of both the carbonyl and the alkene units.

Compound **7c** does not undergo the ODPM rearrangement on acetone-sensitized irradiation; only recovered starting material is obtained as a 2:1 mixture of *E*/*Z* diastereoisomers. Surprisingly, direct irradiation of **7c** using Pyrex-filtered light yields the ODPM product (*Z*)-**10c** and the diene **15** (Scheme

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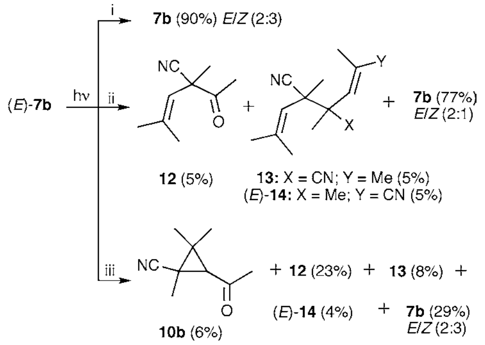
[4] Armesto, D.; Ortiz, M. J.; Agarrabeitia A. R.; Aparicio-Lara, S. *Synthesis* **2001**, 1149−1158.

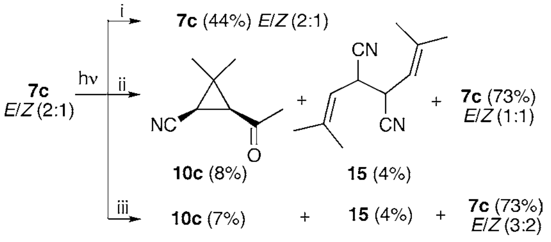
Scheme 2 [a]



[a] Conditions: (i) acetone, 7 h; (ii) direct, Pyrex, 6 h; (iii) direct, quartz, 254 nm.

3). Compounds **10c** and **15** should arise from the S_1 (n,π^*) or the T_2 (n,π^*) excited states. As mentioned before there is only one report in the literature of ODPM reactions via the S_1 or T_2 states.[2] These two products are also obtained on irradiation at 254 nm. Under these conditions the excited state involved in the ODPM and Norrish type I reactions could be the S_2 (π,π^*) or, alternatively, the S_1 arising from internal conversion.

Scheme 3 [a]

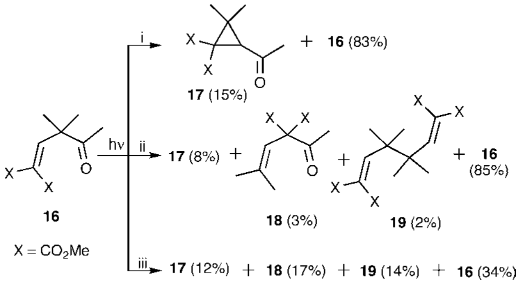


[a] Conditions: (i) acetone, 8 h; (ii) direct, Pyrex, 6 h; (iii) direct, quartz, 254 nm.

The unusual reactivity observed for compounds **7** raises the question whether these reactions only occur when cyano groups are present at the γ-position of the enone. To clarify this point, we have investigated the photochemical reactivity of enone **16** in which cyano groups are replaced by methoxycarbonyl groups.

Acetophenone-sensitized irradiation of **16** leads to formation of the ODPM product **17** (15%) arising from the T_1 (π,π^*) excited state. Thus, replacing the cyano groups in **7a** by methoxycarbonyls restores the normal ODPM reactivity pattern. Direct irradiation of **16**, through Pyrex, also affords **17** (8%), compound **18**, resulting from 1,3-acyl shift, and **19**, obtained by decarbonylation and dimerization of the resulting radical (Scheme 4). The formation of **17** under these conditions could be a result of intramolecular triplet energy transfer from the carbonyl to the alkene grouping. Finally, irradiation of **16** through quartz, at 254 nm, using a low-pressure Hg arc lamp, affords the ODPM product **17**, compound **18**, and diene **19**. These results demonstrate that the ODPM and Norrish type I reactions take place via the S_2 (π,π^*) state in photoreactions of β,γ-unsaturated ketones possessing electron-withdrawing γ-substituents other than cyano.

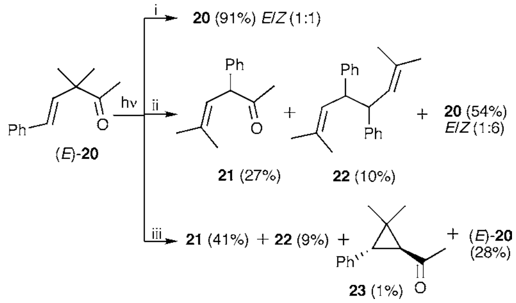
Scheme 4 [a]



[a] Conditions: (i) acetophenone, 14 h; (ii) direct, Pyrex, 14 h; (iii) direct, quartz, 254 nm.

The substitution effects observed for compounds **7** and **16** are both surprising and difficult to explain at this point. The short wavelength promoted reactivity of these compounds could be due to either the electron-withdrawing properties of the cyano and ester groups or their ability to conjugatively stabilize biradical intermediates. If the latter effect predominates, it should operate control on the excited reactivity profiles of other β,γ-unsaturated ketones that contain substituents that alter the energies of radical intermediates involved in the OPM process. This possibility can be probed by using the enone (*E*)-**20**, which has monophenyl substitution at the γ-position that should provide stabilized radical intermediates. Acetophenone triplet-sensitized irradiation of (*E*)-**20**[5]gives recovered starting material only, as a 1:1 mixture of *E*/*Z* diastereoisomers, whereas direct irradiation, through Pyrex, affords ketone **21**, resulting from 1,3-acyl shift and diene **22** arising from decarbonylation and dimerization of the resulting radicals. Compounds **21** and **22** are also formed on direct irradiation at 254 nm. However, under these conditions the corresponding ODPM product (*E*)-**23** is obtained in very low yield (ca. 1%) (Scheme 5). These results demonstrate that when electron-withdrawing groups

Scheme 5 [a]

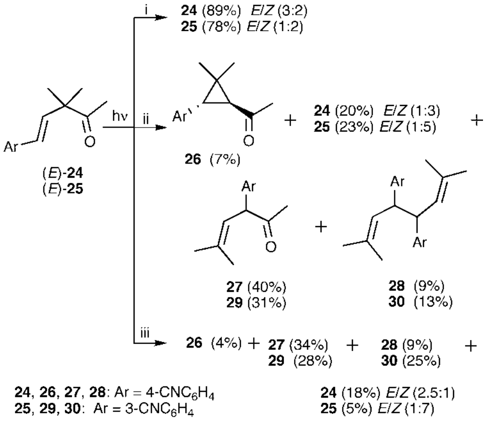


[a] Conditions: (i) acetophenone, 5 h; (ii) direct, Pyrex, 1 h; (iii) direct, quartz, 254 nm.

are not present at the γ-position of β,γ-unsaturated ketones, the efficiency of the ODPM rearrangement taking place via a S_2 (π,π^*) excited state decreases considerably.

We have studied the 4-cyano- and 3-cyano-substituted enones **24** and **25** in order to obtain additional information on the influence of electron-withdrawing groups on singlet excited-state ODPM rearrangement reactions of β,γ-unsaturated ketones. The results of this investigation are summarized in Scheme 6. Triplet-sensitized irradiation of **24** using 3-methoxyacetophenone gives recovered starting material only as a 2:3 mixture of *E*/*Z* diastereoisomers. In contrast, direct irradiation of **24** through Pyrex for 1 h affords the ODPM product (*E*)-**26**, the ketone **27** resulting from 1,3-acyl shift, and the diene **28** arising from decarbonylation and dimerization of the resulting radicals. The three products are also formed on direct irradiation at 254 nm, showing that 4-cyano substitution does help to promote ODPM rearrangements and Norrish type I reactions in the S_2 (π,π^*) excited state and also by excitation of the carbonyl to the S_1 or T_2 states (Scheme 6). However, when the cyano group is at *meta*-position ((*E*)-**25**), only Norrish type I products, **29** and **30**, are observed (Scheme 6). This result suggests that conjugation of the biradical intermediates with cyano groups is important for the success of the rearrangement.

Scheme 6 [a]



[a] Conditions: (i) 3-methoxyacetophenone, 8 h; (ii) direct, Pyrex, 1 h; (iii) direct, quartz, 254 nm.

In summary, earlier studies of the photoreactivity of β,γ-unsaturated ketones have established that these compounds usually undergo ODPM rearrangements on triplet-sensitized irradiation via the T_1 (π,π^*) excited state. In contrast, direct irradiation of β,γ-unsaturated ketones promotes 1,3-acyl migration and decarbonylation reactions that occur in S_1 (n,π^*) or T_2 (n,π^*) excited states.[1] The results obtained in the current study show that β,γ-unsaturated methyl ketones with electron-withdrawing groups at γ-position undergo ODPM rearrangements and Norrish type I reactions on direct irradiation at 254 nm. The findings are consistent with the involvement of a S_2 (π,π^*) excited state in these reactions. Under these conditions bond formation and bond cleavage must be extremely fast to compete with internal conversion. In some instances ODPM reactions occur on direct irradiation using Pyrex-filtered light, probably via the S_1 (n,π^*) or the T_2 (n,π^*) states. The reasons for the unusual ODPM reactivity in the S_2 state are unclear at this point. In this regard it is worth noting that Zimmerman et al.[6] have reported that the multiplicity and regiochemistry of the DPM reaction are affected by cyano and methoxycarbonyl substitution at 1- and 3-positions of the 1,4-diene. Norrish type I reactivity of S_2 (π,π^*) excited states of these substrates might be due to the high energy content of this excited state that promotes homolytic bond fission at the allylic position. Further studies will be necessary to determine the scope and the structural factors that control these novel reactions. In our opinion, the results obtained in this study open new lines of research on the photoreactivity of β,γ-unsaturated carbonyl compounds.

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Supporting Information Available: Experimental procedures for the preparation of enones **7a−c**, **16**, **24**, and **25**; experimental details for the photolysis; analytical and spectroscopic data for all photoproducts; and ^{1}H NMR spectra for all compounds lacking analyses. This material is available free of charge via the Internet at http://pubs.acs.org.

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