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Perfect Switching of Photoreactivity by Acid: Photochemical Decarboxylation versus Transesterification of Mesityl Cyclohexanecarboxylate

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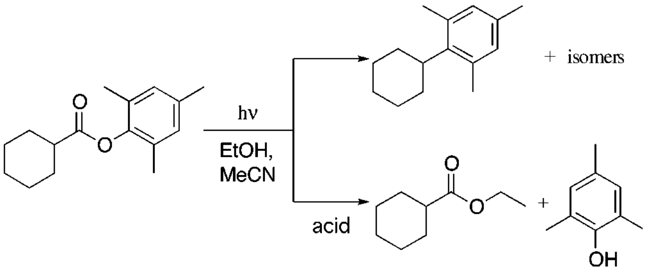
ABSTRACT



Mesityl cyclohexanecarboxylate has been photodecarboxylated upon excitation at 254 nm to form cyclohexylmesitylene in good yield in neutral acetonitrile solutions. In the presence of a catalytic amount of the acid and ethanol as a nucleophile, however, the same compound undergoes facile transesterification upon irradiation, affording its ethyl ester in almost quantitative yield.

Photochemical transformations of carboxylic esters have been studied extensively in terms of cycloaddition, hydrogen abstraction, isomerization, and rearrangement.[1] However, due to the lack of intense absorption bands in the conventional ultraviolet region for a simple carboxyl chromophore, the previous photochemical studies have concentrated mostly on arenecarboxylates, in which the carboxyl chromophore is conjugated with the aromatic moiety, providing a readily accessible π,π^* transition.[2] Consequently, the photochemistry of such aromatic esters has attracted much attention from the mechanistic and synthetic points of view, but unfortunately, a complex mixture of several minor products is always obtained with a poor material balance.[1] For instance, the photolysis of moderately hindered 2,4-alkylphenyl (aryl)-alkanoate leads to at least five competing reactions.[3] In contrast to the several competing photochemical reactions reported for most of the aromatic esters mentioned above, mesityl benzoate has been reported to undergo photohydrolysis in aqueous acetonitrile in the absence of acid, but with poor product yield (7%).[4]

Herein, we report an unprecedented photoreactivity switching of an aryl alkanoate controlled by the acid concentra-

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(1) For general reviews on the photochemistry of carboxylic acids and esters, see: (a) Givens, R. S.; Levi, N. In *The Chemistry of Functional Groups, Supplement B, The Chemistry of Acid Derivatives*; Patai, S., Ed.; John Wiley & Sons, Ltd.: London, 1979; p 641. (b) Pincock, J. A. In *CRC Handbook of Organic Photochemistry and Photobiology*; Horspool, W. M., Song, P.-S., Eds.; CRC Press: Boca Raton, 1995; p 393 (Chapter 32).

(2) A Study of photodecarboxylation of simple aliphatic carboxylic acids was carried out in the gas phase, and in general the reaction is more complicated due to several competing reactions. For reviews: (a) Coyle, J. D. *Chem. Rev.* **1978**, *78*, 97. (b) Budac, D.; Wan, P. *J. Photochem. Photobiol. A: Chem.* **1992**, *67*, 135. (c) Reference 1b, p 384 (Chapter 31).

(3) Bradshaw, J. S.; Loverridge, E. L.; White, L. *J. Org. Chem.* **1968**, *33*, 4127.

(4) Pacifici, J. G.; Zannucci, J. S.; Lappin, G. R.; Ownby, J. C.; Kelly, C. A. *Mol. Photochem.* **1971**, *3*, 175.

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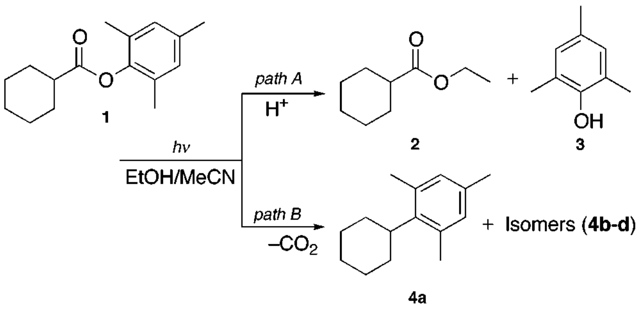
tion: from decarboxylation in neutral acetonitrile to transesterification in acidic acetonitrile containing ethanol, both of which give their respective products in quantitative yields. The results, exemplified by mesityl cyclohexanecarboxylate (**1**) in Scheme 1, provide not only a convenient, powerful tool for controlling the photoreactivity of aromatic esters but also a versatile photolabile protecting group[5] which is readily converted to other ester groups upon irradiation in the presence of an appropriate acidic alcohol. Alternatively, decarboxylation to the corresponding alkylmesitylene may be performed in neutral solvents.

Scheme 1



First of all, it should be emphasized that thermally the mesityl ester **1** was entirely stable under the acidic conditions employed in the present study, i.e., acetonitrile solutions containing 0.34 M ethanol and ≤ 5 mM methanesulfonic acid, and was recovered in >99% yield after 72 h of standing in the dark at 25 °C. Even in the presence of 20 mM of the acid, no transesterification product was detected on GC after 1 week at 25 °C. In photochemical runs, acetonitrile solutions of **1** (2 mM) containing ethanol (0.34 M) were irradiated at 254 nm under an argon atmosphere, mostly at 0 °C, in the presence and absence of acid (0–5 mM). The irradiations led to the efficient formation of the transesterification products, i.e., ethyl cyclohexanecarboxylate (**2**) and mesitol (**3**), and/or the decarboxylation products (**4**), depending on the conditions employed. The conversions and product yields obtained after 2 h irradiation under a representative variety of conditions are listed in Table 1.

In the absence of acid, the photolysis of **1** exclusively afforded the decarboxylation products, i.e., 2,4,6-trimethyl-1-cyclohexylbenzene (**4a**) and its positional isomers (**4b–d**), in a ratio of 87:3:2:8; **4a** was identified by comparison with an authentic specimen synthesized independently,[6] while the latter three were tentatively assigned to the positional isomers of **4a**, produced in the secondary photorearrangement upon prolonged irradiations[7] on the basis of the GC retention times and mass spectra.

Table 1. Competitive Photochemical Transesterification and Decarboxylation of Mesityl Cyclohexanecarboxylate (**1**) in the Presence/Absence of Acid[a]

additive	(mM)	temp, °C	convn, %	yield, %		
				2	**3**	**4**
none	(0)[b]	0	91	0	0	91
	(0)[b]	0	86[c]	0	4	82
$MeSO_3H$	(0.0036)	0	91	0	0	91
	(0.034)	0	92	33	34	48
	(0.051)	0	96	87	91	5
	(0.062)	−40	34	27	18	2
	(0.062)	25	93	13	64	19
	(0.17)	0	93	88	93	0
	(0.23)	0	84[d]	78[e]	83	0
	(0.93)	0	84[c]	38	37	45
	(1.02)	0	86	84	86	0
	(4.92)	0	89	83	89	0
CF_3CO_2H	(5.49)	0	94	94	72	0
BF_3/OEt_2	(0.64)	0	94	94	90	0

[a] Irradiated for 2 h in quartz tubes under Ar with a low-pressure mercury lamp (254 nm) in acetonitrile containing **1** (1.8–2.3 mM) and ethanol (0.34 M), unless otherwise indicated. [b] No ethanol added. [c] Irradiation was performed in pentane. [d] In 2-propanol (0.34 M) instead of ethanol. [e] Yield of isopropyl ester.

In contrast, the addition of a very small amount of acid to the system (in the μM order) dramatically switched the mode of photolysis from decarboxylation to transesterification, maintaining an equally excellent material balance (Scheme 1). As shown in Table 1, even in the presence of methanesulfonic acid concentrations as low as 0.034 mM, the photolysis afforded the transesterification (**2** and **3**) and decarboxylation (**4**) products in comparable yields. Upon increasing acid concentrations of up to 0.10 mM, the yields of **2** and **3** rapidly dominate, at the expense of **4**, reaching a plateau thereafter. Other typical Brønsted and Lewis acids, such as trifluoroacetic acid and trifluoroborane etherate, also switched the photoreaction mode to the transesterification, affording **2** and **3** in excellent yields. The use of 2-propanol instead of ethanol also led to the smooth formation of the corresponding ester, though at slightly slower rates but in correspondingly excellent yields under similar conditions.

The irradiation temperature moderately affected both the reaction rate and the product distribution. At −40 °C the reaction rate (consumption of the starting material) was significantly reduced, although the material balance remained good-to-excellent. At 25 °C the reaction rate increased; however, the material balance (particularly that of yield of **2**) was lowered and the decarboxylation product **4** was appreciably favored. Both the decreased yield of **2** and the increased yield of **4** at 25 °C may be rationalized by an increased escape of the radical pairs from the solvent cage, resulting in the enhanced decarbonylation[8] and decarboxy-

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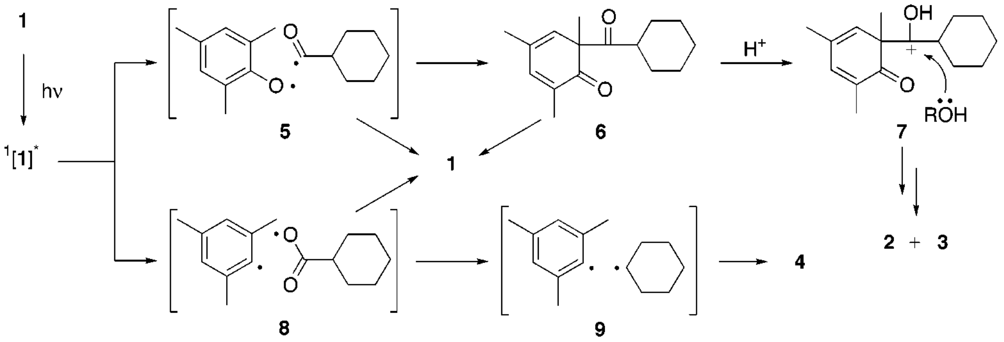
(5) For a general review on photoprotecting groups: Pillai, V. N. R. *Org. Photochem.* **1987**, *9*, 225.

(6) (a) Kim, J. N.; Chung, K. H.; Ryu, E. K. *Tetrahedron Lett.* **1994**, *35*, 903. (b) Kotsuki, H.; Ohishi, T.; Inoue, M.; Kojima, T. *Synthesis* **1999**, 603. (c) Kotsuki, H.; Ohishi, T.; Inoue, M. *Synlett* **1998**, 255. (d) Hickinbottom, W. J.; Rogers, N. W. *J. Chem. Soc.* **1957**, 4124.

(7) The three positional isomers **4b–d** are known to be formed through the 1,2-shift of the alkyl group via a benzvalene intermediate. Indeed, control experiments with pure **4a** under similar photochemical conditions gave the same isomers. See: (a) Kaplan, L.; Wilzbach, K. E.; Brown, W. G.; Yang, S. S. *J. Am. Chem. Soc.* **1965**, *87*, 675. (b) Burgstahler, A. W.; Chien, P.-L. *J. Am. Chem. Soc.* **1964**, *86*, 2940. (c) Wilzbach K. E.; Kaplan, L. *J. Am. Chem. Soc.* **1964**, *86*, 2307. Thus, the isomers **4b–d** are tentatively assigned to 2,3,5-, 2,3,6-, and 2,4,5-trimethyl-1-cyclohexylbenzenes.

Scheme 2



lation of the relevant precursors **5** and **8** at the elevated temperature.

The solvent effect provides us with valuable information about the nature of the intermediates. As shown in Table 1, the photolysis of **1** in acetonitrile ([MeSO$_3$H] = 1.02 mM) exclusively afforded the transesterification products **2** and **3**, whereas the formation of decarboxylation product **4** was favored upon irradiation in pentane ([MeSO$_3$H] = 0.93 mM), yet with comparable conversion for both solvents. This can be accounted for in terms of a charge-transfer character of intermediate **5**, i.e., [acyl$^{\delta+}$ ··· phenoxy$^{\delta-}$].[9]

To elucidate the origin and mechanism of this unique pH-controlled photoreactivity switching, spectroscopic examinations of **1** in the ground and excited states were carried out in the presence/absence of acid in acetonitrile containing ethanol (0.34 M). In the UV spectral examinations of **1** with added acid, no noticeable ground-state interactions were observed between **1** and methanesulfonic acid concentrations of up to 0.7 M. However, the fluorescence spectrum did not appear to be influenced by the addition of acid up to a concentration of 0.03 M. Further addition of the acid (0.1–2.2 M) caused a bathochromic shift of the fluorescence peak from 290 to 296 nm, as well as gradual significant decreases in fluorescence intensity. The fluorescence quenching behavior of **1** with higher concentrations of methanesulfonic acid was analyzed quantitatively to give a linear Stern–Volmer plot with a slope of 1.10 M^{-1}. From the fluorescence lifetime of **1** ($\tau = 1.7$ ns), measured independently by the single-photon-counting technique,[10] we could determine the quenching rate constant as $k_q = 6.5 \times 10^8$ M^{-1} s^{-1}, which is lower by more than 1 order of magnitude than the diffusion-controlled rate constant in acetonitrile (1.9×10^{10} M^{-1} s^{-1}).[11]

Since the reactivity switching from decarboxylation to transesterification is complete at acid concentrations as low as 0.1 mM, and no appreciable fluorescence quenching is observed at such a low acid concentration, the excited singlet state of **1** cannot be the immediate precursor to **2**/**3** or **4**. A mechanism postulating the formation of a ketene intermediate and the subsequent alcoholysis has been proposed,[12] but this possibility is clearly ruled out in the present case since deuterium incorporation was not found in the product **2** when the photolysis was carried out in ethanol-*O*-*d*. Attempted triplet sensitizations with acetophenone and fluorene[13] have failed to give any product under similar conditions, ester **1** being completely recovered. In search of transient species formed upon irradiation, we performed spectroscopic monitoring of the sample solution during irradiation to find a moderate absorption band centered at ca. 320 nm, which is assigned as the n,π^* transition of a cyclohexadienone derivative.[14] On the basis of the smooth reactivity switching with increasing acid concentration and the spectroscopic evidence, we tentatively propose the mechanism shown in Scheme 2 for this photoreaction.[15]

In neutral solutions, the singlet excited state of **1** undergoes three possible processes, i.e., deactivation to **1** and two types of bond dissociations, giving the radical pair intermediates **5** and **8**. The radical pair **5** may afford the cyclohexadienone derivative **6**, which is similar to the intermediate postulated in the photo-Fries rearrangement. Both **5** and **6** can easily revert to the starting material **1** in the absence of any trapping agent such as a proton.[16] On the other hand, the radical pair

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(8) (a) Finnegan, C. C.; Kuntson, D. *Chem. Commun.* **1966**, 172. (b) *J. Am. Chem. Soc.* **1967**, *89*, 1970. (c) Barton, D. H. R.; Chow, Y. L.; Cox, A.; Kirby, G. W. *Tetrahedron Lett.* **1962**, 1055. (d) Barton, D. H. R.; Chow, Y. L.; Cox, A.; Kirby, G. W. *J. Chem. Soc.* **1965**, 3571. (e) Horspool, W. M.; Pauson, P. L. *J. Chem. Soc.* **1965**, 5162.

(9) Coppinger and Bell claimed that in photo-Fries rearrangement the radical pair should exist on the experimental basis but it is very hard to explain why the two components in the pair always remain associated only in terms of solvent cage. Hence, they envisaged the charge-transfer interaction developed in the radical pair on the basis of the substituent effect on the quantum yield. Coppinger, G. M.; Bell, E. R. *J. Phys. Chem.* **1966**, *70*, 3479.

(10) Mori, T., unpublished results: $\tau = 1.7$ ns (25 °C) at 0.28 mM in MeCN in the presence of EtOH (0.34 M) and $\tau = 1.6$ ns in the presence of MeSO$_3$H (57 mM) at 25 °C.

(11) Murov, S. L.; Carmichael, I.; Hug, G. L. In *Handbook of Photochemistry*, 2nd ed.; Mercel Dekker: New York, 1993; p 210.

(12) Gutsche, C. D.; Oude-Alink, A. M. *J. Am. Chem. Soc.* **1968**, *90*, 5855.

(13) Triplet state energies (E_T) of sensitizers are 311 and 284 kJ/mol, respectively. E_T of ester **1** is assumed to be ~320 kJ/mol. See, ref 11, Section 1.

(14) (a) Grabner, G.; Köhler, G.; Marconi, G.; Monti, S.; Venuti, E. *J. Phys. Chem.* **1990**, *94*, 3609. (b) Weiner, S. A.; Mahoney, L. R. *J. Am. Chem. Soc.* **1972**, *94*, 5029. See also: (c) Mahoney, L. R.; DaRooge, M. A. *J. Am. Chem. Soc.* **1970**, *92*, 890. (d) Becker, H.-D. *J. Org. Chem.* **1965**, *30*, 982.

(15) We thank reviewers of ACS for suggestions and comments on the reaction mechanism.

(16) (a) Jackson, L. B.; Waring, A. J. *J. Chem. Soc., Perkin Trans. 1* **1988**, 1791. (b) Waring, A. J.; Zaidi, J. H. *J. Chem. Soc., Perkin Trans. 1* **1985**, 631.

8 either regenerates **1** or decarboxylates to give radical pair **9**, which in turn recombine in the solvent cage to afford **4**. In the presence of acid, the labile intermediate **6** is trapped by acid and the resulting intermediate **7** undergoes solvolysis to give the products **2** and **3**.[17]

In the present study, we have demonstrated that the presence of acid completely switches the photoreactivity of mesityl alkanecarboxylate from decarboxylation to transesterification. In this context, recent reports[18] by Hoffmann and Pete of the acid-induced intramolecular photocycloaddition of alkenyloxybenzene derivatives are quite intriguing from the viewpoint of controlling photobehavior by acids. This research shows that acids can play a more vital role in photochemistry, with the active control of photobehavior by acids applied as a more general idea to a much wider range of photoreactions. Work on the scope, limitations, and detailed mechanism of the present acid-controlled photobehavior is currently in progress.

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Supporting Information Available: Figures of the spectral changes during the irradiation of mesityl cyclohexanacarboxylate **1**. This material is available free of charge via the Internet at http://pubs.acs.org.

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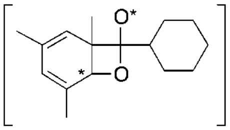
[17] Bicyclic biradical/zwitterionic intermediates bearing a fused-oxetane ring, such as **10** in the present case, have been suggested previously in the photo-Fries rearrangement of phenyl esters. The radical pair intermediate **5** is accepted in general in the mechanism of photo-Fries rearrangement, and indeed, ab initio calculations clearly demonstrate that the fused-oxetane intermediate **10** ($\Delta H_f = -91.4$ kJ mol^{-1}, relative to the energy of excited singlet state of **1**) is less stable than the radical pair **5** ($\Delta H_f = -201.6$ kJ mol^{-1}). However, **10** is much more stable than the radical pair **8** ($\Delta H_f = -6.0$ kJ mol^{-1}), suggesting that intermediate **10** could not rigorously be ruled out from the energetic point of view. See: (a) Reese, C. B.; Anderson, J. C. *J. Chem. Soc.* **1963**, 1781. (b) Sander, M. R.; Hedaya, E.; Trecker, D. J. *J. Am. Chem. Soc.* **1968**, *90*, 7249. (c) Sander, M. R.; Trecker, D. J. *J. Am. Chem. Soc.* **1967**, *89*, 5725.



10 (* = • or +/-)

[18] (a) Hoffman, N.; Pete, J.-P. *J. Org. Chem.* **1997**, *62*, 6952. (b) Hoffman, N.; Pete, J.-P. *Tetrahedron Lett.* **1998**, *39*, 5027.