

ENHANCED PHOTODECARBOXYLATION EFFICIENCY OF α -HYDROXY-SUBSTITUTED ARYLACETIC ACIDS IN AQUEOUS SOLUTION

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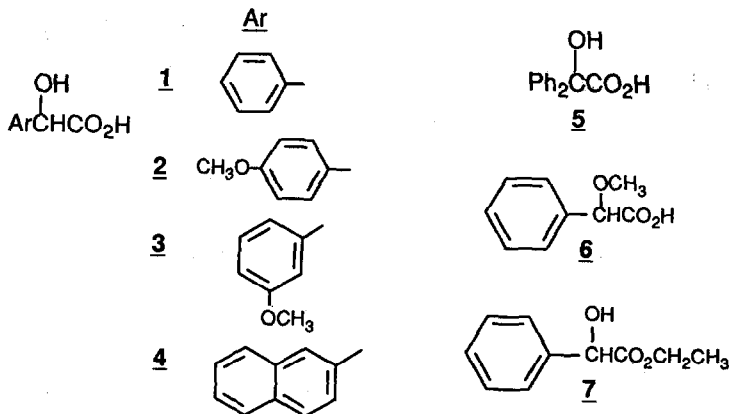
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SUMMARY: The photochemistry of several α -hydroxyarylacetic acids, including mandelic and benzilic acids, was studied in aqueous solution; these compounds photodecarboxylate, via α -hydroxyarylmethyl carbanions, with high quantum yields ($\Phi \approx 0.2-0.7$), to give the corresponding arylmethanols in high yield ($> 50\%$), in contrast to the parent arylacetic acids, which typically have $\Phi \approx 0.01-0.03$.

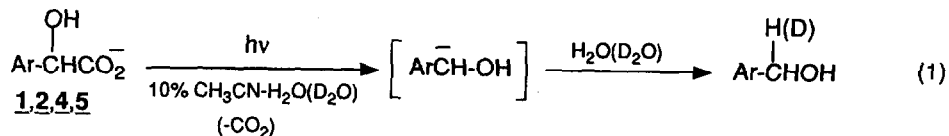
There is continuing interest in the study of photodecarboxylation, especially of arylacetic acids since these simple systems provide a benzyl moiety, which is capable of stabilizing an incipient carbanion or radical intermediate¹⁻¹⁰. For example, the effect on photodecarboxylation efficiency of the "electron count" in the internal cyclic array of several benzannelated acetic acids has been reported by us¹. One of these systems (suberene-5-carboxylic acid)¹ photodecarboxylates with $\Phi \approx 1$. In addition, use of a nitro substituent in the phenyl ring to enhance the photodecarboxylation efficiency in these systems is well-known, the mechanism of which has been studied in some detail²⁻⁴. One of the goals of studying photodecarboxylation is to understand the basic structural requirements necessary for efficient C-C bond heterolysis (as opposed to homolysis) from electronically excited states, giving rise to carbanion intermediates in the primary step. Because C-C bond heterolysis is in general rare in organic photochemistry, we have continued efforts in search of simple arylacetic acids which will photodecarboxylate with high quantum yield¹¹. The availability of such systems will enable the study of reaction mechanism of such a simple process significantly easier, unencumbered by low reactivity. We report here that most simple α -hydroxy-substituted arylacetic acids photodecarboxylate with quantum yields in the range 0.2-0.6 in aqueous solution if $\text{pH} > \text{pK}_a$. The magnitude of these quantum yields is *unprecedented* for relatively simple arylacetic acids. Evidence suggest that the initial primary step in these photodecarboxylations is C-C bond heterolysis, giving rise to α -hydroxyarylmethyl carbanion intermediates.

The photodecarboxylation of α -hydroxyarylacetic acids **1-5** was studied in aqueous solution (10% CH_3CN cosolvent; 10^{-3} M substrate; Rayonet RPR 100 photochemical reactor with 254 nm lamps; photolysis time 5-20 min; pH 0-12) and compared with their parent arylacetic acids, as well as with related systems **6** and **7**. Except for **3**, all of **1-5** photodecarboxylated cleanly (yields $> 50\%$), to give the corresponding arylmethanols (eq 1), with quantum

yields for product formation (Φ) in excess of 0.2 (Table I). When the photolyses were carried out in D_2O ($pD \approx 7$), the products isolated were the corresponding α -deuterated- α -arylmethanols (eq 1), after the initial products were



washed with H_2O to back-exchange the hydroxyl proton. At low pH ($pH < pK_a$), the photodecarboxylation efficiency of these compounds drops off dramatically; they are non-reactive below pH 2. This implies that the carboxylate form of these compounds are photoreactive. At $pH > 12$, photodecarboxylation efficiency also drops off considerably for all substrates, with concurrent formation of side products which remain to be characterized. It is believed at this stage that a change in photodecarboxylation mechanism occurs high pH, presumably to one involving radicals or radical ions. However, it is clear that these compounds do react *cleanly* over a wide pH range (*viz.* pH 3-12). Noteworthy is the observation that **6** also showed enhanced reactivity (to give methyl benzyl ether on photodecarboxylation) but **7** failed to react. In addition, all the *parent* arylacetic acids except for 2,2-diphenylacetic acid ($\Phi \approx 0.12$)¹ (e.g., phenylacetic acid and 2-naphthylacetic acid) failed to react under the same conditions ($\Phi < 0.01$); complete recovery of the starting materials was possible in these cases. A striking observation



is the apparently anomalously low Φ observed for α -hydroxy-3-methoxyphenylacetic acid (**3**) (Table I). However, this observation is consistent with a mechanism of reaction involving primary benzylic C-C bond heterolysis from S_1 ¹⁵; the 3-methoxy group, being a better electron donor than the 4-methoxy group in the excited state^{17,18}, would exert a destabilizing effect on the incipient α -hydroxybenzyl carbanion intermediate, resulting in a lower quantum yield for reaction. The effect is another example of "meta-activation" (in this case "deactivation") commonly observed in photochemical reactions of substituted benzenes¹⁷⁻²⁰. This is the first instance in which this effect has been

observed for photogenerated *benzyl carbanion* intermediates. It is well-known that electronegative α -heteroatoms stabilize carbanions via an inductive effect²¹. The α -hydroxyl substituent in arylacetic acids probably enhances the photodecarboxylation efficiency, by stabilizing the incipient carbanion. We have found that other electronegative atoms at the α -position have a similar enhancing effect. Thus, all of α -chloro, α -fluoro and α -aminophenylacetic acids photodecarboxylate with good quantum yields ($\Phi \approx 0.1-0.3$), whereas α -alkylphenylacetic acids (e.g., α -methyl, α -cyclopentyl and α -cyclohexyl) did not display enhanced reactivity ($\Phi < 0.03$), compared with the parent arylacetic acids.

In summary, we have discovered a general way to enhance the photodecarboxylation efficiency of simple arylacetic acids, by placing an electronegative substituent at the α -position in these compounds. The availability of these much more reactive systems will facilitate the study of the details of the photodecarboxylation mechanism of these and related compounds. *In addition, these reactions provide a way to photochemically generate α -hydroxycarbanions, which have been elusive but theoretically interesting carbanions*²².

Acknowledgment

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References and Notes

1. I. McAuley, E. Krogh and P. Wan, *J. Am. Chem. Soc.*, 1988, **110**, 600.
2. B. B. Craig, R. G. Weiss and S. J. Atherton, *J. Phys. Chem.*, 1987, **91**, 5906.
3. J. D. Margerum and C. T. Petrusis, *J. Am. Chem. Soc.*, 1969, **91**, 2467.
4. P. Wan and S. Muralidharan, *J. Am. Chem. Soc.*, 1988, **110**, 4336.
5. G. A. Epling and A. Lopes, *J. Am. Chem. Soc.*, 1977, **99**, 2700.
6. J. V. Castell, M. J. Gomez-L., M. A. Miranda and I. M. Morera, *Photochem. Photobiol.*, 1987, **46**, 991.
7. F. R. Stermitz and W. H. Huang, *J. Am. Chem. Soc.*, 1971, **93**, 3427.
8. J. D. Coyle, *Chem. Rev.*, 1978, **78**, 97.
9. M. A. Fox, *Chem. Rev.*, 1979, **79**, 253.
10. T. O. Meiggs, L. I. Grossweiner and S. I. Miller, *J. Am. Chem. Soc.*, 1972, **94**, 7981.
11. Simple arylacetic acids photodecarboxylate with only low quantum efficiency ($\Phi \approx 0.01-0.03$)^{5,10}, making detailed studies of their reaction mechanism difficult, and in many cases inconclusive. For example, radical derived products observed in the photolysis of simple arylacetic acids suggest homolysis as a competing if not the major pathway^{5,8-10}. Because overall quantum yields are low, it has been difficult to quantify the importance of either the homolytic or heterolytic pathway in these reactions. Photoinduced electron ejection from the carboxylate anion has also been suggested as a primary pathway^{5,9,10}. A number of recent reports¹²⁻¹⁴ of highly efficient photodecarboxylations have appeared but the mechanisms of these do not involve carbanion intermediates.
12. K. Okada, K. Okamoto and M. J. Oda, *J. Am. Chem. Soc.*, 1988, **110**, 8736.
13. A. Defoin, R. Defoin-Straatmann and K. Hildenbrand, E. Bittersmann, D. Krefit and H. J. Kuhn, *J. Photochem.*, 1986, **33**, 237.
14. W. G. Dauben, B. A. Kowalczyk and D. P. Bridon,

Tetrahedron Lett., 1989, 2461. 15. Triplet sensitization ($\lambda_{ex} = 350$ nm; pH 12) using sodium benzophenone-2-carboxylate ($E_T \approx 68$ kcal mol⁻¹)¹⁶ as the sensitizer with **4** ($E_T \approx 60$ kcal mol⁻¹)¹⁶ failed to give any reaction. In addition, the fluorescence emission intensity (at pH's > 5) of α -hydroxyarylacetic acids is significantly weaker than the emission of the corresponding parent arylacetic acid (by a factor of ≈ 4). These observations suggest that the photodecarboxylations are from the singlet excited state. 16. S. L. Murov, *The Handbook of Photochemistry*, Marcel Dekker, New York, 1973. Triplet state energies were estimated based on related model compounds. 17. (a) H. E. Zimmerman and V. R. Sandel, *J. Am. Chem. Soc.*, 1963, **85**, 915; (b) N. J. Turro and P. Wan, *J. Photochem.*, 1985, **28**, 93. 18. That the 3-methoxy group is a better electron donor than 4-methoxy in the excited state may not be universally true, especially if the photochemical reaction proceeds via radical pairs; see for example, D. P. DeCosta and J. A. Pincock, *J. Am. Chem. Soc.*, 1989, **111**, 8948. 19. H. E. Zimmerman and S. Somasekhara, *J. Am. Chem. Soc.*, 1963, **85**, 922. 20. S. J. Cristol and T. H. Bindel, *Org. Photochem.*, 1983, **6**, 327. 21. J. C. Stowell, *Carbanions in Organic Synthesis*; Wiley: New York, 1979; Chapter 4. 22. K. M. Downard, J. C. Sheldon, J. H. Bowie, D. E. Lewies and R. N. Hayes, *J. Am. Chem. Soc.*, 1989, **111**, 8112.

Table I. Quantum Yields for Photodecarboxylation of α -Hydroxyarylacetic Acids **1-7**.

Compound	Φ^a	Compound	Φ^a
1 ^b	0.40	5 ^c	≈ 0.7
2	0.27	6	0.27
3	<0.01	7	0.00
4	0.42		

^a Quantum yields (for product formation, i.e., arylmethanols in the case of **1-4**) were measured at pH ≈ 11.5 (10% CH₃CN cosolvent), using the photodecarboxylation of suberene-5-carboxylic acid ($\Phi = 1$)¹ as the secondary actinometer. Conversions were calculated by GC and ¹H NMR and kept below 30%. Solutions (10⁻³ M) were photolyzed in quartz vessels degassed with a stream of argon and kept at $\approx 12^\circ\text{C}$ during the course of the photolysis. The pH of the solution was adjusted with aq. NaOH prior to irradiation. No dark reactions were observed with any of the compounds. The identity of all products was confirmed by ¹H NMR and mass spectral analysis, and by comparison with authentic material. Estimated errors in Φ , $\pm 20\%$ of quoted value.

^b Commonly known as mandelic acid.

^c Commonly known as benzilic acid.