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Tetrahedron Letters

Tetrahedron Letters 47 (2006) 1965–1968

Photolytic decarboxylation of α-arylcarboxylic acids mediated by HgF_2 under a dioxygen atmosphere

Saeid Farhadi,[a,*] Parisa Zaringhadam[a] and Reza Zarei Sahamieh[b]

[a]*Department of Chemistry, University of Lorestan, Lorestan, Khoramabad 68135-465, Iran*
[b]*Faculty of Science, University of Lorestan, Lorestan, Khoramabad 68135-465, Iran*

Received 29 September 2005; revised 4 January 2006; accepted 16 January 2006

Abstract—Mercuric fluoride (HgF_2), as a light-sensitive inorganic compound, in the presence of dioxygen is able to convert various α-aryl- and α,α-diarylcarboxylic acids into the corresponding aldehydes and ketones selectively under photoirradiation via trapping of the benzylic radical by O_2.

Among the various carboxylic acids, decarboxylation of α-arylcarboxylic acids and their salts has received a good deal of attention, especially since several nonsteroidal anti-inflammatory drugs (NSAIDs), for example, ketoprofen and ibuprofen, are α-arylpropionate salts.[1–3] Indeed, decarboxylation of these acids provides a benzylic moiety, which is capable of stabilizing an incipient ionic or radical intermediate.

In this context, thermal decarboxylation of various α-arylcarboxylic acids has been extensively investigated for the transformation of these acids to aldehydes or ketones, alcohols and arylalkanes by using metallic and nonmetallic oxidants including $(NH_4)_2Ce(NO_3)_6$,[4] $Co(OAc)_3$,[5] NaClO,[6] n-Bu_4NIO_4,[7] $K_2S_2O_8$–$AgNO_3$,[8] CuI–O_2,[9] Fe(TPP)(X)–PhIO,[10] $NaIO_4$-crown ethers,[11,12] $Mn(OAc)_3$[13] and KO_2–nitrobenzenesulfonyl chloride.[14] Also, photolytic decarboxylation (PD) reactions of arylacetic acids and their derivatives have been extensively reported in the presence of various electron acceptors or photosensitizers such as aza aromatic compounds, dicyanonaphthalene, tetracyanobenzene and heterocyclic *N*-oxides.[15–17]

PD is important in several areas of study. In synthetic organic chemistry, several groups have utilized PD to prepare radical intermediates and organic compounds such as cyclophanes, the syntheses of which are difficult using conventional methods.[18–21] PD is also important in pharmaceuticals[22–25] and agriculture,[26,27] as many drugs, herbicides and pesticides containing the –COOH groups can extrude CO_2 when exposed to sunlight producing potentially toxic materials. PD is also the basis of the photo-Kolbe reaction.[28] The PD of α-arylcarboxylic acids thus continues to be an area of active research interest.[29–32]

In continuation of this work, we decided to examine photolysis of α-aryl acids in the presence of mercuric halides (HgX_2, X = F, Cl, Br and I) under an oxygen atmosphere. Herein, we report results obtained on PD of various α-aryl- and α,α-diarylcarboxylic acids using HgF_2 in CH_3CN under a dioxygen atmosphere at room temperature which resulted in the formation of the corresponding aldehydes and ketones in good yields.

In initial experimental studies on photoirradiation of α-aryl acids in the presence of inorganic mercury compounds, we found that illumination of a CH_3CN solution of diphenylacetic acid and HgF_2 with a 400 W high pressure mercury lamp under oxygen for 1 day, gave benzophenone in 95% yield along with elemental mercury, carbon dioxide (the limewater test) and HF, while the use of $HgCl_2$, $HgBr_2$, HgI_2, Hg_2Cl_2 and also $Hg(NO_3)_2$ instead of HgF_2, did not initiate the reaction. While other mercuric halides are less- or nonphotosensitive, the high sensitivity of HgF_2 to light is well known.[33] Without irradiation, benzophenone was scarcely

Keywords: α-Arylcarboxylic acids; Photolytic; Decarboxylation; Mercuric fluoride; Carbonyl compounds.
* Corresponding author. Fax: +98 6614600088; e-mail: sfarhad2001@yahoo.com

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doi:10.1016/j.tetlet.2006.01.082

obtained even in the presence of HgF_2. Therefore, we concluded that high sensitivity of HgF_2 to light plays an important role in this process. This reagent, that is not a decarboxylating agent in the absence of light, can probably be activated photochemically, affording selectively decarboxylated product. The formation of appreciable amounts of elemental Hg and carbon dioxide in the course of the reaction support suggestion that the present photoreaction involves a photoinduced one-electron transfer from the carboxylate moiety (–COOH) to HgF_2.[34] In addition to HgF_2, oxygen proved to be an oxidizing reagent in this reaction and, in the absence of this reagent (under N_2), a dimeric product was observed instead of the corresponding carbonyl product, as the only product, in excellent yield (see below).

To evaluate the scope of this method, the decarboxylation of various α-arylcarboxylic acids, in which their α-carbon atom is attached to an aryl group were studied. The results for PD of various aryl acids are summarized in Table 1. As can be seen in Table 1, all of the α-aryl acids decarboxylated selectively to give the corresponding carbonyl compounds under our reaction conditions. In all cases, in addition to the corresponding carbonyl compounds, large amounts of Hg, CO_2 and HF were formed during irradiation.

Table 1. Photolytic decarboxylation of α-aryl acids using HgF_2 under an O_2 atmosphere

$$\text{Ar—C(X)(Y)COOH} \xrightarrow[\text{CH}_3\text{CN / r.t}]{\text{HgF}_2\text{ / O}_2\text{ / }h\nu} \text{Product}$$

Entry	Ar	X	Y	Product[a]	Yield[b] (%)
1	C_6H_5	H	H	C_6H_5CHO	78
2	4-MeC_6H_4	H	H	4-MeC_6H_4CHO	88
3	2-MeC_6H_4	H	H	2-MeC_6H_4CHO	85
4	4-$MeOC_6H_4$	H	H	4-$MeOC_6H_4CHO$	88
5	2-$MeOC_6H_4$	H	H	2-$MeOC_6H_4CHO$	84
6	3-$MeOC_6H_4$	H	H	3-$MeOC_6H_4CHO$	82
7	4-$NO_2C_6H_4$	H	H	4-$NO_2C_6H_4CHO$	65
8	4-FC_6H_4	H	H	4-FC_6H_4CHO	60
9	4-HOC_6H_4	H	H	4-HOC_6H_4CHO	72
10	2-ClC_6H_4	H	H	2-ClC_6H_4CHO	70
11	4-ClC_6H_4	H	H	4-ClC_6H_4CHO	78
12	2,4-$Cl_2C_6H_3$	H	H	2,4-$Cl_2C_6H_3CHO$	80
13	2,6-$Cl_2C_6H_3$	H	H	2,6-$Cl_2C_6H_3CHO$	76
14[c]	1-$C_{10}H_7$	H	H	1-$C_{10}H_7CHO$	74
15[c]	2-$C_{10}H_7$	H	H	2-$C_{10}H_7CHO$	70
16	4-PhC_6H_4	H	H	4-PhC_6H_4CHO	66
17	C_6H_5	C_6H_5	H	$(C_6H_5)_2C{=}O$	95
18	C_6H_5	CH_3	H	$C_6H_5(CH_3)C{=}O$	94
19	C_6H_5	C_2H_5	H	$C_6H_5(C_2H_5)C{=}O$	94
20	C_6H_5	*n*-C_3H_7	H	$C_6H_5(n\text{-}C_3H_7)C{=}O$	91
21	4-ClC_6H_4	C_6H_5	H	4-$ClC_6H_4(C_6H_5)C{=}O$	95
22	4-ClC_6H_4	4-ClC_6H_4	H	$(4\text{-}ClC_6H_4)_2C{=}O$	96
23	4-$MeOC_6H_4$	4-$MeOC_6H_4$	H	$(4\text{-}MeOC_6H_4)_2C{=}O$	98
24[d]	4-*iso*-BuC_6H_4	CH_3	H	$(4\text{-}iso\text{-}BuC_6H_4)(CH_3)C{=}O$	88
25[e]	6-MeO-2-$C_{10}H_6$	CH_3	H	$(6\text{-}MeO\text{-}2\text{-}C_{10}H_6)(CH_3)C{=}O$	78
26	C_6H_5	C_6H_5	OH	$(C_6H_5)_2C{=}O$	93
27	C_6H_5	OH	H	C_6H_5COOH	79
28[f]	C_6H_5	C_6H_5	H	$(C_6H_5)_2C{=}O$	97
29	4-CNC_6H_4	H	H	4-CNC_6H_4CHO	66
30	4-$Me_2NC_6H_4$	H	H	4-$Me_2NC_6H_4CHO$	84
31	4-$(Me_2NCO)C_6H_4$	H	H	4-$(Me_2NCO)C_6H_4CHO$	74
32	4-$(CHO)C_6H_4$	H	H	4-$(CHO)C_6H_4CHO$	72
33	4-$(MeCO)C_6H_4$	H	H	4-$(MeCO)C_6H_4CHO$	70
34	4-$(MeO_2CCH_2)C_6H_4$	H	H	4-$(MeO_2CCH_2)C_6H_4CHO$	78
35	4-$(EtO_2CCH_2)C_6H_4$	H	H	4-$(EtO_2CCH_2)C_6H_4CHO$	76
36	4-$AcOC_6H_4$	H	H	4-$AcOC_6H_4CHO$	75
37[g]	4-TBDMS–OC_6H_4	H	H	4-TBDMS–OC_6H_4CHO	78
38[g]	4-TMS–OC_6H_4	H	H	4-TMS–OC_6H_4CHO	75

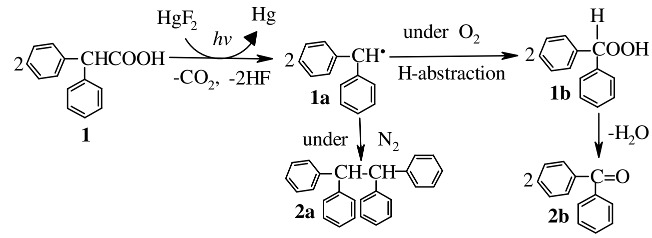
[a] All products were characterized on the basis of mass, IR and ^1H NMR spectral data and comparison with data reported in the literature.
[b] Yields are for isolated products.
[c] 1-$C_{10}H_7$ and 2-$C_{10}H_7$ are 1-naphthyl and 2-naphthyl, respectively.
[d] Ibuprofen = 2-(*p*-*iso*-buthylphenyl)propionic acid.
[e] Naproxen = 2-(6-methoxy-2-naphthyl)propionic acid.
[f] Sodium salt of diphenylacetic acid.
[g] TBDMS and TMS are *tert*-$BuMe_2Si$- and Me_3Si-protecting groups, respectively.

Phenylacetic acids having electron-donating groups on their phenyl ring, for example, Me and OMe groups, were converted into the corresponding benzaldehydes in excellent yields (entries 2–6) while 4-nitro- and 4-fluorophenylacetic acids which possess an electron-withdrawing group were less reactive (entries 7 and 8). Other ring-substituted phenylacetic acids and arylacetic acids gave the corresponding aldehydes in moderate to high yields (entries 9–16). Various secondary α-aryl and α,α-diaryl acids were also converted with high selectivity to the corresponding ketones with yields better than the primary α-aryl acids (entries 17–25). Benzilic and mandelic acids, which are α-hydroxyarylacetic acids, gave benzophenone and benzoic acid, respectively, under the reaction conditions (entries 26 and 27).

Whereas α-aryl acids were decarboxylated in an efficient way, aliphatic acids, benzoic acid and arylcarboxylic acids such as 3-phenylpropionic and 3,3-diphenylpropionic acids, which possess no aryl group at the α-position, were inert under the reaction conditions, and only the starting materials were recovered quantitatively even after 2 days of irradiation. It is noteworthy to mention here that in contrast to methyl diphenylacetate, which was inert towards PD, the sodium diphenylacetate salt was decarboxylated efficiently (entry 28). Moreover, the method is compatible with common functionalities such as cyano (entry 29), *tert*-amino (entry 30), *N*,*N*-dimethylamido (entry 31), aldehyde and ketone (entries 32 and 33), and esters (entries 34 and 35) groups. Furthermore, common *O*-protecting groups such as acyl (entry 36) and silylethers (entries 37 and 38) remain unchanged during oxidation.

In an attempt to detect intermediates and to clarify the reaction pathway, the photolysis of diphenylacetic acid was carried out under the conditions outlined above, except in nitrogen—rather than oxygen-saturated solution which resulted in the formation of 1,1,2,2-tetraphenylethane in 92% yield as the only photoproduct. For further confirmation, phenylacetic acid and 4-methylphenylacetic acid were allowed to react under the same conditions as diphenylacetic acid and were found to give 1,2-diphenylethane (80%) and 1,2-di(4-methylphenyl)ethane (86%), respectively, similar to the result obtained for diphenylacetic acid. Clearly, the formation of these dimeric photoproducts under an inert atmosphere is attributed to coupling of the corresponding benzylic radicals.

Therefore, although the mechanism of this reaction is not yet clear and intermediates have not been observed directly, the formation of dimeric products under N_2 indicates that benzylic radicals are possible intermediates. A plausible reaction pathway is shown in Scheme 1 using diphenylacetic acid **1** as the prototype. Under an O_2 atmosphere, the benzylic radical intermediate **1a** trapped by O_2 and forms the corresponding hydroperoxide **1b**. The intermediate **1b** is known to eliminate H_2O readily to give the corresponding carbonyl compound **2b**.[3,14,35] Under an inert atmosphere (N_2 gas), the dimeric product **2a** is formed via homocoupling of **1a**.



Scheme 1. A plausible photoreaction pathway for decarboxylation of diphenylacetic acid.

The generation of **1b** during the photoreaction was confirmed by a positive KI–starch test on the photolysate. This test provided evidence for involvement of the benzylic radical intermediates **1a**, which are highly reactive towards O_2.

In conclusion, we have developed a new and efficient method for PD of arylacetic acids by the use of HgF_2, as an inorganic photooxidant. This reaction is an interesting example of the application of PD in the transformation of arylacetic acids to carbonyl compounds. It is suggested that arylacetic acids are decarboxylated via a radical pathway although the exact role of HgF_2 in the generation of radical intermediates is not yet known. Studies on a more detailed mechanism and applications to other substrates are now in progress in our laboratory.

General procedure for photolysis of α-arylcarboxylic acids: To a solution of 1 mmol of each α-aryl acid in 25 mL of acetonitrile in a Pyrex flask containing a Teflon-coated magnet bar was added 1 mmol of HgF_2. Oxygen was passed through the mixture which were kept under an oxygen atmosphere (O_2 balloon). It was then placed in a water bath with the temperature adjusted to 25±2 °C. The mixture was magnetically stirred and irradiated. During the course of the reaction a grey precipitate of mercury was formed. The photoreaction was followed by TLC and, after 1 day (24 h) which the mixture darkened completely, the irradiation was stopped and the precipitate was filtered off. The filtrate was concentrated on a rotary evaporator under a reduced pressure at room temperature and the residue was subjected to silica gel plate or column chromatography using carbon tetrachloride–diethyl ether as eluent. Yields are shown in Table 1. All of carbonyl products obtained were characterized by MS, ^1H NMR and IR spectra and by comparison with known compounds.

Acknowledgements

This work was supported by the University of Lorestan Research Council.

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