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PHOTOCHEMISTRY OF HYDROXAMIC ACIDS

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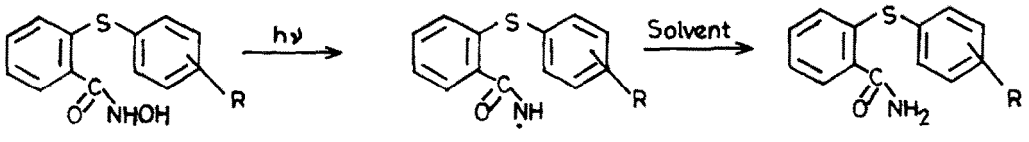
Abstract - Photochemical reactions of hydroxamic acids have been studied. The intermediacy of a RCONH radical is postulated, based on oxidations achieved with DCA under photochemical conditions.

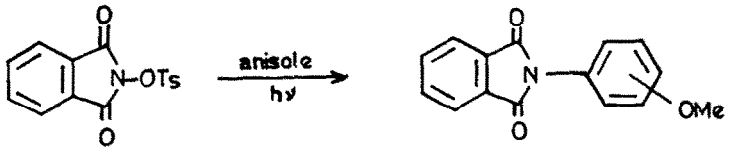
While investigating acid catalysed intramolecular amidation of 2-(aryloxy)benzohydroxamic acids and 2-(arylthio)benzohydroxamic acids, as a route to lactams, we have explored interesting chemistry.[1-4] As an adjunct, we have also explored possibility of photochemical amidation which was published in a preliminary communication (eq. 1).[5] We now report results of that study in full detail.

2-(arylthio)benzohydroxamic acids on irradiation were expected to lead either to lactams via ring closure or to 2-arylsulfinylbenzamides via oxygen transfer as observed during acid catalysed reactions. Instead, 2-(arylthio)benzamides were obtained as photo products. The assumption of intermediacy of an amidyl (RCONH.) radical for the apparent deoxygenation seems to be valid in view of recent studies by Barton and coworkers[6-11] who have reported extensively on photochemistry of esters of thiohydroxamic acids. The main thrust of their studies however, is on generation and synthetic consequences of $RCO_2^{\cdot}$ radical, rather than on the fate of -(C=S)N- radical except in some cases where S-alkyl derivatives are formed. The amidyl radical if formed in photolysis of 2-(arylthio)benzohydroxamic acids, seemed to present interesting synthetic potential. Cadogan et al[12] have, for instance, reported arylation of imidyl radical (eq. 2).

Equation 1



Equation 2



Before pursuing synthetic implications of trapping of $\dot{C}ONH$ radical, it was thought necessary to confirm the generality of photodeoxygenation. For this purpose several hydroxamic acids were prepared.

Synthesis of Hydroxamic Acids.

The known hydroxamic acids 2,4,5,7,9,11,13-18 were prepared from commercially available carboxylic acids using hydroxylamine hydrochloride and dicyclohexylcarbodiimide (DCC) (Figure-1).

O-methyl benzohydroxamic acids 3,6,8,10,12 were prepared from corresponding benzoyl chloride derivatives and O-methyl hydroxylamine hydrochloride (Scheme-1).

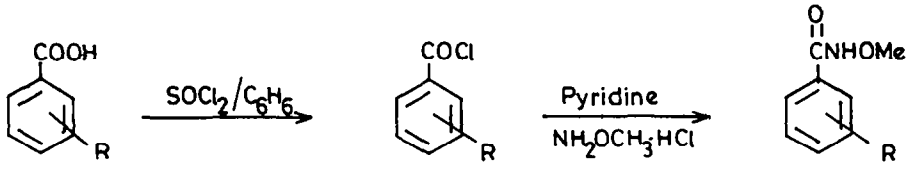
O-methyl-2-(arylthio)benzohydroxamic acids (19-23) were similarly prepared from 2-(arylthio)-benzoic acids[13] (Scheme-2).

O-ethyl-2-(2-methoxyphenylthio)benzohydroxamic acid (29) was prepared from 2-(2-methoxyphenyl-thio)benzoyl chloride[13] and O-ethyl hydroxylamine hydrochloride (Scheme-3).

Photolysis of Hydroxamic Acids. (Table-1).

Hydroxamic acids 2-18 were irradiated with high pressure Hg-lamp. To our surprise all of them were recovered quantitatively. It seemed possible that though these hydroxamic acids do form amidyl radical, due to very efficient cage-recombination process, they fail to react with solvent matrix. Therefore an attempt was made to oxidize these radicals to hydrazines or diazenes. Thus when benzohydroxamic acids 9 and 11 were irradiated in acetonitril saturated with oxygen in presence of DCA[14], formation of diacyldiazenes 30 and 31 was observed (Scheme-4). The structures of diacyl-diazenes 30 and 31 were confirmed by unambiguous synthesis by the method of Tsuneo[15] (Scheme-4).

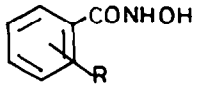
Scheme 1



3a, 6a, 8a, 10a, 12a — 3b, 6b, 8b, 10b; 12b — 3,6,8,10,12

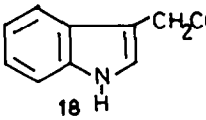
3,3(a b). R=H ; 6,6(a b). R=2-Cl ; 8,8(a b). R = 3-NO_2 ;
10,10(a b). R = 4-OMe ; 12,12(a b). R=4-Me .

Figure 1

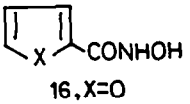


2,4,5,7,9,11

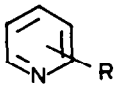
2, R = H
4, R = 2-NH_2
5, R = 3-Cl
7, R = 4-NO_2
9, R = 4-OMe
11, R = 4-Me



18

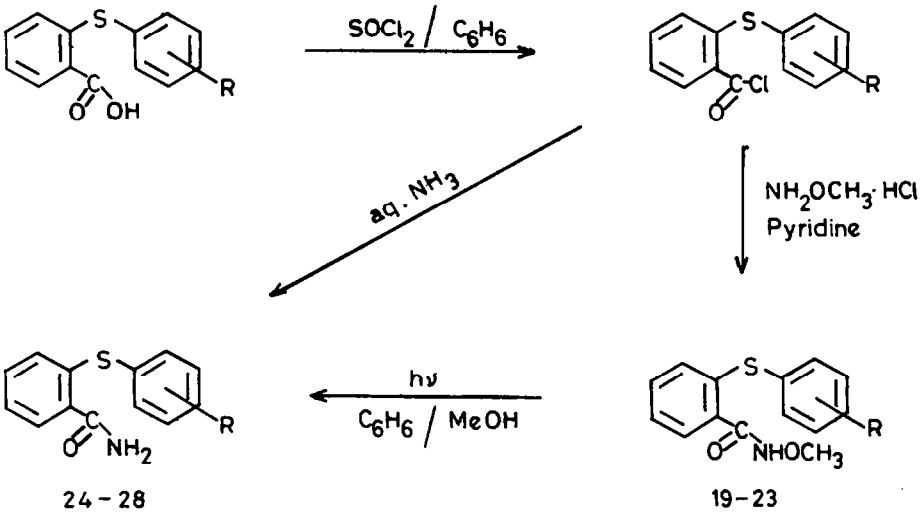


16, X=O
17, X=S

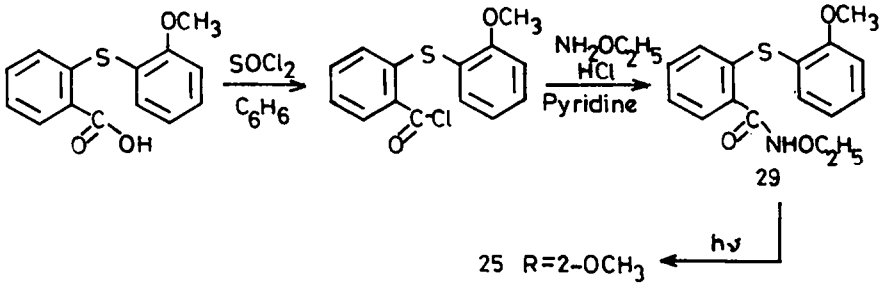


13, R = 2-CONHOH
14, R = 3-CONHOH
15, R = 4-CONHOH

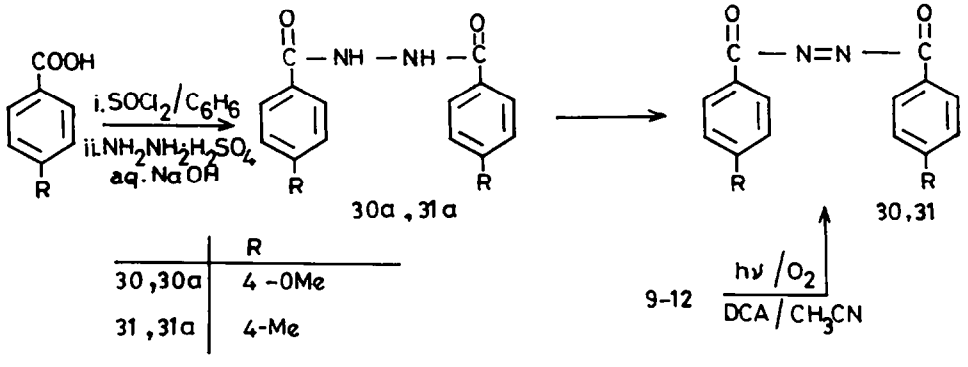
Scheme 2



Scheme 3



Scheme 4



	R
30 ,30a	4 -OMe
31 ,31a	4-Me

If amidyl radical (RCONH) is indeed formed on irradiation of RCONHOH, the same species can also be formed by irradiation of RCONHOR' (R' = Me or Et). To test the hypothesis, O-methyl-2-(arylthio)benzohydroxamic acids 19-23 and O-ethyl-2-(2-methoxyphenyl)benzohydroxamic acid 29 were irradiated under identical conditions. In each case corresponding 2-(arylthio)benzamide (24-28) was formed, confirming the intermediacy of common amidyl radical (RCONH). The structures of 2-(arylthio)benzamide (24-28) were confirmed by independent synthesis from corresponding 2-(arylthio)benzoic acids[13].

Assuming that formation of diazenes 30,31 also involved amidyl radical, the same products should be obtained by irradiation of the corresponding O-methyl benzohydroxamic acids 10,12. On irradiation in oxygen saturated acetonitril, 10 and 12 afforded 30 and 31.

In conclusion it can be stated that an amidyl radical is produced both in case of 2-(arylthio)benzohydroxamic and other hydroxamic acids. In case of the former, synthetic consequence is photodeoxygenation arising from hydrogen capture by the amidyl radical from solvent matrix. In case of the latter, the apparent photoinactivity can be ascribed to efficient cage recombination which however can be precluded under oxidizing conditions. The observed difference in photo behaviour of 2-(arylthio)benzohydroxamic acids and benzohydroxamic acids may be attributed to extended conjugation in former, resulting in different energy profile of radical intermediates. We have already reported similar difference in behaviour of 2-(arylthio)benzohydroxamic acids and benzohydroxamic acids in acid catalysed reactions leading to oxygen transfer.[4] It has been shown that on protonation 2-(arylthio)benzohydroxamic acids, due to peculiar extended conjugation, lead to very fascinating oxygen transfer.

EXPERIMENTAL

All melting points reported are uncorrected. IR spectra were recorded on Hilger Watts infracord model H-900 and Beckman spectrophotometer model IR 4250. Mass spectra were recorded on Varian Mat CH-7 and Varian Mat-6 spectrometers. UV spectra (λ_{max} in nm) were recorded in spectral grade methanol on Shimadzu UV-240 Graphicord spectrophotometer. Photoirradiations were carried out using high pressure Hg-lamp USHIO UM-452 (450 Watts). An induction period of 10 minutes was given to lamp prior to photolysis. Compounds 2-18 have been reported earlier.[15-23] 2-Arylthiobenzoic acids were prepared as described earlier.[1-3,12] Diacyldiazenes 30,31 were prepared unambiguously as described earlier. Spectral data of some of the compounds are given in Table-2. All new compounds gave satisfactory elemental analyses.

Preparation of O-methyl Benzohydroxamic Acids (3,6,8,10,12) and O-methyl-2-(arylthio)benzohydroxamic acids (19-23).

O-methylhydroxylamine hydrochloride[24] (0.01 mole) and corresponding acid chloride (0.01 mole) and dry pyridine (5 ml) were heated on steambath for 30 mins. The mixture was diluted with anhydrous ether. Pyridine hydrochloride, which precipitated, was filtered off. The ether layer was successively washed with saturated sodium bicarbonate (2 x 50 ml) and solution of sodium hydroxide (10%, 2 x 50 ml). Acidification of sodium hydroxide extract gave desired compounds in 50-60% yields.

Preparation of 2-(arylthio)benzamides 24-28.

2-(arylthio)benzoic acid (0.02 mole), thionyl chloride (0.04 mole) in benzene (70 ml) were refluxed for 4 hours. The excess of thionyl chloride was distilled off along with benzene. The residue was cooled to 15°C. Aqueous ammonia (10%, 100 ml) was added to this cooled residue. Desired amides 24-28 precipitated out in 90-95% yields.

Preparation of O-ethyl-2-(2-methoxyphenylthio)benzohydroxamic acid 29.

O-ethylhydroxylamine hydrochloride[26] (0.01 mole), 2-(2-methoxyphenylthio)benzoyl chloride (0.01 mole) and pyridine (1 ml) were heated on steam bath for 30 minutes. The mixture was diluted with anhydrous ether. Pyridine hydrochloride, which precipitated, was filtered off. The ether layer was washed successively with saturated solution of sodium bicarbonate (2 x 50 ml) and sodium hydroxide solution (10%, 2 x 50 ml). Acidification of sodium hydroxide extract afforded 29.

Irradiation of Hydroxamic Acids 2-23,29.

Hydroxamic acid (50 mg) was dissolved in benzene (50 ml) and irradiated with high pressure Hg-lamp in a merry-go-round set-up for 6 hours. Products obtained after rotary evaporation were purified by crystallization. The structures of these compounds were confirmed by comparison (IR, TLC) with authentic samples.

DCA Sensitized Oxidation of O-methyl Benzohydroxamic Acids (9-12).

Hydroxamic acid (50 mg), 9,10-dicyanoanthracene (DCA)[27] were dissolved in acetonitril (50 ml). The solution was irradiated using high pressure Hg-lamp. Oxygen was bubbled throughout the experiment. The residue obtained after solvent removal was purified by passing over column of silica gel. Benzene fraction afforded diacyldiazenes 30,31.

Table - 1

Starting compound (R)	Method	Product
9	B	30
10	B	30
11	B	31
12	B	31
19 (H)	A	24
20 (2-OMe)	A	25
21 (3-Me)	A	26
22 (4-OMe)	A	27
23 (4-Me)	A	28
29	A	25

A : hν / Benzene / MeOH
B : hν / DCA / MeCN / O_2

Table - 2

Compound	IR(KBr) cm^{-1}	NMR($CDCl_3$) δ ppm	m/e
19	3150, 1650, 1600	3.91 (s,3H), 7.26-7.63 (m,9H), 9.13(bs,1H)	259
20	3160, 1640, 1590	3.88(s,3H), 3.94(s,3H), 7.16-7.58(m,8H), 9.06(bs,1H)	289
21	3200, 1650, 1590	2.23(s,3H), 3.90(s,3H), 6.96-7.42 (m,8H), 9.22(bs,1H)	273
22	3240, 1680, 1626	3.82(s,3H), 3.92(s,3H), 7.08-7.66(m,8H), 9.12(bs,1H)	289
23	3140, 1655, 1595	2.38(3H), 3.88(3H), 7.1-7.6(m,8H), 9.06(bs,1H)	273
30	1775, 1685	3.87(s,3H), 3.91(s,3H), 7.28(d,4H, J=7 Hz), 8.02(d,4H, J=7 Hz)	298
31	1785, 1680	2.41(s,3H), 2.43(s,3H), 7.27(d,4H, J=7 Hz), 8.05(d,4H, J=7 Hz)	266

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