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RADICAL DECARBOXYLATIVE BROMINATION OF AROMATIC ACIDS†

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Thiohydroxamic esters (mixed anhydrides) of aromatic and α,β-unsaturated carboxylic acids undergo clean decarboxylative bromination on treatment with bromotrichloromethane in the presence of a radical initiator.

In a recent series of articles,[1] we have described the synthetic potential of a new radical decarboxylation reaction of carboxylic acids via their esters 2 (mixed anhydrides) with appropriate thiohydroxamic acids (e.g. 1).

This decarboxylation was found to be general for primary, secondary and tertiary aliphatic and alicyclic carboxylic acids. However, when we attempted to extend the reaction to aromatic and α,β-unsaturated acids, the results were initially disappointing. Thus, for example, heating or irradiating the p-nitrobenzoic acid derivative 7 gave in a slow, unclean reaction, p-nitrobenzoic acid and its anhydride as the major acid derived products. Little (<10%) of the expected sulphide 8 could be isolated (Scheme 1, path a). The anhydride is formed in an ionic reaction (elimination of 2-pyridyl-disulphide mono-N-oxide) and the persistent carboxyl radical[2] (3, R = p-nitrophenyl) is not involved. The latter extrudes CO_2 some 10^4-10^5 times slower[3] than a carboxyl radical derived from an aliphatic acid (3, R = aliphatic). Under similar experimental conditions, high yields of the corresponding sulphides 4 could be obtained from aliphatic and alicyclic carboxylic acids[1a] (Scheme 1).

In the hope of developing a synthetically more useful reaction, we studied the interception of the aromatic radical with bromotrichloromethane ($CBrCl_3$) to give the bromo derivative 5 (the Hunsdiecker reaction[4]) (Scheme 1, path b). As we have previously shown, this reaction is very efficient for aliphatic acids.[1b]

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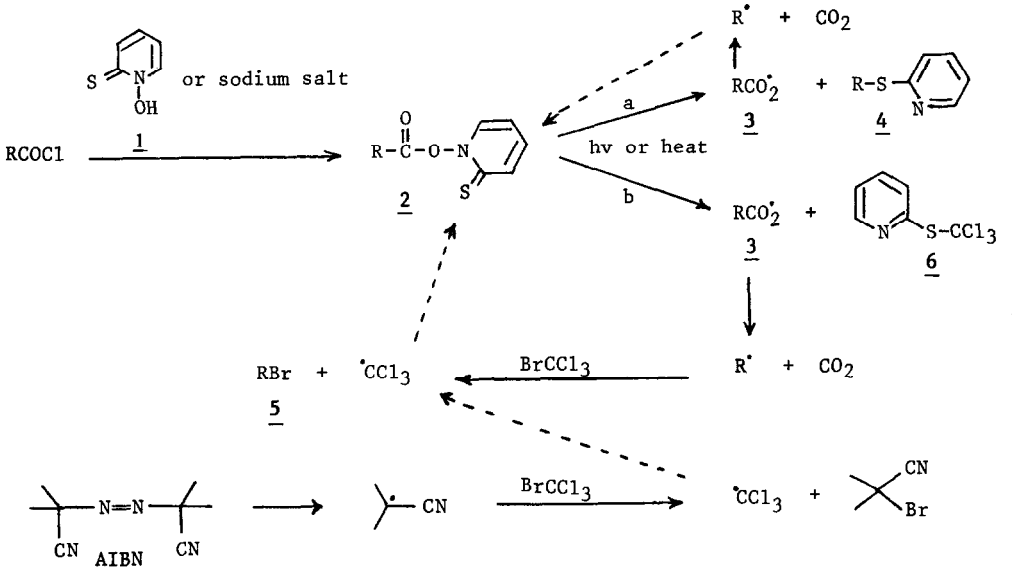
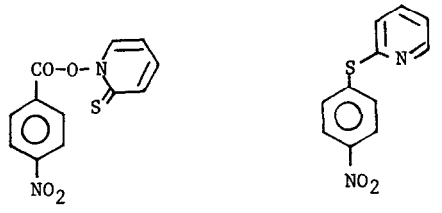
† *Dedicated with appreciation to Prof. Harry H. Wasserman on the occasion of his 65th birthday.*

To favour decarboxylation and minimize side products, we performed the experiments at a higher temperature (~130°C) than usual in a mixture of $CBrCl_3$ and o-dichlorobenzene. The commercially available sodium salt of 1 was suspended in the hot mixture and the acid chloride was added slowly in order to keep the concentration of the ester to a minimum.

Under these conditions, p-nitrobenzoic acid and α-naphthoic acid could be transformed into p-bromonitrobenzene and α-bromonaphthalene in 69 and 80% yield respectively. However, extension to other acids was not so successful. Thus, cinnamic acid gave only 12.5% of trans bromostyrene. The yield could be increased to 22% by lowering the temperature, but extensive formation of cinnamic acid anhydride was observed. Although we had succeeded in establishing the desired chain reaction, clearly, the build up of the ester concentration and a relatively slow decarboxylation step were still a major problem. We examined the effect of adding an external initiator (AIBN azobisisobutyronitrile) on the reaction. We hoped that by generating more trichloromethyl radicals (Scheme 1) we would favour the desired pathway to the detriment of unwanted side reactions and yet keep the temperature within an acceptable range.

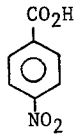
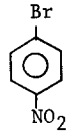
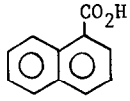
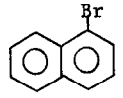
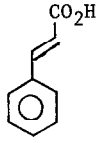
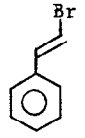
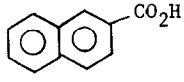
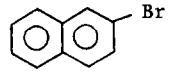
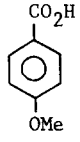
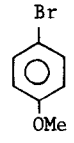
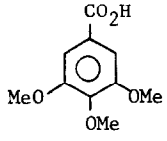
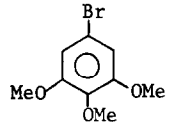
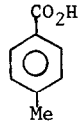
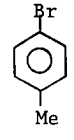
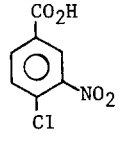
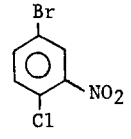


Scheme 1



7 8

Indeed, incorporation of AIBN (~30%) to the acid chloride prior to addition to the hot (100°C) bromotrichloromethane caused a marked improvement in yield. A variety of aromatic acids as well as cinnamic acid could be transformed cleanly into the corresponding bromo derivatives (Table).

Entry	Acid	Bromo Derivative	Yield (%)	Yield of 6 (%)	Lit. Yield (%)
1			69[a]	66[a]	79[4a] 95[4c] 42[4e]
2			82 80[a]	90 60[a]	4.5[4a]
3			68 12.5[a]	70 39[a]	17.5[4a]
4			85	78	0[4a]
5			84	87	0[4a]
6			62	68	26[4d]
7			55[b]	78	17[4a] 11[4e]
8			43	49	-

a) Reaction performed at 130°C in $BrCCl_3$-C_6H_5Cl without AIBN. All others in neat $BrCCl_3$ at 100°C with 30% AIBN.
b) Low yield due to volatility of the product.

Worthy of note is the success of the reaction with electron rich substrates which undergo multiple bromination on the aromatic ring under the usual conditions for the Hunsdiecker reaction, or any of its more recent modifications[4] (Table, entries 2,4,5,6,7). Our method avoids electrophilic intermediates. It is well adapted for preparative purposes.

Professor Shiro Ikegami (Teikyo University, Japan) has kindly informed us of the successful application of our procedure to acids with multiply skipped dienes, where traditional methods failed. Prof. E. Vogel (Cologne University, Federal Republic of Germany) has applied this method to the difficult problem of the brominative decarboxylative of a sensitive triene-acid with success. We thank Prof. Vogel for helpful discussion and for the suggestion to increase the concentration of $^{\cdot}CCl_3$ radicals by addition of an initiator.

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