

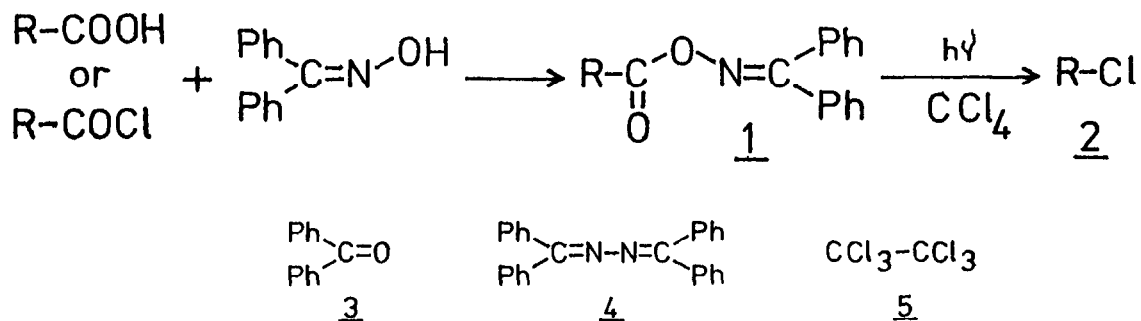
PHOTODECARBOXYLATIVE CHLORINATION OF CARBOXYLIC ACIDS
via THEIR BENZOPHENONE OXIME ESTERS

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Summary: Decarboxylative chlorination of various aromatic and aliphatic carboxylic acids is performed successfully by the photolysis of their benzophenone oxime esters in carbon tetrachloride and corresponding chloro compounds are prepared in good yields. High selective generation of the certain radical and efficiency of the stable radical precursor, benzophenone oxime ester, afford much advantage for radical chemistry.

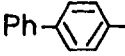
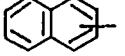
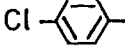
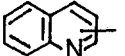
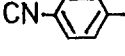
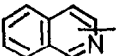
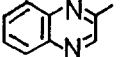
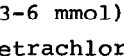
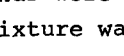
Carboxylic acids derivatives and halo compounds are often used as versatile compounds in synthetic chemistry.¹ Transformation of carboxyl group of common carboxylic acids to other functional group must be one of the useful synthetic procedure in organic chemistry. Especially halo compounds are useful material to prepare organometallic compounds and halogen atom can be easily transformed to other functional groups. The famous Hunsdiecker reaction requires highly purified metal carboxylate and its reaction conditions are rather drastic to transform carboxyl group to halogen atom.² Furthermore, carboxylic acids having other functional groups afford much difficulties to protect those groups during the reaction. Though D.H.R. Barton reported the radical chain decarboxylative halogenation by aid of radical initiator recently, their multi-step spontaneous procedure at rather high temperature still makes the reaction a little complicated.³ On the other hand, poor stability of radical precursors and difficulties of selective generation of desired radicals have restricted the utility of radical reactions.

In the series of our study for radical reactions, we have recently examined the synthetic utility of benzophenone oxime esters of common carboxylic acids as versatil radical precursors for various aliphatic and aromatic radicals by simple photolytic reactions.⁴ We report here the extention of their synthetic applications for potent decarboxylative chlorination of various aromatic and primary, secondary and tertiary aliphatic carboxylic acids under mild photolytic conditions. The efficient radical precursors, benzophenone oxime esters (1), are prepared easily from corresponding carboxylic acids and benzophenone oxime, and they are quite stable under ambient conditions (Scheme I).



Scheme I

Table I, Yields of Aryl Chlorides

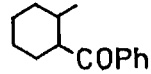
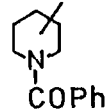

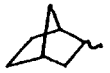

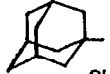
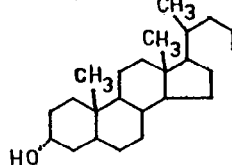
<u>1</u>	R	<u>2</u> (%)*	<u>1</u>	R	<u>2</u> (%)*
a.		88	g.		80
b.		80	h.		87
c.		98	i.		76
d.	α	80	j.		72
e.	β	82	k.	γ	80
f.	γ	77	l.		56
			m.	4	77
			n.		74

* isolated yield

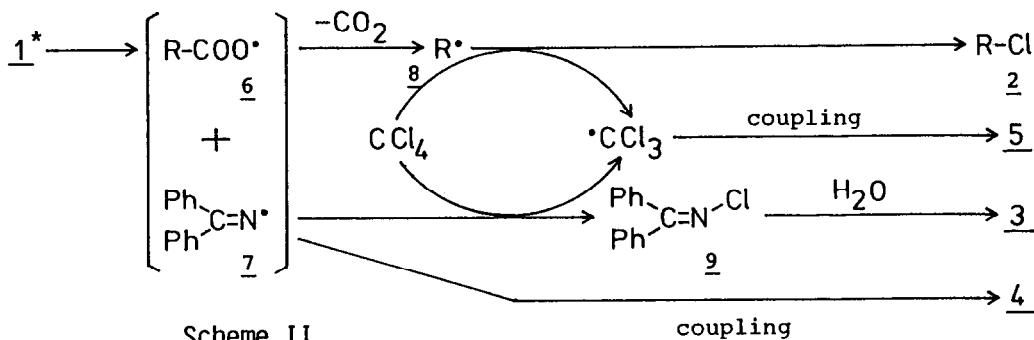
The oxime esters of aryl carboxylic acids (1a-n) (3-6 mmol) were irradiated (400W high pressure Hg lamp, Pyrex filter) in carbon tetrachloride under N_2 gas flow at room temperature until all the starting compounds were consumed. The clean reaction proceeded and photolyzed reaction mixture was washed with aq. K_2CO_3 (3%) solution to remove hydrogen chloride generated by decomposition of carbon tetrachloride during the reaction. The products were isolated by silica gel or alumina column chromatography and they were identified by their spectral data and by comparison of their spectral data with those of authentic samples. In every case, desired radicals were generated efficiently and then they abstracted a chlorine atom of carbon tetrachloride to afford aryl chlorides (2a-n) in good yields together with benzophenone (3, 70-90%), benzophenone azine (4, 6-25%) and some amount of hexachloroethane (5) (Table I). This photoreaction could be applied to wide variety of aromatic carboxylic acids which included not only substituted benzoic acids but also many aza-aromatic carboxylic acids.

Heating those oxime esters in refluxing carbon tetrachloride with or without radical initiator, azobisisobutyronitrile (AIBN), failed to initiate the reaction and most of the starting oxime esters were recovered. Inefficiency of the radical initiator to benzophenone oxime esters explained

Table II, Yields of Aliphatic Chlorides

<u>1</u>	R	<u>2</u> (%)*	<u>1</u>	R	<u>2</u> (%)*
o.	CH ₃ -(CH ₂) ₁₆ -	82	u.		74
p.	CH ₃ -(CH ₂) ₂₀ -	80	v. β w. γ		72 76
q.	 -(CH ₂) ₃ -	82	x.		88**
r.	 -C(=O)-(CH ₂) ₃ -	70	y.		82
s.	CH ₂ -CH ₂ -CH ₂ - NH-COPh	73	z.		81
t.	CH ₃ -CH-CH ₂ - NH-COPh	92			

* isolated yields, **GC analysis



that these decarboxylative chlorination did not proceed in chain mechanism.

Photodecarboxylative chlorination of primary, secondary and tertiary aliphatic and alicyclic carboxylic acids, even steroidal carboxylic acid, was also successful via their benzophenone oxime esters (10-z) under the present reaction conditions to afford corresponding chloro compounds selectively in good yields, respectively (Table II). Moreover, ketone, amide and hydroxy groups of the parent carboxylic acids did not inhibit the reaction and they were tolerated under the present reaction conditions without any protection. Though *w*-1 effect is commonly observed in direct radical chlorination of organic compounds by chlorine atom, selectivity of the reaction is not satisfactory and a mixture of isomers is obtained.⁵ Other alternate decarboxylative halogenations have been exploited and usually those reactions are performed under rather strong oxidative conditions with halogen donor.⁶

The photolysis of the oxime ester (1) may proceed from its excited triplet state and homolytic cleavage of the weak N-O bond initiates the reaction.⁷ Then decarboxylation of the generated carboxylyl radical (6) affords radical (8) which abstracts a chlorine atom of carbon tetrachloride to produce the chloro compound (2). It is assumed that benzophenone (3) is generated from the iminyl radical (7) via the N-chlorimine (9) which is hydrolyzed during work up of the reaction mixture. The coupling of iminyl radicals (7) produces benzophenone azine (4) (Scheme II).

The utility of novel radical precursor, benzophenone oxime esters (1), was proved to be applicable to the photodecarboxylative chlorination of variety of aromatic and aliphatic carboxylic acids under mild photolytic conditions. Moreover, easy preparation of the oxime esters and high selective generation of certain radicals by simple procedure must afford much advantage for radical chemistry, and many carboxylic acids could be used as convenient radical sources via their oxime esters.

Further development of this reaction is in progress.

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