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PHOTOCHEMICAL GENERATION OF ALIPHATIC RADICALS FROM BENZOPHENONE OXIME ESTERS: SIMPLE SYNTHESIS OF ALKYLBENZENES AND ALKYLPYRIDINES

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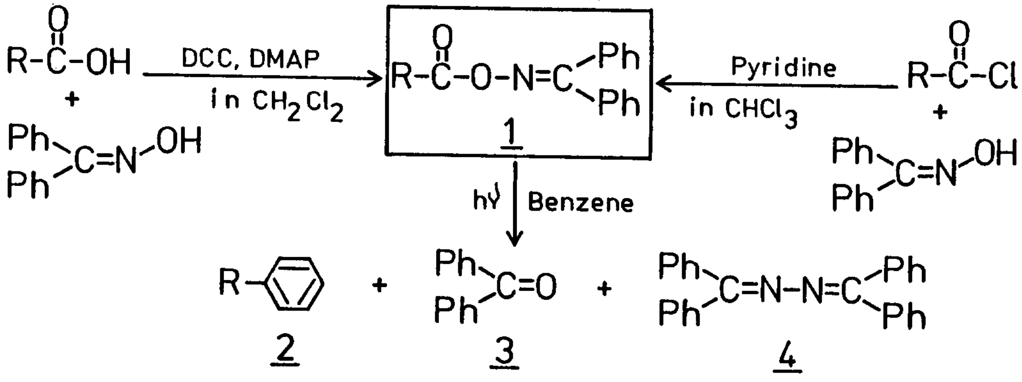
Summary: Photolysis of benzophenone oxime esters, prepared with aliphatic carboxylic acids and benzophenone oxime, in benzene and pyridine generates various primary, secondary and tertiary aliphatic radicals selectively, and corresponding alkylbenzenes and alkylpyridines are produced in good yields, respectively.

In the chemistry of free radicals, effective radical precursors are required for decades to generate desired radicals selectively. Thermal and photochemical decomposition of arenecarbonyl peroxides,[1] arene diazonium salts,[2] acylarylnitrosoamines,[3] and triazenes[4] are commonly used for the generation of aromatic radicals. Although photo-induced decomposition of some haloaromatic compounds also produces aromatic radicals under appropriate reaction conditions, their utilities seem to be somewhat limited.[5,6]

On the other hand, fewer methods are known for generation of aliphatic radicals than aromatic radicals because of poor stability of their precursors such as dialkylacyl peroxides,[7] dialkyl peroxides[8] and alkyl peresters.[9] Particulary, regioselective formation of desired aliphatic radicals is rather difficult; if some common radical initiators are employed, only abstraction of active hydrogen atom occured predominantly.[10]

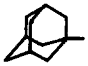
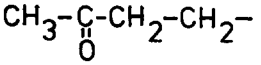
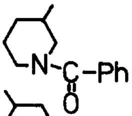
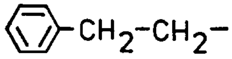
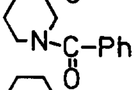
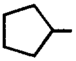
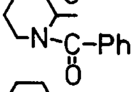
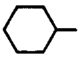
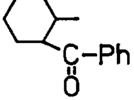
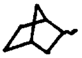
In the series of our study for radical reactions, the utility of some easily prepared benzophenone oxime esters of aromatic carboxylic acids as precursors for various aromatic radicals and their synthetic applications are examined recently.[11] We report here the extention of their synthetic utilities for regioselective generation of various primary, secondary and tertiary aliphatic radicals under mild photolytic conditions in benzene and pyridine to give the corresponding alkylbenzenes and alkylpyridines in good yields, respectively. Furthermore, these oxime esters are prepared easily from common aliphatic carboxylic acids and benzophenone oxime (Scheme I), and they are quite stable under ambient conditions.

The efficient radical precursors, benzophenone oxime esters (1a-i, 5-10 mmol), were irradiated (Pyrex filter, 400 W high pressure Hg lamp) in benzene under N_2 gas flow at room temperature until all the starting compounds were consumed. The products were isolated by silica gel or alumina column



Scheme I. DCC: N,N'-Dicyclohexylcarbodiimide
DMAP: 4-Dimethylaminopyridine

Table I. Yields of Alkylbenzenes

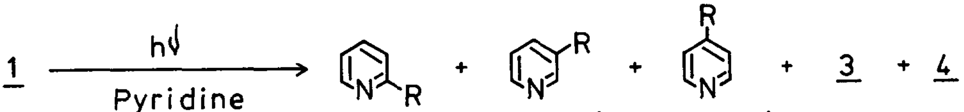
1	R	2 (%)*	1	R	2 (%)*
a.	$CH_3-(CH_2)_6-$	70	g.		90
b.	 $CH_3-\underset{O}{\overset{\parallel}{C}}-CH_2-CH_2-$	72	h.		67
c.		79	i.		59
d.		60	j.		—
e.		62	k.		—
f.		74			

* isolated yield

chromatography and identified by their spectral data and by comparison of their spectral data with those of authentic samples. In each case, corresponding alkyl radicals were produced in benzene and homolytic aromatic substitution on benzene ring proceeded to give alkylbenzenes (2a-i) in good yields, respectively, together with benzophenone (3, 70-95%) and benzophenone azine (4, 5-22%) (Table I). The diphenylmethylene imino group of those oxime esters has quite important role as potent chromophore to initiate the photo-reactions, since parent unconjugated aliphatic carboxylic acids do not have proper absorption above 300 nm of UV light.

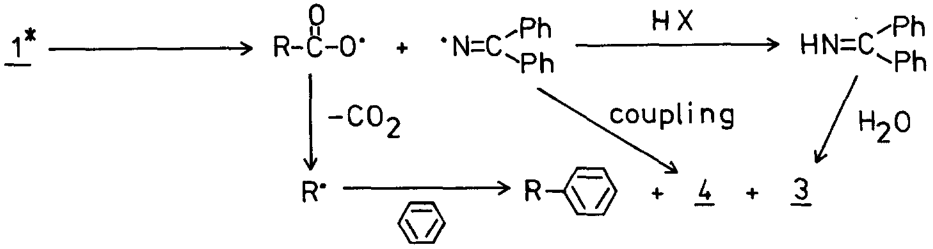
Introduction of benzoyl group adjacent to the carboxyl group inhibited

Table II. Yields of Alkylpyridines



	5(%)*	6(%)*	7(%)*	5+6+7(%)
a.	35	11	20	66
b.	40	15	31	86
c.	53	11	16	80
d.	42	12	40	94
e.	42	15	38	95
f.	52	12	28	92
g.	38	13	29	80

* isolated yield



Scheme II

the formation of alkylbenzenes and giving complex mixture under the present reaction conditions (1j,k) (Table I). Although the reason of this substituent effect is still ambiguous, steric effect of the benzoyl group is assumed to be one of the strong factors of the inhibition.[12]

Photolysis of those oxime esters (1a-g, 5-10 mmol) in pyridine was also successful to produce corresponding three isomers of alkylpyridines (5a-g, 6a-g, 7a-g) in high total yields, respectively, together with 3 (75-90%) and 4 (7-18%) (Table II). The ratio of products depends strongly on the reactivity of pyridine ring for free radicals and β-position of pyridine ring has the least reactivity among the three positions ($\alpha > \gamma > \beta$).[13] Various desired aliphatic radicals could be generated by photolysis of the oxime esters formed with proper employment of starting carboxylic acids. No compounds formed by the alkylcarboxylation on benzene and pyridine ring were obtained under the present photolytic conditions.

In addition, heating those oxime esters in benzene and pyridine did not afford any alkylbenzenes or alkylpyridines and most of the starting compounds were recovered.

The homolytic cleavage of the weak N-O bond of the oxime ester may proceed from its excited triplet state under the present photolytic conditions.[14] Then formed alkylcarboxylyl radical expels carbon dioxide generating the alkyl radical which reacts with benzene and pyridine to afford arylated products. Benzophenone (3) and benzophenone azine (4) might be derived from the iminyl radical as shown in the Scheme II.

Those photochemical reactions reveal that various common aliphatic carboxylic acids could be used as useful radical precursors via their stable benzophenone oxime esters and, moreover, they are extremely efficient to generate all of the primary, secondary and tertiary aliphatic radicals selectively under mild photolytic conditions.

Further synthetic application of this reaction are in progress.

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