

HEPTAFLUORO-1-METHYLETHYL PHENYL KETONE — A NEW BENZOYLATING AGENT

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A mixture of heptafluoro-1-methylethyl phenyl ketone (1) and N,N,N',N'-tetramethylethylenediamine was found to be a facile benzoylating agent, providing O-, N-, and C-benzoyl compounds. The characteristic reactivity of the heptafluoro-1-methylethyl ketone was compared with that of trifluoromethyl and pentafluoroethyl ketones.

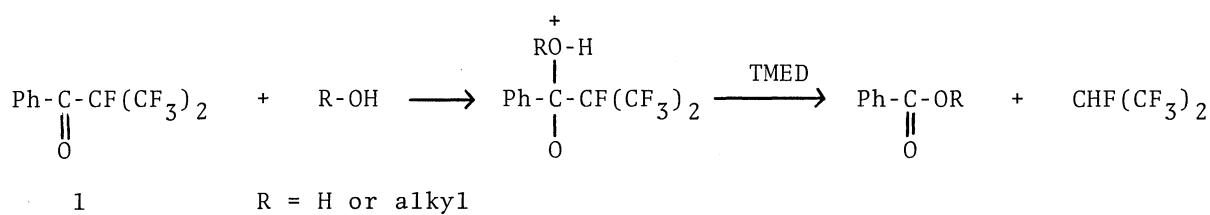
Introduction of a benzoyl group into organic molecules is an important technique in synthetic works, especially for the protection of hydroxylic or amino functions. As benzoylating agents, benzoyl chloride and benzoyl anhydride have been commonly used, and benzoyl cyanide with tertiary amine for C-benzoylation has also been reported recently.¹⁾

These reagents have some problems in use, because (i) they sometimes need a prolonged or an elevated temperature which may not be suitable for the use with sensitive substances, and (ii) they sometimes generate harmful by-products such as hydrochloric acid, benzoic acid or hydrogen cyanide.

We now wish to report a new benzoylating agent which obviates the difficulties mentioned above. Heptafluoro-1-methylethyl phenyl ketone, 1, which is easily obtained by the reaction between benzoyl chloride and hexafluoropropene in the presence of fluoride ion,²⁾ reacted with water or alcohol when tertiary amine such as N,N,N',N'-tetramethylethylenediamine (TMED) was present, affording benzoic acid and alkyl benzoate, respectively. The reactions took place smoothly at room temperature accompanying an evolution of 1,1,1,2,3,3,3-heptafluoropropane, 2, a stable inert gas, and finished within 30 min.

The heptafluoro-1-methylethyl ketone (1) reacted also with primary amines, with or without TMED depending on the basicity of the amine. The reaction with butylamine proceeded without any tertiary amine to give N-butylbenzamide, while that with aniline

to give benzanilide required a higher temperature, even when TMED was present (Table 1).



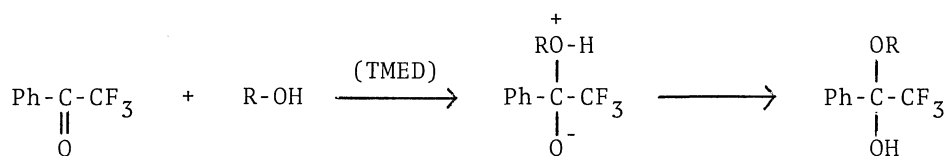
Nitromethane, which carries the acidic methyl group, also reacted with 1 in the presence of TMED to give α -nitroacetophenone, although the reaction was relatively slow and the yield was moderate. For example, a mixture of 1, nitromethane (1.3 mol), and TMED (1.3 mol) was stirred at room temperature for 24 hr, and the resulted crystals were taken into chloroform. The solution was washed with dilute hydrochloric acid and water successively, dried over magnesium sulfate, and evaporated. The residue was recrystallized from hexane-benzene to give α -nitroacetophenone, mp 105°C (52%).

Table 1 Benzoylation with $\text{PhCO}-\text{CF}(\text{CF}_3)_2$ (1)

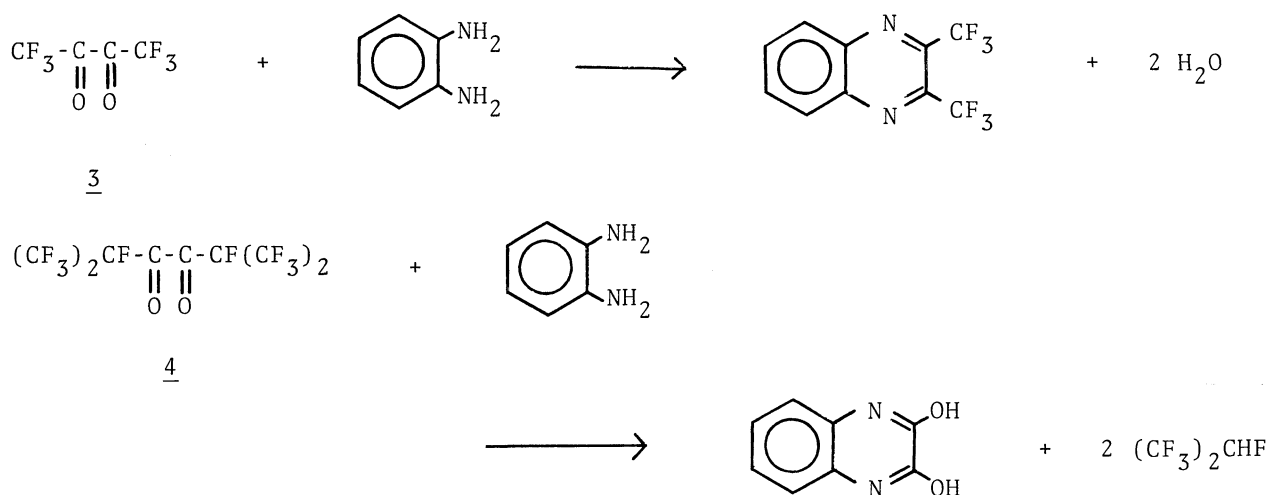
Reactant	Molar ratio of			Reaction conditions		Product	Yield %
	<u>1</u>	:	TMED : Reactant	Temp.	Time		
H_2O	1	:	1 : 1	R.t.	30 min	PhCO_2H	100
MeOH	1	:	1 : 1	"	30 min	PhCO_2Me	89*
BuNH_2	1	:	0 : 1	"	5 min	PhCONHBu	100
PhNH_2	1	:	1.5 : 1.5	55°C	12 hr	PhCONHPh	99
CH_3NO_2	1	:	1.3 : 1.3	R.t.	24 hr	$\text{PhC}(\text{CH}_2\text{NO}_2)_2$	52

* Determined by glc.

In order to compare the reactivity of the heptafluoro-1-methylethyl ketone with other perfluoroalkyl phenyl ketones, we also examined the similar reactions using trifluoromethyl phenyl and pentafluoroethyl phenyl ketones. Interestingly, addition of the nucleophiles to carbonyl double-bond,³⁾ rather than the benzoylation, occurred in the cases of these ketones carrying primary perfluoroalkyl groups.



Similar tendency was observed in the reactions of o-phenylenediamine with perfluorobiacetyl (3) and with perfluoro-2,5-dimethyl-3,4-hexadione (4). Thus the reaction with 4 proceeded with an evolution of heptafluoropropane to give 2,3-dihydroxyquinoxaline,³⁾ while that with 3 proceeded normally to give 2,3-bis(trifluoromethyl)quinoxaline.⁴⁾



Since the electronic effects of various perfluoroalkyl groups are almost similar,⁵⁾ the differences of reactivity among these perfluoroalkyl ketones can be explained by considering the following characteristics of heptafluoro-1-methylethyl ketone.

1. The formation of heptafluoro-1-methylethyl carbanion, $\bar{\text{C}}\text{F}(\text{CF}_3)_2$, which is highly stabilized by two electron-withdrawing trifluoromethyl groups, is easier than that of primary perfluoroalkyl anions.⁶⁾
2. The C-C linkage between the carbonyl group and the heptafluoro-1-methylethyl group must be destabilized sterically because of the bulkiness of the latter group.

These factors were presumed to have made the heptafluoro-1-methylethyl group a good leaving group, and have facilitated the cleavage of the C-C bond.

The experiments mentioned above demonstrate the possibility of the system of aryl heptafluoro-1-methylethyl ketone and tertiary amine as a convenient aroylating agent, especially when mild conditions are required.

References

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- 5) W. A. Sheppard and C. M. Sharts, "Organic Fluorine Chemistry", Benjamin Inc. (1969), p. 37.
- 6) See, for example, R. D. Chambers, "Fluorine in Organic Chemistry", John-Wiley & Sons (1973), p. 85.

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