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A Novel Carbonyl to CF_2 Transformation Using BrF_3

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Summary: This work demonstrates that BrF_3 is very efficient in converting various carbonyls through their azines, oxime methyl ethers, or various hydrazones into the corresponding CF_2 moiety.

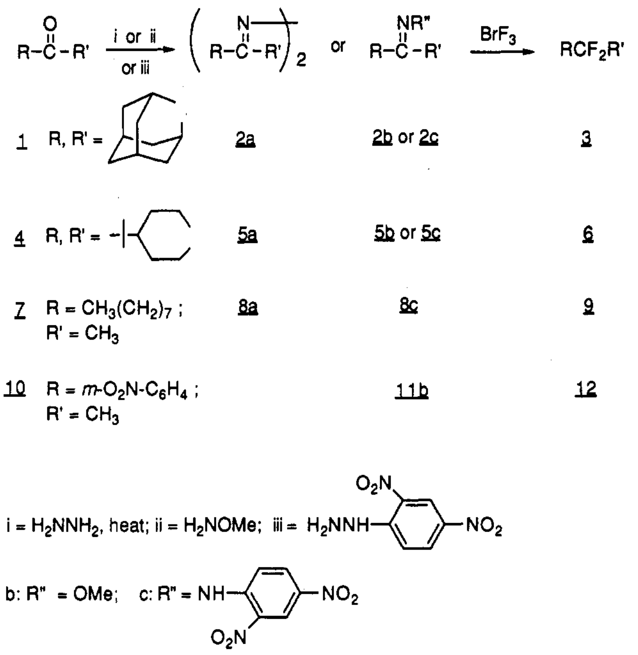
BrF_3 is a commercial reagent which has seldom been used in organic chemistry because of fear and prejudice arising from lack of information. Very recently we demonstrated that BrF_3, which if desired could easily be made directly from its elements, performs some nondestructive reactions even with compounds which are not heavily halogenated.[1]

Less than 3 years ago we described a new way to achieve the important CO → CF_2 transformation via the corresponding hydrazones, using IF made directly from F_2 and I_2.[2] While the method gave satisfactory results, it required a large excess of IF which is not a commercial reagent and has to be prepared just prior to its use. What is more, most of the unsubstituted hydrazones are not very stable and, if not handled carefully, convert spontaneously to azines which are unreactive toward IF. Resistance to that reagent was observed with oxime methyl ethers as well. We report here on a new reaction with BrF_3, which compensates for the above limitations.

When a 25-mL solution of cold $CFCl_3$ containing 6 mmol (0.3 mL) of BrF_3[3] was slowly (10 min) added to a $CFCl_3$ solution of 1 equiv (3 mmol) of adamantanylazine (**2a**), easily prepared from the parent adamantanone (1) and 1 equiv (6 mmol) of hydrazine, an immediate reaction took place forming 2,2- difluoroadamantane (**3**)[4] in 95% yield. When the same reaction was performed on adamantane oxime methyl ether (**2b**) or adamantane dinitrophenylhydrazone (DNP) (**2c**), **3** was obtained in 50 and 65% yields correspondingly, accompanied by 25% of the starting adamantanone (**1**). Excess BrF_3 did not provide higher yields, but increased the formation of many unidentified products.

The reaction is not confined only to the robust adamantane system and 4-*tert*-butylcyclohexanone (**4**), through its azine (**5a**) as well as its oxime methyl ether **5b** and DNP **5c** were all converted to 4,4-difluoro-*tert*-butylcyclohexane (**6**)[2] in 65, 50, and 75% yields, respectively. Similar results were obtained with aliphatic straight chain ketones, 2-decanone (**7**) serving as an example. Its azine **8a** and DNP **8c** were both converted to 2,2-difluorodecane (**9**, 60 and 80% yields) in a matter of seconds, with practically none of the additional corresponding α-halo derivatives which characterize the reaction of IF with hydrazones.[2] Some complications may arise with benzylic ketones, since BrF_3 is also capable of brominating aromatic rings.[5] However, with deactivated rings such as *m*-nitroacetophenone (**10**) the reaction proceeds satisfactorily, since the initial attack of the reagent on the nitrogen atom seems to be considerably faster than on the ring itself. Thus, applying 2 mol/equiv of BrF_3 on the oxime methyl ether of *m*-nitroacetophenone (**11b**) resulted in 90% yield of the desired (1,1-difluoroethyl)-*m*-nitrobenzene (**12**), mp 48 °C,[6] although in 80% conversion. It should be emphasized that the reaction is not sensitive to the stereochemistry of the configuration around the carbon–nitrogen double bond, and *cis*- and *trans*-azines, methyl oxime ethers, and various hydrazones react apparently with the same efficiency.

Scheme 1



In conclusion, this general method can be a very good alternative to the conventional one based on the gaseous and expensive SF_4 (or its derivative DAST) which in many cases require drastic reaction conditions. It is also superior to the method using IF which has to be prepared prior to the fluorination step.

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[1] Rozen, S.; Mishani, E. *J. Chem. Soc., Chem. Commun.* **1993,** 1761.See references cited therein also for some reactions of BrF_3 with extensively halogenated compounds.

[2] Rozen, S.; Zamir, D. *J. Org. Chem.* **1991,** *56,* 4695.

[3] *Caution:* BrF_3 should be treated with care since it reacts violently with solvents such as water and acetone. All our reactions were conducted with diluted BrF_3, otherwise they become too exothermic and lead to production of excess tars. Dry trichlorofluoromethane, chloroform, carbon tetrachloride, and in some cases acetonitrile are suitable as reaction solvents. All reactions were conducted in glass vessels.

[4] Prakash, G. K. S.; Reddy, V. P.; Li, X. Y.; Olah, G. A. *Synlett* **1990,** 594.

[5] Rozen, S.; Lerman, O. *J. Org. Chem.* **1993,** *58,* 239.

[6] Mathey, F.; Bensoam, J. *Tetrahedron* **1975,** *31,* 391.

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