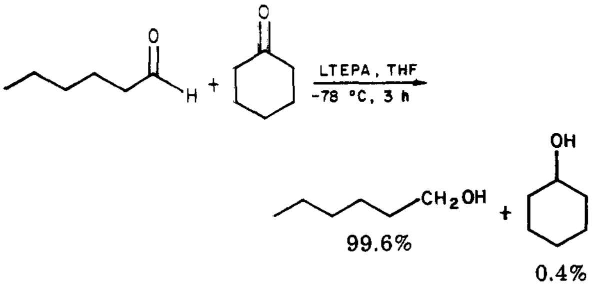

(3)

Interestingly, even benzaldehyde, often less reactive in hydride reductions, is selectively (97.7%) reduced in the presence of cyclohexanone (2.3% attack).

The reactions are quite rapid even at -78 °C (2–4 h), and the conversions are over 90%. The results summarized in Table I clearly indicate that the new reagent is far superior to any of the reducing systems[2] currently available for the selective reduction of aldehydes in the presence of ketones.

Influence of the steric requirements of *tert*-alkoxy substituents on the chemoselectivity was also examined. Lithium tri-*tert*-butoxyaluminum hydride (LTBA)[3] is less chemoselective than LTEPA. Yet the chemoselectivity observed with LTBA is equal to or better than that of the previously reported reagents[2] for the selective reduction of aldehydes in the presence of ketones. Lithium tri-*tert*-amyloxyaluminum hydride (LTAA)[3] and lithium tris[(3-methyl-3-pentyl)oxy]aluminum hydride (LTMPA)[8] are slightly better than LTBA. Thus, it is quite evident that increasing the steric requirements of the *tert*-alkoxy group enhances the chemoselectivity of the reagent to the aldehyde group, an interesting and useful observation.

In summary, lithium tris[(3-ethyl-3-pentyl)oxy]aluminum hydride and other tri-*tert*-alkoxyaluminum hydrides are convenient reagents for reducing aldehydes, even in the presence of reactive ketones, with 98–100% chemoselectivity under mild conditions. The reagents are readily synthesized from $LiAlH_4$ and the corresponding alcohols. Further, the mildness and the remarkable functional group tolerance of these hindered lithium tri-*tert*-alkoxyaluminum hydrides[9] should permit their use for chemoselective reductions in multifunctional molecules. Other unique reduction characteristics of these highly hindered trialkoxyaluminum hydrides are being actively investigated.

Acknowledgment. I thank Professor Herbert C. Brown of Purdue University for stimulating discussions.

Registry No. Hexanal, 66-25-1; 2-heptanone, 110-43-0; benzaldehyde, 100-52-7; acetophenone, 98-86-2; cyclohexanone, 108-94-1; LTEPA, 79172-99-9.

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[8] Synthesized from 3-methyl-3-pentanol and $LiAlH_4$ in THF.

[9] Brown, H. C.; Weissman, P. M. *Isr. J. Chem.* **1963**, *1*, 430–440.

[10] Address for correspondence.

Acetyl Hypofluorite as a Taming Carrier of Elemental Fluorine for Novel Electrophilic Fluorination of Activated Aromatic Rings

Summary: The new fluorinating reagent CH_3COOF, which is prepared in situ from F_2, is used for electrophilic aromatic fluorinations of activated aromatic rings.

Sir: Several methods dealing with specific introduction of a fluorine atom into an aromatic ring are described in the literature. Yet this transformation is not a trivial task. The most widely used method is probably still the Balz–Schiemann procedure which requires a suitable aromatic amino group.

Recently, however, the use of electrophilic fluorinating agents is increasing. The expensive XeF_2 and CF_3OF, for example, were used several times with some success.[1] In quite a few cases, the latter reagent adds across double bonds or produces *gem*-difluorides and ketones.[2] Very recently a new and potentially explosive reagent $CsSO_4F$ was used for fluorination of some substituted benzenes.[3] Several groups also tried direct fluorination with elemental fluorine, but on a preparative scale these reactions are inefficient and produce mainly tars.[4]

We describe in this paper an indirect use of elemental fluorine for electrophilic fluorination of activated aromatic compounds in which relatively clean reactions were obtained unlike those employing direct action of F_2, CF_3OF, and other reagents on aromatic rings.

We have already described the in situ synthesis and some of the chemistry of CF_3COOF and CF_3CF_2OF.[5] The oxygen-bound fluorine in these compounds is similar or even more reactive than the one in CF_3OF. Thus, when several aromatic rings were treated with these fluoroxy reagents, usually low to very low yields of the desired fluorinated compounds were obtained along with various polymeric tars. However, we have found that bubbling elemental fluorine through a suspension of CH_3COONa or NaF in $CFCl_3$ (Freon) and acetic acid produces the novel acetyl hypofluorite, CH_3COOF (1).[6] While this compound still possesses an electrophilic fluorine, it should be less polarizable and hence less reactive than the other known compounds possessing the OF moiety. In reactions with 1, neither a purification nor any isolation of this oxidizing reagent is necessary. Two methods were employed. In method A an aromatic compound is added to the reaction vessel in which 1 was formed at -75 °C, and in method B the acetyl hypofluorite is transferred with the aid of a stream of nitrogen into a cold (-75 °C) solution of the substrate in $CFCl_3$ or $CFCl_3/CHCl_3$. We found that usually method B is more suitable, especially when very activated rings are present. Some typical experiments are summarized in Table I.

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[1] For excellent reviews on the reactions of XeF_2 and CF_3OF with organic compounds, including aromatic compounds, see (a) Filler, R. *Isr. J. Chem.* **1978**, *17*, 71 and references therein. (b) Hesse, R. H. *Ibid.* **1978**, *17*, 60 and references therein.

[2] (a) Patrick, T. B.; LeFaivre, M. H.; Koertge, E. T. *J. Org. Chem.* **1976**, *41*, 3413. (b) Patrick, T. B.; Cantrell, G. L.; Chang, C. *J. Am. Chem. Soc.* **1979**, *101*, 7434.

[3] (a) Stavber, S.; Zupan, M. *J. Chem. Soc., Chem. Commun.* **1981**, 148. (b) Ip, D. P.; Arthur, C. D.; Winans, R. E.; Appelman, E. H. *J. Am. Chem. Soc.* **1981**, *103*, 1964.

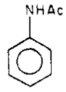
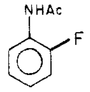
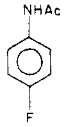
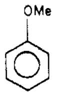
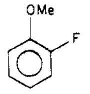
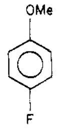
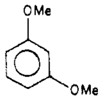
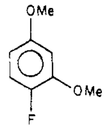
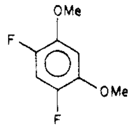
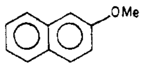
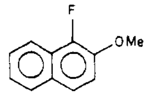
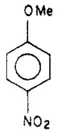
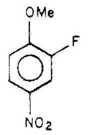
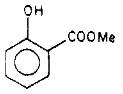
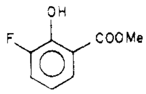
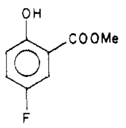
[4] Cacace, F.; Giacomello, P.; Wolf, A. P. *J. Am. Chem. Soc.* **1980**, *102*, 3511 and references therein.

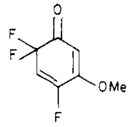
[5] (a) Rozen, S.; Lerman, O. *J. Org. Chem.* **1980**, *45*, 672. (b) Lerman, O.; Rozen, S. *Ibid.* **1980**, *45*, 4122.

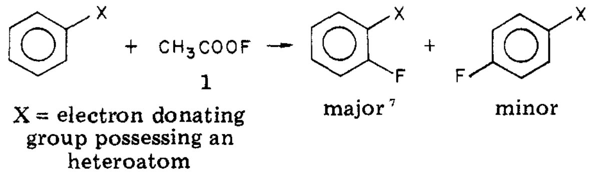
[6] Rozen, S.; Lerman, O.; Kol, M. *J. Chem. Soc., Chem. Commun.* **1981**, 443.

0022-3263/81/1946-4629$01.25/0

Table I

substrate[a]	product[b]	% yield (ortho/para)	% conversion[c]	method[d]
	 	55 (7:1)	92	A
	 	85 (9:1)	75	A
	 	99[e] (1:2)	86	B[f]
		65	100	A
		43	78	B
	 	20 (2:3)	70	B

[a] In a typical reaction an oxidizing solution consisting mainly of 1 was prepared by passing 5–8% of F_2 in N_2 through a suspension of about 10 g of sodium acetate in 400 cm^3 of acetic acid: Freon (1:9) at −70 °C (see ref 6). Usually the passing of fluorine was stopped when 60–80 mmol of the oxidizing material was formed. The oxidizing power was measured by treating a sample with KI and titrating the liberated iodine. A cold solution of 30–40 mmol of substrate (2–5 g) in Freon or $CHCl_3$ was added to the oxidizing solution (method A) or the oxidizing substance was transferred by a cold stream of nitrogen into another vessel containing the cold solution of the substrate (method B). The course of the reactions was monitored by GC and usually the time required for the reaction to take place was from a few seconds up to 20 min for the nitroanisole and the methyl salicilate. Detailed description of how to handle and use elemental fluorine appears in ref 5. [b] The spectral data (IR, ^{1}H NMR, ^{19}F NMR, and MS) of all fluorinated compounds as well as their melting points are in excellent agreement with the proposed structures and with the data published in the literature. The ratio of ortho to para isomers was determined by ^{19}F NMR. No meta isomers were detected. [c] The yields are of the isolated fluorinated compounds based on the reacted starting material. No special attempts were made to increase the conversion, although it should be noted that sometimes when the reaction is forces to completion, the formation of the tar increases. [d] If method B is employed, one has to take care that the glass, Teflon, monel, or brass pipes through which CH_3COOF is transferred are clean, since dirt may decompose the reagent catalytically. [e] 2,4-Dimethoxyfluorobenzene is a liquid at room temperature: NMR δ 3.76 and3.85 (two s, 6 H), 6.2–7.07 (m, arom, 3 H); ^{19}F NMR ϕ^* 146.3 ppm; mass spectrum, *m/e* 156 (M$^+$). 1,5-Difluoro-2,4-dimethoxybenzene: mp 99 °C; NMR δ 3.88 (s, 6 H), 6.63 (t, J = 9.2 Hz, 1 H), 6.9 (t, J = 10.9 Hz, 1 H); ^{19}F NMR ϕ^* 141.9 ppm; mass spectrum, *m/e* 174 (M$^+$). [f] When method A was applied on this very activated compound, the aromaticity was lost. Although not isolated in a pure form, there are indications (IR, UV, ^{1}H NMR, and ^{19}F NMR) that the main product has a quinoidic structure  which is formed from the addition of an excess of 1 to the difluorodimethoxy compound mentioned above.



In contrast to the fluorinations with elemental fluorine, which reacts uncleanly with all types of aromatic compounds, CH_3COOF has the advantage of being a specific fluorinating agent for strongly activated aromatic rings. While the reaction usually takes place within seconds in such systems, various alkyl benzenes,[6] including toluene and *tert*-butylbenzene, react only after relatively long periods (see ref 7). Nitrobenzene and even phenyl acetate are still less reactive.

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(7) The quite unusual ortho to para substitution ratio is worth noting. Several mechanisms can be proposed for such a preference but none is firmly established as yet. The addition–elimination mechanism, for example, suffers from the fact that it usually produces a fluorocarbonyl group with a loss of the aromaticity (ref 1b and 2). A one-electron oxidation of the aromatic ring provides an attractive mechanism and was used for reactions with XeF_2 (ref 1a). In our case, if the resulting radical anion of the hypofluorite would decompose to CH_3COO^- and a F atom, the latter should be attracted to the ortho and ipso sites where the combined electron density is higher than in the para position. Such a mechanism, however, had been discharged by Hesse for reactions with CF_3OF (ref 1b). Another approach is to consider the possible mutual interaction, although not very strong, between the electron lone pairs of the fluorine and the oxygen or nitrogen atoms (ref 8). It is possible that

In contrast to the reaction with CF_3OF,[2] the amide group survives our reaction conditions as is demonstrated by the reaction of acetanilide. Thus, it is also possible to apply this method on various aniline derivatives. Phenol, on the other hand, reacts too vigorously and produces various oligomers, polymers, and carbonyl-containing compounds. The reaction can be tamed to some extent by introducing an electron-withdrawing group as in the case of methyl salicilate although the yield is only 20%. Yet, when such a deactivated group is present, but the phenolic hydroxyl is protected as in the case of *p*-nitroanisol, the yield is more than doubled (see Table I). Good yields are also obtained in the fluorination of 2-methoxynaphthalene. The yield is even better with the more activated 1,3-dimethoxybenzene. Its reaction with CH_3COOF produces mainly the 1,5-difluoro-2,4-dimethoxybenzene along with the monofluoro derivative in practically quantitative yield.

Acknowledgment. We thank the Israel Commission for basic research and The Israel Academy of Sciences and Humanity for financial support.

Registry No. 1, 78948-09-1; acetanilide, 103-84-4; anisole, 100-66-3; 1,3-dimethoxybenzene, 151-10-0; 2-methoxynaphthalene, 93-04-9; 1-methoxy-4-nitrobenzene, 100-17-4; methyl 2-hydroxybenzoate, 119-36-8; *o*-fluoroacetanilide, 399-31-5; *p*-fluoroacetanilide, 351-83-7; *o*-fluoroanisole, 321-28-8; *p*-fluoroanisole, 459-60-9; 1-fluoro-2,4-dimethoxybenzene, 17715-70-7; 1,5-difluoro-2,4-dimethoxybenzene, 79069-70-8; 1-fluoro-2-methoxynaphthalene, 27602-71-7; 2-fluoro-1-methoxy-4-nitrobenzene, 455-93-6; methyl 3-fluoro-2-hydroxybenzoate, 70163-98-3; methyl 5-fluoro-2-hydroxybenzoate, 391-92-4.

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such interactions are also operative in transition states. In any case, it is clear at this stage, that there is an interaction between the heteroatom and the hypofluorite 1, resulting in a subsequent attack mainly at the ortho position. The reaction of 1 with toluene also supports this idea. Being less activated toward electrophilic substitutions, toluene reacts slowly, and after 2 h the conversion is less than 50%. The part that does react yields a lot of tar, but still a small amount of fluorinated toluenes can be detected. However, since in this case no interactions are likely between the aromatic methyl group and the hypofluorite 1, the ratio of the *o*-fluoro- to *p*-fluorotoluene is about 1:1.

(8) Zefirov, N. S.; Samoshin, V. V.; Sabotin, O. A.; Baranenkov, V. I.; Wolfe, S. *Tetrahedron* **1978**, *34*, 2953.

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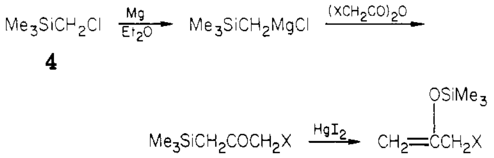
3-Chloro-2-(trimethylsiloxy)-1-propene as an Electrophilic Acetonyl Equivalent. A Novel Regioselective Synthesis of 1,4-Dicarbonyl Compounds[1]

Summary: α-Metalated imines, hydrazones, and activated methylene compounds are acetonylated with 3-chloro-2-(trimethylsiloxy)-1-propene in high yield. Highly regioselective acetonylation at either the tertiary or secondary α-carbon of 2-methylcyclohexanone can be carried out by selecting the reaction condition.

Sir: Acetonylation of ketone enolates is one of the most important routes to the synthesis of 1,4-diketones which can serve as precursors for the synthesis of naturally occurring cyclopentanoids, furans, and pyrroles,[2,3] and therefore numerous efforts have been directed to the development of new acetonylating reagents.[4] For instance, 3-bromo-2-methoxypropene[4j] and in situ generated 3-bromo-2-[(tetrahydropyran-2-yl)oxy]propene[4k] have been proposed as convenient electrophilic reagents for introducing an acetonyl group by a single-step process, but these reagents are rather thermally unstable. Preparation of the pure reagents requires tedious procedures in low yield. We have previously described that allylsilanes can be viewed as useful nucleophilic acetonyl equivalents.[5]

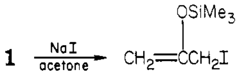
In this report we show that 3-chloro-2-(trimethylsiloxy)-1-propene (1) serves as a novel and convenient electrophilic acetonylating reagent toward several α-metalated species of imines, hydrazones, and activated methylene compounds. Moreover, we show that highly regioselective acetonylation at either the tertiary or secondary α-carbon of 2-methylcyclohexanone can be carried out by selecting the reaction condition.

The requisite acetonylation reagent 3-chloro-2-(trimethylsiloxy)-1-propene (1) was prepared as reported previously.[6] The corresponding bromo (2) and iodo (3) derivatives are prepared as shown in eq 1.



$$\underset{\mathbf{4}}{Me_3SiCH_2Cl} \xrightarrow[Et_2O]{Mg} Me_3SiCH_2MgCl \xrightarrow{(XCH_2CO)_2O} Me_3SiCH_2COCH_2X \xrightarrow{HgI_2} CH_2{=}C(OSiMe_3)CH_2X$$

1, X = Cl (62% from **4**)
2, X = Br (55% from **4**)



$$\mathbf{1} \xrightarrow[acetone]{NaI} CH_2{=}C(OSiMe_3)CH_2I \quad (1)$$

3 (57%)

1 was thermally and photochemically quite stable and was used most conveniently. Although the reactivity of **2** and **3** are expected to be higher than **1**, these are rather unstable compounds.

For the acetonylation, **1** was allowed to react with metalloenamines (**6**), prepared from imines (**5**) of enolizable ketones and lithium diisopropylamide (LDA) or *sec*-bu-

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[1] Chemistry of Organosilicon Compounds. 148.

(2) For reviews, see (a) Harris, T. M.; Harris, C. N. *Org. React.* **1969**, *17*, 155. (b) Reiff, H. *Newer Meth. Prep. Org. Chem.* **1971**, *6*, 48. (c) Nakai, T. *J. Syn. Org. Chem., Jpn.* **1978**, *36*, 49.

(3) (a) Grieco, P. A.; Pogonowski, C. S. *J. Org. Chem.* **1974**, *39*, 732. (b) Hegedus, L. S.; Stiverton, R. K. *J. Am. Chem. Soc.* **1974**, *96*, 3250. (c) Nakai, T.; Shiono, H.; Okawara, M. *Tetrahedron Lett.* **1975**, 4027. (d) Ito, Y.; Konoike, T.; Harada, T.; Saegusa, T. *J. Am. Chem. Soc.* **1977**, *99*, 1487 and references cited therein.

(4) (a) Stork, G.; Jung, M. E. *J. Am. Chem. Soc.* **1974**, *96*, 3682. (b) Stork, G.; Borch, R. *Ibid.* **1964**, *86*, 935. (c) Nienhouse, N. J.; Irwin, R. M.; Finni, G. R. *Ibid.* **1967**, *89*, 4557. (c) Dox, A. W.; Houston, B. *Ibid.* **1924**, *46*, 252. (e) Miyashita, M.; Yanami, T.; Yoshikoshi, A. *Ibid.* **1976**, *98*, 4679. (f) Islam, A. M.; Raphael, R. A. *J. Chem. Soc.* **1952**, 4086. (g) Miller, R. M. *Synth. Commun.* **1972**, *2*, 267. (h) Deboer, A.; Ellwanger, R. E. *J. Org. Chem.* **1974**, *39*, 77. (i) Miyano, M.; Dorn, C. R. *Ibid* **1972**, *37*, 268. (j) Greenwood, G.; Hoffmann, H. M. R. *Ibid.* **1972**, *37*, 611. (k) Horning, D. E.; Kavadias, G.; Muchowski, J. M. *Can. J. Chem.* **1970**, *48*, 975. (l) Jacobson, R. M.; Raths, R. A.; McDonald III, J. H. *J. Org. Chem.* **1977**, *42*, 2545 and references cited therein.

(5) Hosomi, A.; Kobayashi, H.; Sakurai, H. *Tetrahedron Lett.* **1980**, *21*, 955.

(6) Sakurai, H.; Shirahata, A.; Araki, Y.; Hosomi, A. *Tetrahedron Lett.* **1980**, *21*, 2325. 1, bp 61–63 °C (35–37 mmHg); IR (neat) 2960, 2900, 1635, 1315, 1260, 1225, 1160, 1030, 915, 850 cm^{-1}; NMR (CCl_4) δ 0.40 (s, 9 H), 3.92 (s, 2 H), 4.28 (br s, 1 H), 4.50 (br s, 1 H). 3-Bromo-2-(trimethylsiloxy)-1-propene (2), bp 57 °C (15 mmHg), was prepared similarly from bromoacetic anhydride in 55% yield. The iodo derivative (3) was obtained by the Finkelstein reaction of 1 with NaI in acetone in 57% yield. 1 was thermally and photochemically quite stable, but both 2 and 3 were not.

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