generous support of this research.

Registry No. 1, 71886-29-8; 2, 71886-30-1; 3, 21641-71-4; 3-methyl-1-pentene, 760-20-3; 2-iodo-3-methylpentanal, 71886-31-2; 1-iodo-3-methyl-2-pentanol, 71886-32-3; *N*-phenyl-*N*-(3-methyl-2-oxo-1-pentyl)triflamide, 71901-58-1; *N*-phenyltriflamide, 456-64-4; leucinamide, 13366-40-0.

Reactions of Nitrosonium Tetrafluoroborate in Acetonitrile with Organic Molecules Containing Nonbonding Electrons. Synthesis of Acetamides

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We have recently found that NO_2BF_4 in acetonitrile will abstract hydrogen from saturated hydrocarbons. Under these relatively mild reaction conditions, the incipient carbenium ion is efficiently trapped by the nitrile solvent, and upon hydrolysis of the resulting nitrilium ion acetamides are produced in good yield.[1a] The Lewis acid character of the nitronium (NO_2^+) ion is also manifested in its complexation with the nonbonding (n) electrons of alkyl halides[1b] and ethers, inducing C–X bond heterolysis which results in acetamide formation (eq 1).[1c] Hydrogen,

$$R_3CX + NO_2BF_4 \xrightarrow{CH_3CN} R_3C\text{-}N^+{\equiv}CCH_3 + NO_2X \quad (1)$$

$$\downarrow H_2O$$

$$R_3CNCCH_3 \quad (\mathrm{HO},\ \mathrm{O})$$

halogen, and alkoxide transfer to the nitronium ion was also observed with $CF_3C(O)ONO_2$ in trifluoroacetic acid and $CH_3C(O)ONO_2$ in acetic acid, affording alkyl trifluoroacetates and alkyl acetates, respectively.[1d] We now report a comparable series of reactions with $NOBF_4$ as the electrophilic reagent in acetonitrile.

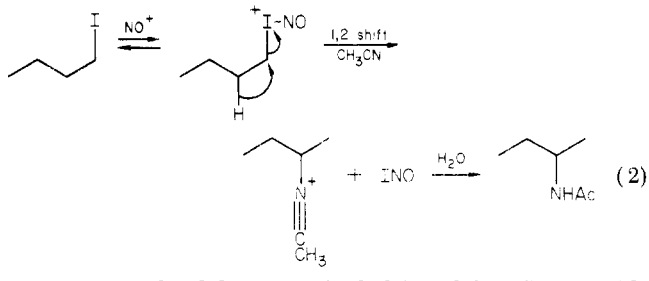
The nitrosonium ion, NO^+, is a reactive electrophilic species that has been utilized synthetically with alkenes,[2] amines,[3] amides,[4] sulfoxides,[5] and activated aromatic compounds.[6] Nitrosonium salts, with nonnucleophilic ions like $NOBF_4$ and $NOPF_6$, can be used to advantage in diazonium ion preparation from aryl or primary amines[7] and in the nitrosative decomposition of aliphatic azides.[8] Amides and sulfonamides were found to react with $NOBF_4$ under mild conditions to give the corresponding acids.[4] This versatile electrophilic reagent has been shown to abstract hydride ion from activated benzylic positions,[9a] to oxidize benzyl alcohols, and to oxidize trimethylsilyl and tributylstannyl ethers to carbonyl compounds.[9b] Activated benzyl and benzhydryl esters are also oxidatively cleaved to the parent acid or ketone.[9c] Alkenes also undergo electrophilic addition by $NOBF_4$ in acetonitrile to afford 2-methyl-*N*-hydroxyimidazolium salts.[9d]

Results and Discussion

To date there has been no systematic study of the reaction of $NOBF_4$ with alkyl halides or ethers in the condensed phase. In the gas phase, ion–molecule reactions of NO^+ with organic halides[10] closely paralleled our results with both NO^+ and NO_2^+ in solution.[9] In the absence of solvent, NO^+ exhibits a high electron affinity and will abstract hydrogen from normal, branched, or cyclic hydrocarbons.[10,11] It was the goal of the present study to provide a comparison between the reactivity of NO_2BF4 and $NOBF_4$ in acetonitrile and to develop a convenient synthetic procedure for the conversion of alkyl halides and ethers to their respective acetamides.

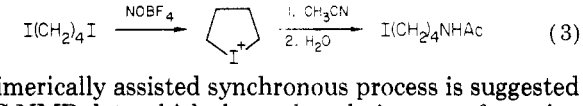
In a typical reaction, the alkyl halide or ether is added to 1 equiv of $NOBF_4$ in acetonitrile at 0 °C and allowed to stir at room temperature; the reaction is then quenched with water. Product isolation is not complicated by the formation of side products which give difficult separation problems. The results given in Table I serve to define the scope and utility of this new procedure.

The reactivity of $NOBF_4$ toward alkyl iodides was very similar to that observed with NO_2BF_4/CH_3CN. Both tertiary and secondary alkyl iodides reacted smoothly with $NOBF_4$ to afford their acetamides. As anticipated on the basis of relative carbenium ion stability, *n*-butyl iodide reacted slowly and gave equal amounts of 1-butyl- and 2-butylacetamides. The latter product arises from a 1,2 hydride shift to the developing adjacent positive center (eq 2).[12] The selective reaction of only one functional



(2)

group in 1,4-diiodobutane afforded (4-iodobutyl)acetamide. The absence of rearranged product is most likely a result of neighboring-group participation by iodine (eq 3). An



(3)

anchimerically assisted synchronous process is suggested by ^{13}C NMR data which shows the relative rate of reaction of 1,4-diiodobutane to be at least 10 times greater than that of 1-iodobutane.

The reaction times for the secondary halides were typically longer (24 h) with $NOBF_4$ than with NO_2BF_4. 1-Bromopropane and 1-bromooctane were unreactive toward

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(12) It is doubtful that primary and secondary substrates involve discrete carbenium ions. Optically active 2-bromo- and 2-methoxyoctane react with NO_2BF_4 to provide 2-acetamides with net inversion of configuration.

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Table I. The Reaction of Alkyl Halides and Methyl Ethers with $NOBF_4$ in Acetonitrile[a]

structure (RX) R	X	reaction time, h	product	yield, %
1-adamantyl	I	1.5	R-NHAc	90
	Br	1.0	R-NHAc	95
	Cl	19.0	R-NHAc	87[b]
	OMe	20.0	R-NHAc	89
tert-butyl	Br	3.0	R-NHAc	82
exo-2-norbornyl	Br	6.0	*exo*-2-acetamide	82
	Cl	32.0	*exo*-2-acetamide	67
	OMe	6.0	*exo*-2-acetamide	16
			2-norbornanone	33
endo-2-norbornyl	Cl	32.0	*exo*-2-acetamide	7
	OMe	15.0	*exo*-2-acetamide	10
			2-norbornanone	58
isopropyl	Br	23.0	R-NHAc	33
cyclohexyl	Cl	32.0	R-NHAc	1
2-butyl	I	2.5	R-NHAc	65
1-butyl	I	2.5	1-butylacetamide	26[b]
			2-butylacetamide	27
4-iodobutyl	I	3.0	4-iodobutylacetamide	85[c]
benzyl	Br	20.0	benzylacetamide	30[d]
2-octyl	OMe	20.0	2-octylacetamide	11
			3-octylacetamide	1
			2-octanone	13

[a] Yields are determined by gas chromatography. [b] Two equivalents of $NOBF_4$ were utilized. All other reactions used 1 equiv. [c] Crude isolated product. [d] The acetamide was isolated by column chromatography on silica gel. Its formation was accompanied by several side products.

$NOBF_4$ at room temperature for up to 66 h. (Tertiary alkyl chlorides reacted very sluggishly, and even 1-adamantyl chloride required an extended reaction time and 2 equiv of $NOBF_4$ in order to get a high yield.) In contrast, tertiary alkyl chlorides were readily transformed to acetamides by the action of NO_2BF_4 in CH_3CN.[9c]

The reaction of 1-adamantyl methyl ether was about an order of magnitude slower with $NOBF_4$ than with NO_2BF_4. Secondary alkyl methyl esters gave low yields of product with $NOBF_4$ with α-hydride abstraction, producing a ketone, competing favorably with C–O bond scission. Attempted reaction with 1-octyl methyl ether produced an intractable oil with only 23% starting material being recovered after 20 h.

The reduced electrophilic reactivity of $NOBF_4$ is particularly evident in its reaction with saturated σ-donor hydrocarbons. Treatment of adamantane with 2 equiv of $NOBF_4$ in CH_3CN solvent at room temperature produced less than 10% 1-adamantyl acetamide. However, at reflux (4 h) the acetamide was produced in 97% yield. Under similar reaction conditions norbornane gave only ~1% *exo*-2-acetamide (17 h), and cyclohexane and 2-methylbutane were found to be essentially inert toward $NOBF_4$. These hydrocarbons are readily oxidized at room temperature with NO_2BF_4 in CH_3CN.[9a]

In general, the overall reactivity of $NOBF_4$ toward n-donor molecules was significantly less than that of NO_2BF_4 under otherwise identical reaction conditions. However, we suggest that the mechanism for acetamide formation is essentially the same with both electrophilic reagents. There is little doubt that $NOBF_4$, which has a relatively low-lying empty π^* orbital as its lowest unoccupied molecular orbital (LUMO), is strongly solvated by one or more nitrile functional groups. We therefore choose to represent the "effective electrophile" in CH_3CN by resonance structures **1a** and **1b** (eq 4). Consistent with this sug-

$$CH_3C{\equiv}N: + NOBF_4 \rightleftarrows CH_3C{\equiv}\overset{+}{N}{-}N{=}O \leftrightarrow CH_3C{\equiv}N: \ {}^{+}N{=}O \quad (4)$$

1a **1b**

gestion is a considerable broadening of the ^{13}C NMR resonance for the nitrile carbon of CH_3CN (118 ppm from Me_4Si) upon addition of $NOBF_4$. By analogy to our mechanistic studies with NO_2BF_4[9] we propose the mechanism given in Scheme I. Displacement of solvent by the weakly nucleophilic nonbinding electrons of the substrate provides a Lewis acid–Lewis base complex which facilitates halide transfer to $NOBF_4$ concomitant with ionization of the C–X bond. Indeed, 1-bromoadamantane, which is relatively insoluble in CH_3CN and affords no acetamide in the absence of $NOBF_4$, quickly gives a dark colored solution upon addition of $NOBF_4$.

Scheme I

$$CH_3C{\equiv}\overset{+}{N}NO\ BF_4^- + RX \underset{\longleftarrow}{\overset{CH_3CN}{\rightleftarrows}} RX^+{-}NO\ BF_4^-$$

$$\downarrow$$

$$RNCCH_3 \underset{\longleftarrow}{\overset{H_2O\ CH_3CN}{\rightleftarrows}} R^+ + NOX$$

(HO, ‖ O)

In conclusion, we have established that $NOBF_4$ reacts more slowly than NO_2BF_4 with both n-donor and σ-donor molecules. The reaction of $NOBF_4$ in acetonitrile is the method of choice for the conversion of highly reactive alkyl tertiary halides and ethers to their respective acetamides. This reaction sequence provides an alternative to the use of NO_2BF_4 that should be more highly selective when multifunctional substrates are involved.

Experimental Section

Reaction of Alkyl Halides and Ethers. To 1.33 g (11 mmol) of nitrosonium tetrafluoroborate[13] in 25 mL of dry acetonitrile at 0 °C was added 10 mmol of alkyl halide (or ether). The reactions were stirred at 0 °C and then allowed to warm to room temperature. After a specific period (Table I) the reaction was quenched by addition of water and extracted with methylene chloride (3 × 20 mL). The combined organic layers were washed with 10 mL of water and dried ($MgSO_4$). The volatiles were removed by rotary evaporation, and the crude amides were purified by column chromatography on alumina using methylene chloride as the eluent.

(13) Nitrosonium tetrafluoroborate was purchased from Cationics Inc., Columbia, S.C. Acetonitrile was dried by distillation from H_2SO_4 and stored over 4 Å molecular sieves.

Reaction of 1,4-Diiodobutane. Employing the above procedure, we stirred 3.1 g (10 mmol) of 1,4-diiodobutane for 3 h in the presence of 1.2 g (10 mmol) of $NOBF_4$ in acetonitrile. The combined CH_2Cl_2 extracts were washed with saturated $NaHSO_3$ solution, and upon solvent removal 2.08 g (85%) of a yellow-orange oil was obtained: ^1H NMR ($CDCl_3$) δ 1.2–2.3 (m, 7), 3.0–3.6 (m, 4), 7.0 (1); ^{13}C NMR (relative to $CDCl_3$ at 77 ppm) δ 6.4, 22.9, 30.0, 30.4, 38.2, 170.6 (C=O) ppm; IR (neat) 3290, 2960, 1645, 1540 cm^{-1}.

The structure was confirmed by reduction with powdered zinc (1.1 g) in acetic acid (10 mL) for 1 h at 95 °C. Extraction with CH_2Cl_2 (3 × 10 mL) and washing with saturated $NaHCO_3$ afforded 1.0 g (46%) of 1-butylacetamide upon solvent removal.[14]

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Registry No. 1-Adamantyl iodide, 768-93-4; 1-adamantyl bromide, 768-90-1; 1-adamantyl chloride, 935-56-8; 1-adamantyl methyl ether, 6221-74-5; *tert*-butyl bromide, 558-17-8; *exo*-2-norbornyl bromide, 2534-77-2; *exo*-2-norbornyl chloride, 765-91-3; *exo*-2-norbornyl methyl ether, 10395-53-6; *endo*-2-norbornyl chloride, 2999-06-6; *endo*-2-norbornyl methyl ether, 10395-55-8; isopropyl bromide, 75-26-3; cyclohexyl chloride, 542-18-7; 2-butyl iodide, 513-48-4; 1-butyl iodide, 542-69-8; 4-iodobutyl iodide, 628-21-7; benzyl bromide, 100-39-0; 2-octyl bromide, 557-35-7; 1-adamantylacetamide, 880-52-4; *tert*-butylacetamide, 762-84-5; *exo*-2-norbornylacetamide, 28607-02-5; 2-norbornanone, 497-38-1; isopropylacetamide, 1118-69-0; cyclohexylacetamide, 1124-53-4; 2-butylacetamide, 1189-05-5; 1-butylacetamide, 1119-49-9; 4-iodobutylacetamide, 71988-86-8; benzylacetamide, 588-46-5; 2-octylacetamide, 23602-00-8; 3-octylacetamide, 23602-01-9; 2-octanone, 111-13-7; $NOBF_4$, 14635-75-7.

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Reduction of α,β-Unsaturated Nitriles with a Copper Hydride Complex

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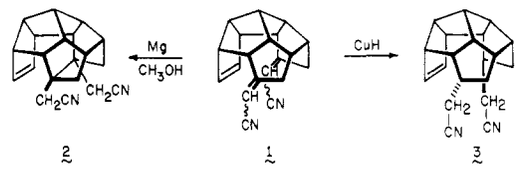
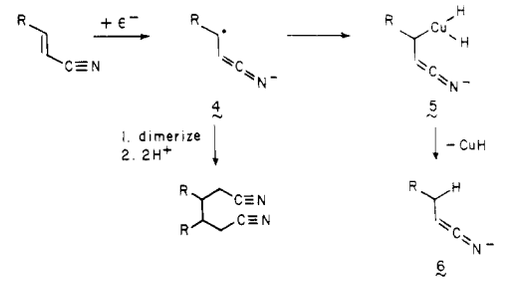
The reduction of conjugated nitriles to their saturated counterparts has long been a vexatious synthetic problem because of oft-encountered overreduction to the amine,[2] hydrodimerization,[3] decyanation,[4] and/or polymerization.[5] Recently, Profitt, Watt, and Corey published results achieved with magnesium metal in methanol.[6] Not only did reductions performed with this reagent proceed readily and in high yield but compatibility with a variety of other functional groups was also demonstrated. Accordingly, when the need arose in these laboratories to reduce the pair of conjugated double bonds in hexaquinane **1** regioselectively, we sought to take advantage of this recent development. However, magnesium in methanol proved versatile in transforming **1** uniquely into the unwanted transannular product **2**. This finding caused us to search for alternative methodology with which to achieve the desired conversion to **3**. Herein we describe our general success with the copper hydride reagent prepared from cuprous bromide, Vitride, and *sec*-butyl alcohol in the solvent tetrahydrofuran.[7]



2 1 3

Table I presents the results obtained with a variety of α,β-unsaturated nitriles which were prepared from the corresponding ketones by the Wadsworth–Emmons procedure[8] or purchased commercially. By means of a similar procedure, **3** was isolated in 70% yield.

The differing behavior of **1** under the two sets of conditions is particularly significant when considering the mechanisms of these complementary reactions. The dissolving action of elemental magnesium is thought to result in electron transfer with formation of a transient radical anion of type **4**. The characteristic[9] dimerization and



6

protonation of this species ensues. A parallel mechanism has been invoked for reduction with copper hydride species.[7,10,11] The absence of detectable transannular bonding in this instance probably has its origins in the rapid conversion of **4** to a covalently bonded copper species exemplified by **5** or perhaps in the direct production of such an intermediate. The copper atom presumably serves to retard hydrodimerization while making possible the delivery of **6** by reductive elimination of CuH or hydrogen abstraction from the medium.

Whatever the actual situation, it would appear that the copper hydride species described herein constitutes a useful reagent for the reduction of conjugated nitriles. Certainly, its reactivity is greater than that of sodium borohydride in refluxing isopropyl alcohol which has been reported not to reduce 2-butenenitrile,[12] as well as that of sodium cyanoborohydride which appears to require the presence of two activating groups at C_1.[13]

Experimental Section

General Reduction Procedure. To 1.86 g (13.0 mmol) of cuprous bromide in anhydrous tetrahydrofuran (10 mL) cooled

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