consumed. The catalyst was recovered, and water was added to the reaction mixture to precipitate the desired isomer, which was recrystallized from glacial acetic acid to provide 5,6,7,8-tetrahydro-1-naphthalenecarboxylic acid: mp 150–151 °C (lit.[1] mp 150–151.5 °C); 60% yield.

The corresponding deuteriated compound, 5,6,7,8-tetrahydro-1-naphthalenecarboxylic-5,6,7,8-d_4 acid (mp 150–151 °C) was prepared in the same way using dideuterium with acetic acid-*d* as the solvent.

Exchange Procedure. The exchange reaction was carried out in the Parr apparatus. The substrate (2.0 g) in acetic acid-*d* (20 mL) was sealed in the reaction bottle with the 10% palladium on carbon catalyst (100 mg, 5% w/w of substrate) and connected to a dideuterium reservoir at an initial pressure of 25 psig. The bottle was vigorously shaken at 55 °C for 24 h. The product was isolated by method A or B.

Method A. The reaction mixture was diluted with water, and the product was extracted into ether. The extract was washed with concentrated aqueous sodium hydroxide and water and then dried over magnesium sulfate. The ether was removed in vacuo, and the product was purified by vacuum distillation.

Method B. The reaction mixture was diluted with water, and the crude product was collected on a filter and recrystallized. The results are summarized in Table I.

Acknowledgment. We are indebted to Dr. R. S. Mahasay for his helpful discussions and comments. We also appreciate the financial support of the Gas Research Institute.

Registry No. $Ph(CH_2)_3Ph$, 1081-75-0; $PhCD_2CH_2CD_2Ph$, 67081-88-3; 1-naphthalenecarboxylic acid, 86-55-5; palladium, 7440-05-3; 5,6,7,8-tetrahydronaphthalene, 119-64-2; 9,10-dihydroanthracene, 613-31-0; 9,10-dihydrophenanthrene, 776-35-2; diphenylmethane, 101-81-5; 1,2-diphenylethane, 103-29-7; triphenylmethane, 519-73-3; 5,6,7,8-tetrahydro-1-naphthalenecarboxylic acid, 4242-18-6; 5,6,7,8-tetrahydro-1-naphthalenecarboxylic acid-5,6,7,8-d_4, 105372-59-6; 5,6,7,8-tetrahydronaphthalene-5,5,8,8-d_4, 92633-06-2; 9,10-dihydroanthracene-9,9,10,10-d_4, 59785-52-3; 9,10-dihydrophenanthrene-9,9,10,10-d_4, 27758-74-3; diphenylmethane-1,1-d_2, 3947-98-6; 1,2-diphenylethane-1,1,2,2-d_4, 20389-19-9; triphenylmethane-*d*, 2913-53-3; 5,6,7,8-tetrahydro-1-naphthalenecarboxylic acid-5,5,8,8-d_4, 105372-60-9; 5,6,7,8-tetrahydro-1-naphthalenecarboxylic acid-6,7-d_2, 105372-61-0.

A New Br^+ Reagent. Oxidation of Alcohols to Carbonyl Compounds by Bis(quinuclidine)bromine(I) Tetrafluoroborate

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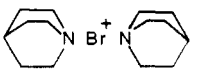
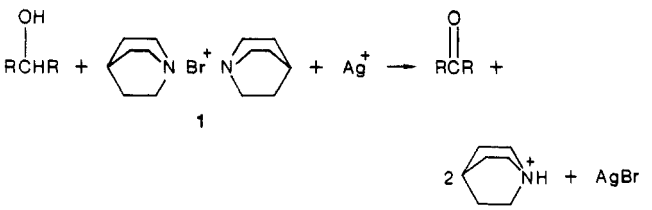
We call attention to a new source of positive bromine[1] for chemical synthesis, the quinuclidine-stabilized Br^+ complex **1**, bis(quinuclidine)bromine(I).



1

Recently,[2] we reported the preparation and crystal structure of the tetrafluoroborate of **1**, called attention to its unusual stability and desirable handling properties, and noted the intriguing electronic structure about the bromine which can be called hypervalent.[3] Now we report that this new reagent[4] effectively oxidizes alcohols to carbonyl compounds, particularly secondary alcohols to ketones. High yields of products are obtained when $AgBF_4$ is employed as a coreactant.

Scheme I



The results of the oxidation of several primary and secondary alcohols are given in Table I. The percent yields are based on GC analysis except for 9-fluorenone which was isolated. 4-*tert*-Butylcyclohexanone was also isolated in one case (86% yield). The yields of carbonyl product and AgBr support the stoichiometry for the oxidation given in Scheme I.

The two quinuclidines in **1** serve as base to absorb the 2 H^+ ions formed in the oxidation of alcohol. Thus, with base incorporated into the reagent itself in proper stoichiometric amount, additional base is unnecessary for oxidation of alcohols.

As the results in Table I show, the oxidation of secondary alcohols to ketones by bis(quinuclidine)bromine(I) tetrafluoroborate and $AgBF_4$ is nearly quantitative. The method compares favorably with other successful procedures.[5] Yields of aldehydes, however, are lower. Tertiary alcohols, which can be degraded if hypobromites are formed,[6] are essentially unaltered by the reagent under the conditions of oxidation of secondary and primary alcohols. Thus, for example, 97% (GC) of 3-ethyl-3-pentanol remained in the reaction mixture after 24 h under conditions that afforded high yields of ketone from secondary alcohols in less that 30 min. Similarly, no acetone was detected by GC after 7 h in the attempted oxidation of *tert*-butyl alcohol. Thus, the reagent shows promise as a selective oxidizing agent for secondary alcohols in the presence of tertiary alcohols.

With the objective to make exploratory applications of **1** to chemical synthesis, we have yet to undertake mechanistic studies of the oxidation of alcohols by **1** in the presence of $AgBF_4$. Although we have not made a rigorous search for products that might be expected to arise from hypobromite[6] intermediates—tetrahydrofurans and ring-opened products, for example—these products are minor ones, if formed at all, in our reactions. Thus, in the context of extensive studies of the role of hypobromites, reaction conditions, and the role of Ag^+ in oxidations of alcohols involving bromine,[7] it is noteworthy to point out that we

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Table I. Oxidation of Alcohols

alcohol	mmol	Br^+ complex, mmol	$AgBF_4$, mmol	reaction time, min	product	% yield
2-pentanol	0.94	1.09	1.49	5	2-pentanone	90
	1.17	1.03	1.22	10		104[a]
2-octanol	1.00	1.00	1.21	30	2-octanone	96
	1.18	1.03	1.13	10		83
	1.07	1.04	1.41	30		81
2,4-dimethyl-3-pentanol	0.94	1.05	1.21	5	2,4-dimethyl-3-pentanone	100
	1.00	1.00	1.21	38		98
cyclopentanol	1.45	0.95	1.19	10	cyclopentanone	93
	1.22	1.17	1.09	30		87
	1.05	0.99	1.27	30		93
cyclohexanol	0.85	1.02	0.99	30	cyclohexanone	102
	1.04	1.02	1.25	30		82
	1.08	1.00	1.24	30		97
	1.13	1.10	1.09	10		92
2-*tert*-butylcyclohexanol	1.03	0.99	1.51	30	2-*tert*-butylcyclohexanone	97
	1.03	0.99	1.27	30		113
	1.03	1.03	1.72	30		103
4-*tert*-butylcyclohexanol	1.03	1.00	1.27	30	4-*tert*-butylcyclohexanone	103
	1.00	1.01	1.23	30		95
cyclododecanol	1.00	1.00	1.23	20	cyclododecanone	84
menthol	1.00	1.00	1.23	34	menthone	72
borneol	1.00	1.00	1.23	23	camphor	91
sec-phenethyl alcohol	2.21	0.97	1.23	10	acetophenone	98
	1.13	1.04	1.13	10		109
9-hydroxyfluorene	1.00	1.09	1.25	40	9-fluorenone	94
	1.01	1.14	1.52	25		82
	1.10	1.08	1.30	33		98
1-pentanol	1.26	1.05	1.25	7	pentanal	59
	0.99	1.00	1.18	7		76
	1.30	1.36	1.24	5		65
1-octanol	0.69	0.90	0.84	5	octanal	51
	0.69	0.86	0.81	5		51
	1.05	1.00	1.00	30		48
neopentyl alcohol	1.01	1.00	1.23	84	trimethylacetaldehyde	60
	1.00	1.00	1.20	120		78
benzyl alcohol	1.21	1.07	1.11	7	benzaldehyde	100
	1.05	1.13	1.44	45		93

[a] Yields in excess of 100% indicate the precision of the analysis.

observe high yields of carbonyl products under the conditions of our reactions.

In an attempt to use the most readily accessible source of **1**, we investigated the oxidation of alcohols by the bromide salt of **1**, which can be prepared in a single step from the 2:1 combination of quinuclidine and bromine.[2] At least in a few preliminary studies of reactions involving 2 mol of $AgBF_4$/mol of the bromide of **1**, we found generally that the yield of carbonyl product was slightly to 50% lower than when the tetrafluoroborate of **1** was used with 1 mol of $AgBF_4$. To reduce the cost of the reagent, we shall continue to search for silver-free applications of **1** and related compounds.

Experimental Section

GC analyses were performed on Perkin-Elmer 810 or Varian 700, 3700, or 3400 instruments equipped with Carbowax 20M and SE-30 columns, 6 ft × 0.25 in., copper. Alcohols were used as supplied by commercial vendors. Quinuclidine and silver tetrafluoroborate were used as supplied by Aldrich. All other reagents and solvents were ACS or spectrophotometric grade and were used without further purification. Chloro- or bromobenzenes were used as internal standards for GC analyses. NMR spectra were obtained on Varian XL-200, Varian EM-360A, and Hitachi Perkin-Elmer R-24 instruments, and δ values are parts per million relative to tetramethylsilane as the internal standard. Melting points were obtained on a Mel-Temp apparatus and are uncorrected.

Characterization of 1 by NMR. Tetrafluoroborate of 1: ^1H NMR (CD_3CN) δ 3.11 (6 H, m, H-2), 1.80 (7 H, m, H-3 and H-4); ^{13}C NMR (CD_3CN) δ 54.3 (C-2), 27.6 (C-3), 20.0 (C-4). For comparison, quinuclidine was investigated: ^{13}C NMR (CD_3CN) δ 48.3 (C-2), 27.4 (C-3), 21.8 (C-4). A mixture of quinuclidine (2 mmol) and the tetrafluoroborate of **1** (1 mmol) in CD_3CN (8 mL) showed a spectrum with six lines that was identical with the superimposed spectra of the individual compounds. Thus, in acetonitrile any exchange of free quinuclidine and complexed quinuclidine takes place at a rate that is slow on the NMR time scale. for additional comparison, quinuclidine hydrobromide was studied: ^{13}C (CD_3D) δ 47.6 (C-2), 23.5 (C-3), 20.2 (C-4).

Oxidation of Cyclohexanol. To a mixture of bis(quinuclidine)bromine(I) tetrafluoroborate[2,8] (0.390 g, 1.00 mmol) and $AgBF_4$ (0.241 g, 1.24 mmol) was added 3 mL of CH_2Cl_2. To this solution was added with stirring a mixture of cyclohexanol (0.107 g, 1.07 mmol) and internal standard chlorobenzene (0.117 g, 1.04 mmol) dissolved in 2 mL of CH_2Cl_2. The reaction mixture was allowed to stir at ambient temperature for 30 min at which time the solid AgBr was collected on a glass-sintered funnel. The filtrate was then analyzed by GC, and the solid AgBr was washed with water, dried, and weighed.

Variation on Oxidation Procedure. For several oxidations, bis(quinuclidine)bromine(I) tetrafluoroborate, internal standard, $AgBF_4$, and alcohol, respectively in this order, were added directly to a 10-mL flask. The CH_2Cl_2 (4 or 5 mL) was then immediately added and the mixture allowed to stir until analysis was performed as described above. This procedure was used for the oxidations of cyclopentanol, 2-octanol, and *sec*-phenethyl alcohol, for example.

(8) In regard to the preparation of Br^+ complex,[2] we recently have observed that a white solid forms in solutions of quinuclidine in CH_2Cl_2 if the solution is allowed to stand at ambient temperatures for a few hours. Thus, it is recommended that the quinuclidine solution be used immediately. Presumably the white solid is the (chloromethyl)ammonium chloride of quinuclidine.

Oxidation of 9-Hydroxyfluorene and Isolation of Product. To a mixture of bis(quinuclidine)bromine(I) tetrafluoroborate (0.419 g, 1.08 mmol), $AgBF_4$ (0.254 g, 1.30 mmol), and 9-fluorenol (0.200 g, 1.10 mmol) was added 5 mL of CH_2Cl_2 and the mixture allowed to stir for 30 min. After the AgBr was collected, the filtrate was washed with water (5 × 10 mL) and evaporated to leave a yellow solid: mp 75–79 °C (lit. mp 81–83 °C for 9-fluorenone); 0.190 g (96%).

Verification of Products. Cyclopentanone and 2-octanone were verified as products by comparison of the NMR spectrum of the filtrate from the reaction mixture with the spectrum of authentic ketone. For analysis by NMR, the filtrate was washed with water, dried with Na_2SO_4, and concentrated by evaporation. Pentanal was verified as product from the NMR spectrum of the fraction collected around 103 °C in the distillation of the filtrate from the reaction mixture.

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Registry No. 1-BF_4, 85282-86-6; $AgBF_4$, 14104-20-2; 2-pentanol, 6032-29-7; 2-octanol, 123-96-6; 2,4-dimethyl-3-pentanol, 600-36-2; cyclopentanol, 96-41-3; cyclohexanol, 108-93-0; 2-*tert*-butylcyclohexanol, 13491-79-7; 4-*tert*-butylcyclohexanol, 98-52-2; cyclododecanol, 1724-39-6; menthol, 1490-04-6; borneol, 507-70-0; *sec*-phenethylalcohol, 98-85-1; 9-hydroxyfluorene, 1689-64-1; 1-pentanol, 71-41-0; 1-octanol, 111-87-5; neopentyl alcohol, 75-84-3; benzyl alcohol, 100-51-6; 2-pentanone, 107-87-9; 2-octanone, 111-13-7; 2,4-dimethyl-3-pentanone, 565-80-0; cyclopentanone, 120-92-3; cyclohexanone, 108-94-1; 2-*tert*-butylcyclohexanone, 1728-46-7; 4-*tert*-butylcyclohexanone, 98-53-3; cyclododecanone, 830-13-7; menthone, 10458-14-7; camphor, 76-22-2; acetophenone, 98-86-2; 9-fluorenone, 486-25-9; pentanal, 110-62-3; octanal, 124-13-0; trimethylacetaldehyde, 630-19-3; benzaldehyde, 100-52-7.

Regiospecific Synthesis of 5-Alkyl-1-(phenoxycarbonyl)-1,2-dihydropyridines

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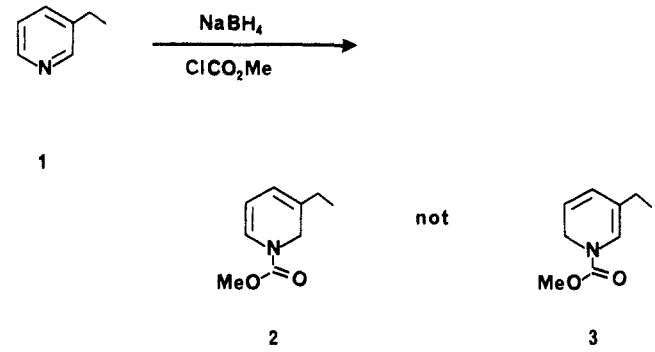
Recently, there has been considerable interest in 1-acyl-1,2-dihydropyridines as intermediates for the synthesis of natural products.[1,2] These relatively stable dihydropyridines are generally prepared by the addition of an organometallic[1,3] or reducing agent[4,5] to a 1-acylpyridinium salt. A substituent at the 5-position of the dihydropyridine intermediate is frequently required in natural product synthesis. Fowler's reduction (pyridine, alkyl chloroformate, $NaBH_4$)[4] is convenient for the synthesis of unsubstituted 1-(alkoxycarbonyl)-1,2-dihydropyridines; however, due to an "ortho" effect,[6] use of this procedure with 3-ethylpyridine (1) and methyl chloroformate leads



1 2 3

to 1-carbomethoxy-3-ethyl-1,2-dihydropyridine (**2**) and not the 5-substituted product **3**.[7] The dihydropyridine **3** is a useful intermediate for the synthesis of the Iboga alkaloid catharanthine[8] and has been prepared from 3-ethylpyridine by Fowler[9] and Raucher.[2h] No regiospecific syntheses of other 1-acyl-5-alkyl-1,2-dihydropyridines have been reported. We report herein a general synthesis of 5-alkyl-1-(phenoxycarbonyl)-1,2-dihydropyridines **8** that does not require a 3-substituted pyridine as an intermediate.

Table I. Synthesis of 5-Alkyl-1-(phenoxycarbonyl)-1,2-dihydropyridines 8

compd[a] 8	R	overall yield of 8,[b] %	compd[a] 8	R	overall yield of 8,[b] %
a	$PhCH_2$	60	**d**	Et	40
b	*n*-Bu	46	**e**	Ph	55
c	Me	46	**f**	C_6H_{11}	42

[a] The reactions were performed on a 2-mmol scale in THF. [b] Yield of purified product obtained from radial preparative-layer chromatography. Yield represents overall yield from **6**. All products were clear oils and gave the expected IR and ^1H NMR spectra. Due to their instability,[4] products **8** were not submitted for elemental analysis.

1-(Phenoxycarbonyl)-1,2-dihydropyridine (**4**) was chosen as starting material; it is a crystalline material that is readily prepared by a modification of Fowler's procedure.[10] Our synthetic plan called for a regiospecific formylation of dihydropyridine **4** at the 5-position (see Scheme I). The 5-position of **4** is electron rich and part of an ene carbamate system, which is susceptible to electrophilic attack. We[11] recently reported a regiospecific Friedel–Crafts β-acylation of 1-acyldihydropyridines, and Shono[12] has described one example of a β-formylation of a 1-acyl-1,4-dihydropyridine.

Formylation of **4** by the Vilsmeier–Haack reaction gave aldehyde **5** in 81% yield. This compound is a crystalline solid that can be stored in a freezer for several months without decomposition. Reduction of **5** with $NaBH_4$/$CeCl_3$[13] gave the alcohol **6** in quantitative yield. Treatment

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