Combination of the two crystalline fractions yielded 200 g (50%) of 12-membered ring lactone free base **2**: mp 186–187 °C; mass spectrum *m/e* 688 (P + 1), 546.3274 (P – 141), 369.2265 (P – 318), 351.2135 (P – 336), 158.1182 (P – 529, base peak), 145.0087 (P – 542). Anal. Calcd for $C_{35}H_{61}O_{12}N$: C, 61.11; H, 8.94; N, 2.03. Found: C, 60.93; H, 8.89; N, 2.08.

X-ray Data. A hexagonal prism of dimensions 0.37 × 0.25 × 0.25 mm suitable for X-ray diffraction studies was mounted on a glass fiber. Diffraction measurements were made on an Enraf-Nonius CAD-4 fully automated diffractometer using graphite-monochromated Cu Kα radiation. Preliminary indications of unit cell based on 25 randomly selected reflections revealed orthorhombic symmetry with the following lattice parameters: a = 37.038 (12) Å, b = 11.685 (2) Å, and c = 8.861 (3) Å, with $\alpha = \beta = \gamma = 90$. On the basis of observed systematic extinctions, the space group could be assigned as $P2_12_12$ (No. 18), $Z = 4$ with one molecule of composition $C_{35}H_{61}O_{12}N$ forming the asymmetric unit. The calculated density was 1.191 g/cm^3. There were 2980 reflections collected with $2\theta \leq 114°$; of those reflections, 2137 (72%) with $I \geq 3\sigma(\mathbf{I})$ were adjudged observed.

The structure was solved by using MULTAN 80. The phasing of 248 E values ≥ 1.648 resulted in an electron density map that revealed 45 out of the 48 non-hydrogen atoms. The complete structure was revealed by using the WFO option in Normal. All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were calculated by using SDP and HYDRO and were added to the structure calculations. The following full-matrix refinement of the non-hydrogen atoms and addition of the hydrogen atoms to the structure factor calculations, without refinement of their positions, resulted in convergence to a standard crystallographic unweighted residual of 0.044 and a weighted residual of 0.044. All intramolecular bond distances and angles are with normal ranges.

4-[(2,6-Dideoxy-3-*O*-methyl-α-L-*arabino*-hexopyranosyl)oxy]-9-hydroxy-9-(5-hydroxy-2,4-dimethyl-1-oxo-2-hexenyl)-3,5,7-trimethyl-6-[[3,4,6-trideoxy-3-(dimethylamino)-β-D-*xylo*-hexopyranosyl]oxy]-[3*R*-[3*R,4*S**,5*R**,6*S**,7*S**,9*R**(2*E*,4*R**,5*R**)]]-2-oxecanone (3).** A suspension of 8.0 g (0.116 mol) of the 12-membered ring lactone **2** and 8.0 g (0.0696 mol) of TMG in 100 mL of acetonitrile was refluxed for 12 h. The initial suspension gradually solubilized, followed by the precipitation of a white solid. The reaction mixture was cooled to room temperature and filtered. The precipitate was crystallized from ethyl acetate to yield 3.9 g (49%) of 10-membered ring lactone **3**: mp 208–210 °C; mass spectrum *m/e* 688 (P + 1), 546 (P – 141), 402 (P – 285), 158 (P – 529, base peak), 145 (P – 542). Anal. Calcd for $C_{35}H_{61}O_{12}N$: C, 61.11; H, 8.94; N, 2.03. Found: C, 60.97; H, 8.80; N, 1.97.

β-[(2,6-Dideoxy-3-*O*-methyl-α-L-*arabino*-hexopyranosyl)oxy]-2-(5-hydroxy-2,4-dimethyl-1-oxo-2-hexenyl)-α,γ,ε-trimethyl-δ-[[3,4,6-trideoxy-3-(dimethylamino)-β-D-*xylo*-hexopyranosyl]oxy]-[2*R*-[2*R(2*E*,4*R**,5*R**),2-(α*R**,β*S**,γ*R**,δ*S**,ε*S**)]]-oxiraneheptanoic Acid (4).** A solution of 1.7 g (2.47 mmol) of the 12-membered ring lactone **2** and 1.7 g (14.8 mmol) of TMG in 50 mL of THF was stirred at room temperature for 48 h. TLC (9:3:0.3 $CHCl_3/CH_3OH/NH_4OH$) of the reaction mixture indicated disappearance of starting lactone **2** (R_f 0.45) and appearance of a new polar product (R_f 0.12). Evaporation of the THF and chromatography of the residue (silica gel; 3:1 $CHCl_3/CH_3OH$) yielded 0.62 g (37%) of carboxylic acid **4** as a white amorphous solid: mass spectrum, *m/e* 688.1 (P + 1), 614 (P – 73), 544 (P – 143), 514 (P – 173), 496 (P – 191), 470 (P – 217), 369 (P – 318), 158 (P – 529), 145 (P – 742); TLC (9:3:0.3 $CHCl_3/CH_3OH/NH_4OH$) R_f 0.12.

Conversion of Carboxylic Acid 4 to 10-Membered Ring Lactone 3. A solution of 0.15 g (0.218 mmol) of the carboxylic acid **4** and 0.15 g of TMG was refluxed in 5 mL of acetonitrile for 24 h. The reaction mixture was cooled to room temperature and the solvent evaporated. The residue was suspended in water and extracted with ethyl acetate. The ethyl acetate extracts were dried (Na_2SO_4) and evaporated to yield 0.11 g (73%) of lactone **3**: mp 184–186 °C. ^{1}H NMR, ^{13}C NMR, and mass spectral data were the same as those reported for the 10-membered ring lactone **3** synthesized from the 12-membered ring lactone **2**.

Supplementary Material Available: Tables containing fractional coordinates, isotropic temperature parameters, bond distances, bond angles, torsion angles, and anisotropic temperature factors for compound **2** (9 pages). Ordering information is given on any current masthead page.

1,3-Dimethyl-2-phenylbenzimidazoline as a Novel and Efficient Reagent for Mild Reductive Dehalogenation of α-Halo Carbonyl Compounds and Acid Chlorides

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1,3-Dimethyl-2-phenylbenzimidazoline (DMBI) has been found to be a powerful, chemoselective, and useful reducing agent for mild reductive dehalogenation of a variety of α-halo carbonyl compounds (halo = Br, Cl, F) and acid chlorides. The reduction of α-halo ketones, aldehydes, esters, lactones, and carboxylic acids with this new reagent in ether is quite selective and clean and generally proceeds in almost quantitative yields at moderate temperatures with no additives. The order of relative reactivities in a series of α-halo carbonyl compounds was Br > Cl > F (for halides), primary > secondary > tertiary (for substitution at the halogenated carbon), and cyclohexyl > cyclododecyl (for ring size). The reduction of α-bromocamphor with DMBI-2-*d* led stereospecifically to the formation of camphor-3-*exo*-*d*. Based on these results together with experiments with para-substituted DMBIs, the mechanism of the present dehalogenation reaction of α-halo carbonyl compounds is postulated to proceed via a simple linear transition state (direct S_N2 displacement) featuring an attack on the halogenated carbon center by hydrogen at the C-2 position of DMBI as a hydride. Reductive dechlorination of acid chlorides to the corresponding aldehydes or aldehyde-*d* with DMBI or DMBI-2-*d* has also been achieved most effectively in the presence of an acetic acid catalyst.

Selective reduction of organic functional groups is an important and frequently encountered synthetic operation in organic synthesis. Many methods have been developed toward this goal and many types of "selective reduction" have been accepted as synthetically useful. Despite much work, however, in the reduction field, there are only a few

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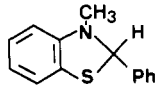
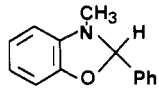
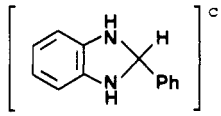
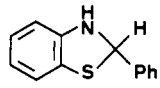
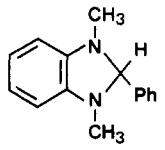
Table I. Reductive Dehalogenation of α-Bromoacetophenone with Benzazolines[a]

entry	H donor	yield,[b] %
1	DMBI	100
2		55
3		11
4	 [c]	12[d]
5		47[d]

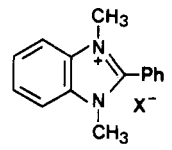
[a] All the reactions were carried out with 2.4 mmol of the substrate and the hydrogen donor in 10 mL of THF at the refluxing temperature for 30 min. [b] Determined by GLC. [c] Prepared in situ from benzaldehyde (2.4 mmol) and o-phenylenediamine (2.4 mmol). [d] Reaction under nitrogen atmosphere.

reports[1] dealing with the practical use of heterocyclic hydrogen donors as selective reducing agents. Recently, several reports[2] have appeared dealing with the use of 1,4-dihydropyridine derivatives (so-called NAD(P)H-model compounds) as synthetic reducing agents. Reduction with these compounds has, so far, been investigated because of its biological, biomimetic, and mechanical interest. Furthermore, the possibilities of dihydropyridines as practical reducing agents in organic synthesis seem to be somewhat low because of their poor reactivity and their instability is a disadvantage to their use.

As a continuation of our work for the development of new reducing systems utilizing the potential reducing ability of heterocyclic compounds,[3] we have investigated the potential reducing ability of a series of 2-phenylbenzazolines on the selective reduction of carbon–halogen bonds in α-halo carbonyl compounds and acid chlorides to a carbon–hydrogen bond and found that DMBI was an excellent candidate as a reducing agent for these reactions because of its high reactivity and selectivity. This paper



DMBI



$DMBI^+X^-$

describes the general reducing properties of DMBI and the

(1) (a) Mashraqui, S. M.; Kellogg, M. *Tetrahedron Lett.* **1985**, *26*, 1453. (b) Tagani, S.; Tabuchi, C.; Morimoto, K.; Shiho, D. *Yakugaku* Zasshi **1974**, *94*, 929.

(2) Yasui, S.; Nakamura, K.; Fujii, M.; Ohno, A. *J. Org. Chem.* **1985**, *50*, 3283. Nakamura, K.; Fujii, M.; Mekata, H.; Oka, S.; Ohno, A. *Chem. Lett.* **1986**, *87*. Yasui, S.; Nakamura, K.; Ohno, A. *Ibid.* **1984**, 377. Nakamura, K.; Ohno, A.; Oka, S. *Tetrahedron Lett.* **1983**, *24*, 3335. Nakamura, K.; Fujii, M.; Oka, M.; Ohno, A. *Chem. Lett.* **1985**, 523. Nakamura, K.; Fujii, M.; Ohno, A.; Oka, S. *Tetrahedron Lett.* **1984**, *25*, 3985.

(3) (a) Itoh, K.; Ishida, H.; Chikashita, H. *Chem. Lett.* **1982**, 1117. (b) Chikashita, H.; Nishida, S.; Miyazaki, M.; Itoh, K. *Synth. Commun.* **1983**, *13*, 1033. (c) Chikashita, H.; Morita, Y.; Itoh, K. *Synth. Commun.* **1985**, *15*, 527. (d) Chikashita, H.; Miyazaki, M.; Itoh, K. *Synthesis* **1984**, 308. (e) Chikashita, H.; Itoh, K. *Bull. Chem. Soc. Jpn.* **1986**, *59*, 1747. (f) Chikashita, H.; Itoh, K. *Chem. Express* **1986**, *1*, 17. (g) Chikashita, H.; Miyazaki, M.; Itoh, K. *J. Chem. Soc., Perkin Trans. I*, in press.

Table II. Rates of Reduction of α-Bromoacetophenone with DMBI in Various Solvents at Refluxing Temperature[a]

	reduction,[b] %				
solvent	5 min	10 min	20 min	30 min	60 min
diethyl ether	69	100			
THF	69	100			
dioxane	60	98	100		
acetonitrile	56	59	60	66	72
benzene	58	72	80	96	100
n-hexane	19	34	63	74	75
methanol	19	29	30	32	35
ethanol	20	25	29	31	35

[a] In all cases, solutions were 0.24 M in the substrate and 0.24 M in DMBI. [b] All yields were determined by GLC using pentylbenzene as internal standard.

usefulness of this new reagent in the reductive dehalogenation of selected halo carbonyl compounds; reduction of α-halo ketones, aldehydes, esters, lactones, and acids, and acyl chlorides.

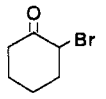
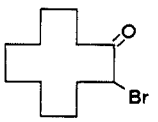
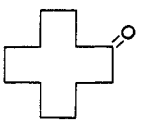
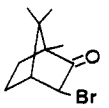
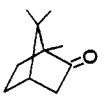
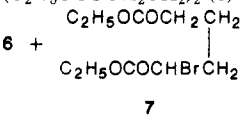
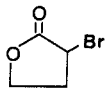
Results and Discussion

Reduction of α-Halo Carbonyl Compounds. Initially, a brief survey of benzazolines as reductants for the reductive dehalogenation of α-bromoacetophenone with no additive using tetrahydrofuran (THF) as solvent was conducted. While all of these reactions selectively proceeded to give acetophenone, it was apparent from Table I that DMBI was superior to the other heterocycles in terms of potential reducing ability toward α-halo carbonyl compounds. Although Kellogg *et al.* reported[1a] that 2-phenylbenzothiazoline does not reduce α-bromoacetophenone under either thermal or photochemical conditions, we had pointed out that this reaction (entry 5) proceeded in THF at reflux temperature to give a quantitative yield of acetophenone during a reaction time of 24 h. It is noteworthy that DMBI is very stable in air and light and 1,3-dimethyl-2-phenylbenzimidazolium bromide ($DMBI^+Br^-$) was formed by the compensating oxidation of the reducing agent and was deposited from the reaction mixture in quantitative yield as insoluble crystals.

Before any detailed study, it was desirable to examine the effect of solvent on the reduction with DMBI. Thus, the yields of acetophenone was monitored by GLC at appropriate intervals for the reduction of α-bromoacetophenone with 1 molar equiv of DMBI in various solvents. The results are summarized in Table II. In general, the reduction was quite selective and proceeded well in most common solvents; however, among the solvents employed, ethereal solvents such as diethyl ether, THF, or dioxane were found to be most effective in terms of rapidity, cleanliness, and recovery of the imidazolium salt ($DMBI^+X^-$).

To establish the generality of the DMBI-reduction, we examined the reaction of DMBI with a variety of α-halo carbonyl compounds. The results are summarized in Table III. Dehalogenation of alicyclic α-bromo ketones (**1a**, **d–f**) and α-chloro ketone **1b** to the parent ketones could be carried out efficiently with 1 equiv of DMBI by using THF as a solvent at reflux temperature. Although reduction of the tertiary bromide, 2-bromo-2,4-dimethyl-3-pentanone (**1g**), is very slow, it gave selectively the corresponding ketone, diisopropyl ketone, in moderate yield with no trace of the elimination product or other byproducts after refluxing for 2 days. Reductive defluorination of α-fluoro ketones is generally believed to be very difficult and virtually no widely applicable method for defluorination is available in the literature.[4] Interestingly, the defluori-

Table III. Reductive Dehalogenation of α-Halo Ketones 1, Aldehydes 2, Esters 3, Lactones 4, and Acids 5 with DMBI

	substrate[a]	product[b]	solvent	time,[c] h	yield,[d,e] %
1a	$PhCOCH_2Br$	$PhCOCH_3$	THF	0.5	95 (88)
1b	$PhCOCH_2Cl$	$PhCOCH_3$	THF	15	95 (85)
1c	$PhCOCH_2F$	$PhCOCH_3$	dioxane	48	84
1d	p-$BrC_6H_4COCH_2Br$	p-$BrC_6H_4COCH_3$	THF	0.5	96 (93)
1e	p-$HOC_6H_4COCH_2Br$	p-$HOC_6H_4COCH_3$	THF	3	93 (89)
1f	n-$C_3H_7COCHBrC_2H_5$	$(n$-$C_3H_7)_2CO$	THF	44	93 (88)
1g	i-$C_3H_7COCBr(CH_3)_2$	$(i$-$C_3H_7)_2CO$	THF	48	55[f,g] (72)
1h			dioxane	15	93 (88)
1i			dioxane	52	95 (93)
1j			dioxane	46	82[f] (89)
2a	$PhCH_2CHBrCHO$	$PhCH_2CH_2CHO$	THF	5	89 (88)
2b	$PhCH_2CHClCHO$	$PhCH_2CH_2CHO$	THF	18	88 (91)
2c	$PhCBr(CH_3)CHO$	$PhCH(CH_3)CHO$	THF	5	95 (97)
2d	n-$C_6H_{13}CHBrCHO$	n-$C_7H_{15}CHO$	THF	5	92 (93)
3a	$PhCH_2OCOCH_2Br$	$PhCH_2OCOCH_3$	THF	1	94 (95)
3b	$PhCH_2OCOCH_2Cl$	$PhCH_2OCOCH_3$	dioxane	4	91 (92)
3c	$PhCH_2OCOCHBrCH_3$	$PhCH_2OCOC_2H_5$	THF	9	90 (97)
3d	$PhCH_2OCOCHClCH_3$	$PhCH_2OCOC_2H_5$	dioxane	11	93 (90)
3e	$C_2H_5OCOCHBrCH_3$	$C_2H_5OCOC_2H_5$	ether	2	90 (95)
3f	$(C_2H_5OCOCHBrCH_2)_2$	$(C_2H_5OCOCH_2CH_2)_2$ (6)	THF	9	93[f] (94)
3f	$(C_2H_5OCOCHBrCH_2)_2$	 6 + 7	THF	6	32[h,i] + 36[h,j] (91)
4			THF	4	95 (93)
5a	$BrCH_2COOH$	CH_3COOH	THF	4	87 (86)
5b	$ClCH_2COOH$	CH_3COOH	THF	23	85 (89)
5c	n-$C_6H_{13}CHBrCOOH$	n-$C_7H_{15}COOH$	THF	6	89 (86)

[a] All the experiments were performed on a 2.4-mmol scale with a molar ratio of substrate to DMBI of 1:1 unless otherwise noted. [b] All the products gave satisfactory spectral (NMR, IR, MS) data which were compared with authentic samples. [c] Reactions were carried out at the refluxing temperature of the solvent. [d] Yield of isolated, pure product unless otherwise noted. [e] Values in parentheses indicate yields of $DMBI^+X^-$. [f] 4.8 mmol of DMBI was used. [g] Yield determined by GLC with an internal standard. [h] Isolated as a mixture of adipic acid diethyl ester (6) and α-bromoadipic acid diethyl ester (7). [i] Yield of adipic acid diethyl ester (6) determined by GLC. [j] Yield of α-bromoadipic acid diethyl ester (7) determined by GLC.

nation of α-fluoroacetophenone (**1c**) proceeded effectively in high yield with 2 equiv of DMBI in dioxane at reflux temperature. This result is an unique feature of the reduction system and presented a new method for the reductive removal of fluorine in α-fluoro ketones. On the other hand, the reduction of common cyclic α-bromo ketones (**1h, i**) proceeded well by using 1 equiv of DMBI, as also with alicyclic α-halo ketones. Even the stericaly hindered halo ketone **1j** could be reduced in high yield with 2 equiv of DMBI. α-Halo aldehydes **2a–d**, esters **3a–e**, lactones **4**, and acids **5a–c** were similarly reduced with no difficulties with 1 equiv of DMBI in an appropriate ethereal solvent (generally THF) in excellent yields. The reduction of α,α′-dibromoadipic acid diethyl ester (**3f**) with 2 equiv of DMBI gave the corresponding complete reduction product **6** in near quantitative yield, although the selective partial reduction of the same substrate to α-bromoadipic acid diethyl ester (**7**) with 1 equiv of DMBI was unsuccessful, giving a mixture of **6** and **7**. In all cases, the $DMBI^+X^-$ was efficiently recovered in excellent yields by simple filtration as shown in Table III. In the reductions shown in Table III, the hydroxyl, arylic bromide, ketonic carbonyl, aldehydic carbonyl, carboxylic ester, acid, and lactone groups were inert toward DMBI reduction. In addition, we have found that other functional groups such as nitro groups, cyano groups, carbon–carbon double bonds, carbon–carbon triple bonds, and common carbon–halogen bond are inert to DMBI under the present conditions. These high chemoselectivities are of great importance and enhance the utility of the present reagent.

In comparing the relative reactivities of α-halo carbonyl compounds with DMBI, several observations are noteworthy. Reduction of α-bromo, chloro, and fluoro carbonyl

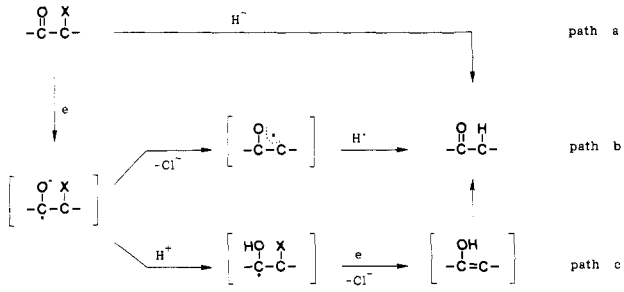
(4) Defluorination of α-fluoro ketones to dithioacetals of the corresponding defluorinated ketones with aluminum chloride and ethanethiol has been reported: Fuji, K.; Node, M.; Kawabata, T.; Fujimoto, M. *Chem. Lett.* **1984**, 1153. α,α,α-Trifluoroacetophenone was electrolytically reduced to a mixture of acetophenone and acetophenone pinacol: Stocker, J. H.; JeneVein, R. M. *J. Chem. Soc., Chem. Commun.* **1968**, 934. The Clemmensen reduction conditions can affect the reductive removal of fluorine with a concomitant reduction of the carbonyl group: Fear, E. J. P.; Thrower, J.; Veitch, J. *J. Appl. Chem.* **1955**, *5*, 589.

Table IV. Rates of Reduction of α-Bromoacetophenone with Some Para-Substituted DMBIs in Refluxing THF[a]

	reduction,[b] %				
subst	5 min	10 min	15 min	60 min	90 min
OMe	72	100			
Me	69	100			
H	69	100			
Cl	35	37	47	100	
NO_2	trace	2	3	5	5

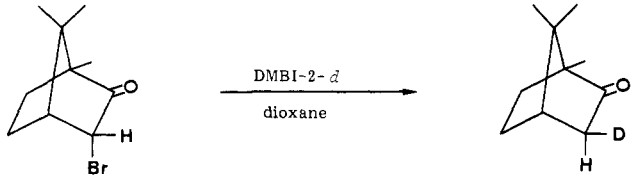
[a] In all cases, solutions were 2.4 M in the substrate and 2.4 M in DMBI or its derivative. [b] All yields were determined by GLC using pentylbenzene as internal standard.

Scheme I



compounds clearly reveals that the rate of reduction markedly decreases in the order Br > Cl > F. Increasing alkyl substitution at the halogenated carbon resulted in a substantial decrease in the rate of reduction. For example, the rate of reduction decreased from α-bromoacetophenone (**1a**) to 3-bromo-4-heptanone (**1f**) to 2-bromo-2,4-dimethyl-3-pentanone (**1g**), revealing the order primary > secondary > tertiary, which is commonly observed in S_N2 substitution reactions. The influence of the ring size on the reactivity varies in the order α-bromocyclohexanone > α-bromocyclododecanone, which also conforms to the order observed for S_N2 halide substitutions of cycloalkyl halides.[5]

In order to further probe the mechanistic pathway of the present DMBI-reduction, we examined the stereochemical course of the reduction of α-bromocamphor with DMBI-2-*d* in dioxane at reflux temperature. This reaction was found to lead stereospecifically to the formation of camphor-3-*exo*-*d*. Since camphor-3-*endo*-*d* was not detected, this result shows that the reaction occurred with complete inversion of configuration (Eq 1).



A comparison of the relative reactivities of several *para*-substituted DMBIs against α-bromoacetophenone was also conducted. As shown in Table IV, when DMBI was substituted by an electron-donating group, the rate of reduction increased. On the other hand, the rate decreased with the increase of electron-withdrawing ability of the substituent. These results indicate that the reduction is most likely involves the transfer of a hydrogen atom from the C-2 position as a hydride. The process involving the movement of a hydride ion from the C-2 carbon is probably the major rate-determining step of the

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Scheme II

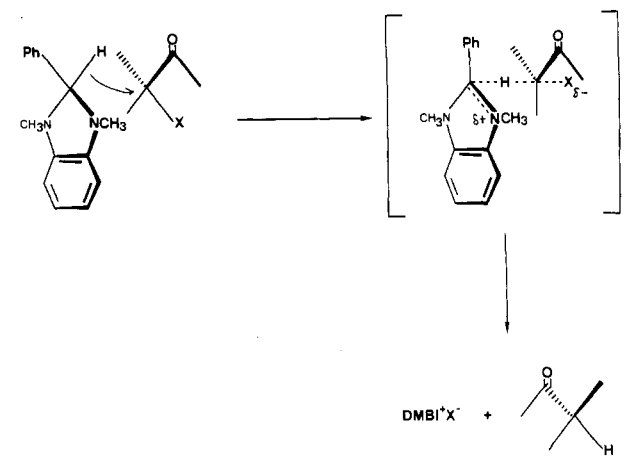


Table V. Effect of Additives on the Reduction of Benzoyl Chloride to Benzaldehyde with DMBI[a]

entry	additive	molar ratio of PhCOCl:DMBI:additive	yield,[b] %
1	none	1:1:0	64
2	CH_3CO_2H	1:1:0.5	88
3	CH_3CO_2H	1:1:1	96
4	CH_3CO_2H	1:1:10	51
5	CH_3CO_2H	0:1:1	0 (93)[c]
6	$AlCl_3$	1:1:1	16
7	$ZnCl_2$	1:1:1	24
8	DMF	1:1:1	79

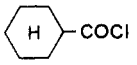
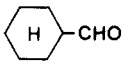
[a] All the reactions were performed in acetonitrile at the refluxing temperature for 2 h. [b] Determined by GLC. [c] Isolated recovery of DMBI.

reduction. Although the present dehalogenation may be viewed as simply a one-step hydride ion transfer (path a), schemes involving sequential transfers of e + H• (path b) and e + H^+ + e (path c) are also possible in theory (Scheme I). The involvement of paths b and c, however, is rather unlikely in view of the forementioned observation that the reduction rate is very sensitive to steric environment. This type of steric sensitivity is not generally expected for paths b and c. Accordingly, we suggest that pathway a is more likely to operate in the DMBI-reduction of α-halo carbonyl compounds; that is, we postulated that the reaction occurred via direct S_N2 displacement of the halides with hydride ion. We believe that all of our data and observations are best explained by a mechanism which includes a simple linear transition state featuring the attack on a halogenated carbon center by hydrogen at the C-2 position of DMBI as a hydride (Scheme II).

Reduction of Acyl Chlorides. We next tried the direct reduction of acyl chlorides to aldehydes. As shown in Table V, the reduction of benzoyl chloride with 1 equiv of DMBI proceeded in acetonitrile in moderate yield (entry 1). However, when 1 molar equiv of acetic acid was added to the system, the reaction was much more effective and benzaldehyde was produced in nearly quantitative yield (entry 3). The use of acetic acid in amounts equimolar with the acyl chloride was most effective in promoting the reaction, while the use of excess of acetic acid reduced the yield of aldehyde (entry 4). Under the present nonaqueous and weakly acidic conditions, no hydrolysis of DMBI to benzaldehyde occurred even after the aqueous workup (entry 5). This stability[6] of DMBI prevents the mixing of

(6) We have found that the hydrolysis of DMBI even under aqueous acidic conditions (pentane/4% aqueous HCl) is very sluggish in sharp contrast to that of 1,3-dimethyl-2-alkylbenzimidazolines.

Table VI. Reductive Dehalogenation of Acid Chlorides to Aldehydes with DMBI in the Presence of Acetic Acid[a]

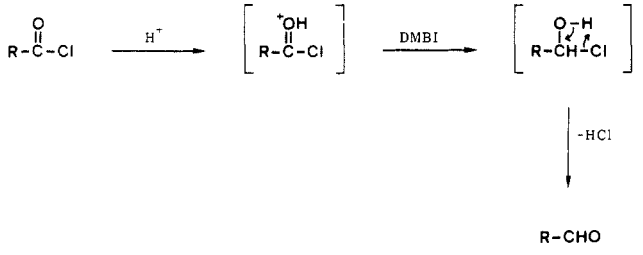
entry	acid chloride	product[b]	time, h	yield,[c] %
1	PhCOCl	PhCDO	2	90[d,e]
2	p-$NO_2C_6H_4COCl$	p-$NO_2C_6H_4CHO$	5	82
3	p-$CH_3OC_6H_4COCl$	p-$CH_3OC_6H_4CHO$	6	85
4	n-$C_7H_{15}COCl$	n-$C_7H_{15}CHO$	7	69
5			5	80

[a] All the experiments were performed on a 2.4-mmol scale with equimolar amounts of substrate, DMBI, and acetic acid. [b] All the products gave satisfactory spectral (NMR, IR, MS) data which were compared with authentic samples. [c] Yield determined by GLC with an internal standard. [d] DMBI-2-d was used in place of DMBI. [e] 99% deuterium incorporation was observed.

benzaldehyde with the reduced product.

The acetic acid catalyzed reduction with DMBI was carried out on five representative acyl chlorides. The results in Table VI show that the reaction can be effectively applied to aliphatic (entries 4, 5) and aromatic (entries 1–3) acyl chlorides. On the whole, the yields of aldehydes are consistently high. When DMBI-2-d was used instead of DMBI in the reduction of benzoyl chloride, benzaldehyde-d was obtained in good yield with almost complete deuteriation (entry 1). In no cases could any appreciable amount of byproducts such as alcohols or esters be detected. Furthermore, chemoselectivity of this reaction was found to be similar to observations during reduction of α-halo carbonyl compounds. Thus, the present DMBI reduction of acyl chlorides tolerates the presence of forementioned reducible functional groups in the molecule.

The mechanism of reductive dechlorination of acyl chlorides is well explained by general acid catalysis. That is, acyl chloride is electrophilically activated toward attack by hydride ion from DMBI via protonation of the carbonyl group (Eq 2).



Conclusions

The present study clearly reveals that DMBI is a powerful, selective, and useful reducing agent for the reduction of a carbon–halogen bond to a carbon–hydrogen bond in a wide variety of α-halo carbonyl compounds. Even α-fluoroacetophenone undergoes efficient reduction to the corresponding ketone. These reactions can be performed under simple and very mild (moderate temperature, aprotic, nonbasic, nonacidic, and no ionic species present) conditions. The products are generally obtained in excellent yields with high purity. The easy and efficient recovery of the imidazolium salt ($DMBI^+X^-$) by simple filtration and the reconvertibility[7] of it to DMBI make the present method more attractive. The reduction of a carbon–chlorine bond in acyl chlorides to a carbon–hydrogen bond with DMBI is also efficiently performed with high selectivity by acetic acid catalysis. The ready availability of DMBI-2-d, high yields of the product, and the excellent deuterium incorporation offer promise for a new method for the synthesis of aldehydes-d from acyl chlorides via deuterium–chlorine displacement. Finally, high chemoselectivity together with the power of DMBI in these reactions enhance the usefulness of the present reduction method.

Experimental Section

Melting points were recorded on a Yanagimoto micro melting point apparatus and are uncorrected. ^1H NMR spectra were measured with a JEOL PMX-60 spectrometer at 60 MHz or a JEOL PS-100 spectrometer at 100 MHz with tetramethylsilane as an internal reference. IR spectra were recorded on a JASCO A-202 spectrophotometer. Mass spectra were obtained on a JMS-QH100 GC–mass spectrometer. GLC analyses were carried out on a Shimadzu gas chromatograph GC-6AM equipped with a hydrogen flame ionization detector using glass columns (1.5 m) packed with 2% Silicone OV-7 on Uniport HP (60–80 mesh). The yields by quantitative GLC were measured on the same columns by the internal standard method using pentylbenzene as an internal standard. Silica gel (Wakogel C-300) was used for short column chromatography.

Materials. THF was distilled over $LiAlH_4$. Dioxane and diethyl ether were distilled over sodium. The other solvents were purified by the usual methods and were freshly distilled. DMBI was prepared from 2-phenylbenzimidazole by a slightly modified method of Craig et al.[7] DMBI-2-d was prepared by the reduction of 2-phenylbenzimidazolium iodide with $LiAlD_4$ according to the same procedure. This gave fully deuteriated material by ^1H NMR; no azomethine proton absorption was detected. 3-Methyl-2-phenylbenzothiazoline[8] and 3-methyl-2-phenylbenzoxazoline[9] were prepared according to the literature procedures. 2-Phenylbenzimidazoline was prepared in situ from benzaldehyde and o-phenylenediamine as described previously.[3b,c] α-Bromo-p-hydroxyacetophenone (**1e**),[10] α-bromocyclohexanone (**1h**),[11] α-fluoroacetophenone (**1c**),[12] α-halo aldehydes **2a–d**,[13] 2-bromobutyrolactone (**4**),[14] and α,α'-dibromoadipic acid diethyl ester (**3f**)[15] were prepared by the methods in the literature. α-Bromo ketones **1f,g,i** were prepared by bromination of the corresponding ketones with $CuBr_2$ according to the method of King et al.[10] α-Halo esters were obtained by esterification of the corresponding acids (**5a–c**) which were commercially available. The other halo carbonyl compounds were obtained commercially and purified by distillation or recrystallization.

Reduction of α-Halo Carbonyl Compounds: General Procedure. To a stirred solution of the halo carbonyl compound (2.4 mmol) in a solvent (10 mL), DMBI (2.4 mmol) was added and the mixture was refluxed with stirring. A white precipitate was formed soon after the addition. This indicated the formation of $DMBI^+X^-$. After completion of the reaction (monitored by TLC; see Table III), the reaction mixture was cooled in an ice bath. The insoluble $DMBI^+X^-$ was filtered off and washed with chloroform. The filtrate was concentrated under reduced pressure to give product. In most cases, the products obtained were almost pure by TLC analysis. When necessary, the crude product was purified by short column chromatography on silica gel.

Identification of products was performed by spectroscopic (NMR, IR, and MS) methods. When the product was a ketone or an aldehyde, the melting point of the 2,4-dinitrophenylhydrazone derivative was also measured. These spectral and physical data were in satisfactory agreement with those of the corresponding authentic samples or expected values.

Reduction of α-Bromocamphor with DMBI-2-d. α-Bromocamphor was treated with 2 equiv of DMBI-2-d in dioxane for

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46 h according to the general procedure. The crude product was purified by short column chromatography on silica gel.

The ^1H NMR ($CDCl_3$/100 MHz) spectrum of the product showed the triplet assigned to the endo-3-H at δ 1.75 (J = 2.5 Hz), and these spectral data together with melting points were in full accord with the literature.[16]

Reduction of Acyl Chlorides: General Procedure. To a refluxing solution of DMBI (2.4 mmol) in acetonitrile (5 mL) was slowly added a mixture of acyl chloride (2.4 mmol) and acetic acid (2.4 mmol) in acetonitrile (5 mL) dropwise under stirring. After refluxing had been continued for the appropriate time (see Table VI), the reaction mixture was cooled in an ice bath and poured into cold $NaHCO_3$ solution. The aqueous solution was extracted with chloroform and the extract dried with Na_2SO_4. The crude product obtained by evaporation of chloroform was subjected to short column chromatography on silica gel to give pure product.

Identification of products was performed by comparison of NMR, IR, and MS spectra and melting points of 2,4-dinitrophenylhydrazone derivatives of the isolated products with those of corresponding authentic samples. The spectral and physical data were in satisfactory agreement.

Reduction of Benzoyl Chloride with DMBI-*2-d*. Benzoyl chloride was treated with an equimolar amount of DMBI-*2-d* for 2 h according to the general procedure. The crude product was purified by short column chromatography on silica gel to give fully deuteriated benzaldehyde-*d*; no aldehyde proton absorption was detected by ^1H NMR analysis.

Registry No. **1a**, 70-11-1; **1b**, 532-27-4; **1c**, 450-95-3; **1d**, 99-73-0; **1e**, 2491-38-5; **1f**, 42330-10-9; **1g**, 3212-63-3; **1h**, 822-85-5; **1i**, 31236-94-9; **1j**, 76-29-9; **2a**, 51075-28-6; **2b**, 19261-37-1; **2c**, 51075-29-7; **2d**, 35066-22-9; **3a**, 5437-45-6; **3b**, 140-18-1; **3c**, 3017-53-6; **3d**, 81577-34-6; **3e**, 535-11-5; **3f**, 869-10-3; **4**, 5061-21-2; **5a**, 79-08-3; **5b**, 79-11-8; **5c**, 2623-82-7; **6**, 141-28-6; **7**, 7209-01-0; DMBI (X = 5-H), 3652-92-4; DMBI (X = 5-OMe), 105282-67-5; DMBI (X = 5-Me), 105282-68-6; DMBI (X = 5-I), 105282-69-7; DMBI (X = 5-NO_2), 14443-02-8; DMBI-2-*d* (X = 5–H), 105282-70-0; $PhCOCH_3$, 98-86-2; *p*-$BrC_6H_4COCH_3$, 99-90-1; *p*-$HOC_6H_4COCH_3$, 99-93-4; $(Pr)_2CO$, 123-19-3; $(i\text{-}Pr)_2CO$, 565-80-0; $PhCH_2CH_2CH_3$, 104-53-0; $PhCH(CH_3)CHO$, 93-53-8; $CH_3(CH_2)_6CHO$, 124-13-0; $PhCH_2OCOMe$, 140-11-4; $PhCH_2OCOEt$, 122-63-4; EtOCOEt, 105-37-3; $CH_3(CH_2)_6CO_2H$, 124-07-2; CH_3CO_2H, 64-19-7; PhCOCl, 98-88-4; *p*-$O_2NC_6H_4COCl$, 122-04-3; *p*-$MeOC_6H_4COCl$, 100-07-2; $CH_3(CH_2)_6COCl$, 111-64-8; PhCDO, 28106-59-4; *p*-$O_2NC_6H_4CHO$, 555-16-8; *p*-$MeOC_6H_4CHO$, 123-11-5; 1-methyl-2-phenylbenzothiazoline, 16192-33-9; 2-phenyl-3-methylbenzoxazoline, 16192-26-0; 2-phenylbenzimidazoline, 53088-00-9; 2-phenylbenzothiazoline, 31230-83-8; cyclohexanone, 108-94-1; cyclododecanone, 830-13-7; camphor, 76-22-2; dihydro-2-furanone, 96-48-0; cyclohexanecarbonyl chloride, 2719-27-9; cyclohexanecarboxaldehyde, 2043-61-0.

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An Enolized Sulfonamide Formed by Strong Hydrogen Bonding to Triphenylphosphine Oxide

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Compound I, 5-methyl-6-phenyl-1,2,3-oxathiazin-4(3*H*)-one 2,2-dioxide, exists in chloroform solution and in crystals grown from chloroform as an amide with NH···O=C intermolecular hydrogen bonds. In the presence of triphenylphosphine oxide [(TPP)O], I tautomerizes to an enol form and complexes with (TPP)O through a very strong hydrogen bond between the phosphoryl oxygen and the enol OH group. In solution and in the solid state the complex exhibits unusually low-frequency OH stretching bands in its infrared spectrum, consistent with the observed hydrogen-bond distance of 2.504 (3) Å [O(H)···O=P], determined from crystal structure analysis. The crystal structures of I and its complex with (TPP)O, II, and the infrared and NMR spectra of I and II are reported. Comparison of solution- and solid-state structures are made, and an analysis of the role of intermolecular hydrogen bonds in the formation of tautomers of I is given.

Hydrogen bonds can be used to orient molecules into predictable aggregate patterns in solution or in the solid state, analagous to the role of single bonds in determining the pattern of functional groups within molecules.[1] Being able to predict which of several possible intermolecular hydrogen bonds will form when multiple hydrogen bond acceptor and donor sites are present in a molecule is of fundamental importance to controlling the structure of molecular aggregates in solution and, ultimately, to determining the structure of nucleation sites for crystal growth.[2]

Usually the process of forming intermolecular hydrogen bonds does not involve intramolecular rearrangement of the complexing species, although conformational changes may be observed,[3] and bond lengths and angles will be altered near the hydrogen-bond site.[4] Benzamide, for

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