is therefore evident that the Afanas'ev equation underestimates whereas the Taft equation overestimates the polar component.

In this sence, the other two equations, YTJ and SL correlations, appear to be normal, and indeed the corresponding components in these two equations are approximately equal.

Inclusion of effects of substituent variation in the leaving group (Z) on the components of the DSP equations given in Table 2 however puts an end to this apparant similarity of the two equations. Now the YTJ equation shows anomalies in that resonance contributions vary in opposite to polar contributions for X = *p*-CH_3O and the resonance to polar ratios R for X = *m*-NO_2 are less than one. These and other types of anomalies were also found with the Taft and Afanas'ev equations when substituent variation in the leaving group is considered. The SL equation is the only one that behaves normally in every respects. Thus of the four major types of DSP correlations, we must regard the Swain-Lupton equation as the most reliable one for correlating substituent effects on rates for S_N2 reactions.

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A New Aldehyde Synthesis from Aliphatic Nitriles with Sodium Diethyldihydridoaluminate in the Presence of Diethylaluminum, 2,6-Di-t-Butylphenoxide

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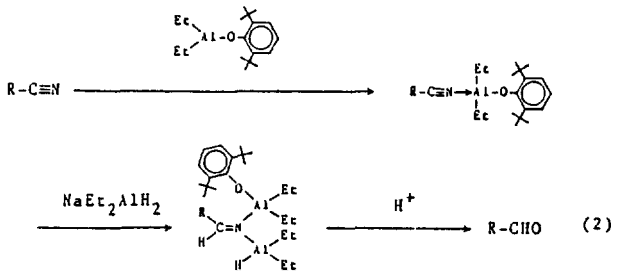
Reduction of nitriles to aldehydes is an important functional group transformation and consequently considerable effort has been expended devising methods for these conversions.[1,2] Such transformations generally take the form of partial reduction of a nitrile to an aldimine followed by hydrolysis of the aldimine to the corresponding aldehyde[3] (eq. 1).

$$R\text{-}C\equiv N \xrightarrow{H\text{-}M} R\text{-}CH=N\text{-}M \xrightarrow{H_2O} R\text{-}CHO \qquad (1)$$

Diisobutylaluminum hydride (DIBAH)[4], and lithium triethoxyaluminohydride (LTEAH)[5] are the two major hydride reducing agents for such transformations (both of which have only one hydride per molecule). In contrast to these hydride reagents, sodium diethyldihydridoaluminate (OMH-1) has two hydrides per molecule and was reported to reduce benzonitrile to benzaldehyde in 86% yield, whereas gives only 14% butyraldehyde from butyronitrile.

We tested several aliphatic nitriles with OMH-1, and the yields of aldehydes were constantly low, comparable to those reported with lithium aluminum hydride. However, it was very interesting to note that the yields of aldehydes increased tremendously from the primary nitrile (n-capronitrile; 10% conversion) to the secondary (isobutyronitriles; 57%) and tertiary (trimethylacetonitrile; 68%) nitriles. The steric effect of alkyl group on the cyano group is presumably interfering the second hydride attack. Since nitriles are known to form adducts with Lewis acids[6], it was felt that bulky Lewis acid-nitrile adduct might accept only one hydride from OMH-1, resulting a new aldehyde synthesis (eq. 2).



(2)

We have tested this possibility with diethylaluminum 2,6-di-*t*-butylphenoxide, which can be readily prepared from the reaction of triethylaluminum with 2,6-di-*t*-butylphenol. We have found that capronitrile reacts with diethylaluminum 2,6-di-*t*-butylphenoxide to form an adduct. Thus the characteristic band of coordinated nitrile group exhibited at 2295.0 cm^{-1} whereas the free nitrile showed at 2243.5 cm^{-1}. The reduction of this adduct with OMH-1 gave caproaldehyde in 90% yield whereas capronitrile itself gave only 10%. In order to test the generality of the reaction, we examined eight representative aliphatic nitriles and benzonitrile. The reactions were carried out in toluene at 0°C for half an hour in the presence of 1.5 equiv of the Lewis acid.

As shown in Table 1, the two secondary nitriles, isobutyronitrile and 2-methyloctanonitrile gave equally good results as capronitrile and trimethylacetonitrile, a tertiary nitrile, gave an even better yield (96%). Cyclopentane- and cyclohexanecarbonitrile also gave good results, however, cinnamonitrile gave a lower yield (68%) and phenylacetonitrile gave no aldehyde, similar to LTEAH.[5]

The reduction of capronitrile is described as a representative procedure. Triethylaluminum (3 mmol) in toluene was added dropwise to 3 m*l* of 2,6-di-*t*-butylphenol (3 mmol) in toluene with a good stirring at 0°C. During this operation, 72 mL of ethane gas was evolved, corresponding to 2.91 mmol. Stirring was continued at 0°C for 1 h, then 2 m*l* of capronitrile (2 mmol) in toluene was added dropwise at this temperature and then 0.51 m*l* of OMH-1 (1.1 mmol) was added to this solution. Further stirring was carried out at 0°C for 0.5 h. The reaction was quenched by the addition of 2 mL of water followed by 1 mL of 5 N-H_2SO_4. The aqueous layer was saturated with sodium chloride and the organic layer was separated. The organic layer was neutralized with a small amount of sodium bicarbonate, dried over sodium sulfate. The GLC analysis, using 5% Carbowax 20 M, showed 90% of caproaldehyde and trace amount of capronitrile.

For isolation of aldehyde, bisulfite procedure[13] was adopted and the aldehyde was regenerated from the bisulfite adduct with formaldehyde.[14] In a preparative run (50 mmol), the procedure was same as above until the separation of organic layer. After neutralization with a small amount of sodium bicarbonate, the organic layer was poured into 150 m*l* of saturated aqueous sodium bisulfite solution and 100 m*l* of tetrahydrofuran was added. The mixture was stirred for 2 h. At this time, the crystalline bisulfite adduct of caproaldehyde was apparent. The solution was cooled in an ice-water bath to insure complete crystallization of the adduct. The adduct was then collected by filtration and washed with 3×50 m*l* of pentane and dried. The adduct was placed in 100 m*l* of saturated aqueous magnesium sulfate solution and then 100 m*l* of pentane and 20 m*l* of 37% formaldehyde solution were added. The mixture was stirred for 2 h. The pentane layer was separated and dried with magnesium sulfate. The volatile materials were evaporated and the distillation of the crude product gave 3.87 g (77%) of pure caproaldehyde: bp 129°C (lit.[15] 131°C), n_d^{25} 1.4040 (lit.[15] n_D^{20} 1.4035).

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Table 1. Partial Reduction of Aliphatic Nitriles to Aldehydes with Sodium Diethyldihydridoaluminate (OMH-1) in the Presence of Diethylaluminum 2,6-Di-*t*-butylphenoxide and Comparisons with the Reductions with OMH-1, Lithium Aluminum Hydride, Diisobutylaluminum Hydride and Lithium Triethoxyaluminohydride

Nitriles	Aldehydes, %				
	Lewis Acid+OMH-1[a]	OMH-1[b]	$LiAlH_4$[c]	DIBAH[d]	LTEAH[e]
n-Capro-	90 (77)[f]	10		87	69
Isobutyro-	93	57	59	85[i]	81
2-Methyloctano-	90	51			
Trimethylaceto-	96	68	68	80[j]	89
Cyclopentanecarbo-	91	37			
Cyclohexanecarbo-	84	13	60[k]		76
Cinnamo-	68	0		85[k]	61
Phenylaceto-	0	0		50	0
Benzo-	93	86[g]		86	96

[a]To 3 mmols of Lewis acid (diethylaluminum 2,6-di-*t*-butylphenoxide), 2 mmols of nitrile was added. After 0.5 h at 0°C, 1.1 mmol of OMH-1 was added and reacted for 0.5 h at 0°C in toluene. [b]1.1 mmol of OMH-1 was added to 2 mmols of nitrile and reacted for 0.5 h at 0°C in toluene. [c]*Ref.* 8. [d]*Ref.* 4. [e]*Ref.* 5. [f]Yield is based on the analytically pure caproaldehyde after distillation of regenerated product from busulfite adduct with formaldehyde. [g]*Ref.* 7. [h]*Ref.* 9. [i,j,k]Yields of 3(R)-[2(R)-isopropenyl-1(R)-cyclopentyl] butanal, 1-(3,4-methylenedioxyphenyl)-cyclopropanecarboxaldehyde and 3,3-dimethyl-$\Delta^{1,4}$-cyclohexaneacetaldehyde from the corresponding nitriles. *Ref.* 10, 11, and 12.

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Synthetic Studies on Penems and Carbapenems (II)[1]. Substitution of the Acetoxy Group in 4-Acetoxyazetidin-2-one with Various Nucleophiles

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The availability and ease with which the acetoxy group could be exchanged with other groups has made 4-acetoxyazetidin-2-one derivatives[1-3] as attractive starting materials for construction of biologically interesting bicyclic systems like penems[4], carbapenems[5] and others[6]. Much attention has been focused on carbon-carbon bond formation at the 4-position of β-lactam compounds and many reports[5,7] have dealt with this carbon-extension reaction; however, there are limitations on the functionalities the extending units may contain. For example, the replacement of the acetoxy group in 4-acetoxyazetidin-2-one analogs by an enolizable carbon atom is fraught with difficulty; generally, the yields of β-lactam compounds having a 2-oxoalkyl group at C-4 position, which are obtained from 4-acetoxyazetidin-2-one by reaction with enolate anions, are poor[5,8,9] presumably due to the ring fragmentation[7]. The stability of a 4-substituted β-lactam compound seems to be very much depend on the availability of the non-bonding electron pair existing at the α-position of the substituent group; the non-bonding electron pair should induce decomposition of the β-lactam ring by breakage of the bond between C-4 and N-1. In this paper, we report new methods for formation of carbon-carbon, carbon-phosphorus, carbon-sulfur, carbon-oxygen, and carbon-nitrogen bonds at the C-4 position of 4-acetoxyazetidin-2-one by nucleophilic substitution of the 4-acetoxy group with various nucleophiles.

4-Acetoxyazetidin-2-one (**1**) was obtained by reaction of chlorosulfonylisocyanate (CSI) with vinyl acetate. Generally, CSI has been shown to react with a variety of olefinic substances through $[_2\pi_s + _2\pi_s]$ cycloaddition reactions to give N-chlorosulfonyl-β-lactams[10,11]. The N-chlorosulfonyl group of the addition product can be reduced to N-H by (a) benzene-2-mercaptopyridine in acetone at −30°C[12,13], (b) potassium iodide in aqueous sodium hydroxide[12,13], and (c) Raney nickel in ethanol[12,13] followed by aqueous hydrolysis[12] with 4N KOH in acetone[13] or saturated methanolic KOH[15]. We modified the Durst and O'Sullivans' method[16] to obtain 4-acetoxyazetidin-2-one in 39% yield, in which CSI was stirred with vinyl acetate at 10°C for 30 min to give the desired CSI addition product, and the N-chlorosulfonyl group was reduced by pouring the reaction mixture into a cold aqueous solution (0-5°C), with crushed ice, of sodium sulfite, sodium bicarbonate and potassium iodide with vigorous stirring.

Recent development of new carbapenem antibiotics, including thienamycin, demand new methods for formation of a new carbon-carbon bond by substitution of the acetoxy group of 4-acetoxyazetidin-2-one derivatives with carbanions. Treatment of 4-acetoxyazetidin-2-one(**1**) with various carbanion nucleophiles did not give good yields of substituted azetidinone products, especially with those of enolizable ones. Several special methods were developed for formation of new carbon-carbon bonds by substitution of the acetoxy group or the phenylsulfonyl group of 4-acetoxy- or 4-phenylsulfonylazetidin-2-one by reaction with silyl enol ether in the presence of Lewis acid catalyst[17,18] or by reaction with monoorganocuprate[19]. For substitution of the acetoxy group in 4-acetoxyazetidin-2-one with alkyl carbanions (Scheme 1), we examined several lithium organocuprates obtained by mixing copper iodide in various ratios to the alkyllithium (CuI-