chloroform and acetone, respectively, and the aflatoxins and averufin were separated and purified by the tlc systems described above. The parent strain culture was found to indeed produce averufin though in small quantity (1 μmol/l. as compared to 43 μmol/l. of aflatoxin B_1). To ascertain the coexistence of the two metabolites, a resting cell culture of the parent wild type strain was incubated with [1-^{14}C]acetate for 10 hr, and 60 μg of unlabeled pure averufin was added to each flask as carrier. After extraction and purification, 1.32 and 0.41% of the labels in [1-^{14}C]acetate were found in the recovered aflatoxin B_1 and averufin, respectively. The relative specific radioactivity, or RIC, of aflatoxin B_1 so obtained was only one-tenth that of the averufin, indicating that averufin is subject to less extent of isotope dilution and hence is an intermediate in the pathway leading from acetate to aflatoxin B_1.

Averufin has been proposed by Thomas[9] as an intermediate in a hypothetical pathway for the biosynthesis of aflatoxin from acetate, involving sterigmatocystin. This pathway, however, does not account for the distribution of labels in the aflatoxin B_1 molecule biosynthesized from [^{14}C]acetate.[1] The biosynthetic scheme proposed by Biollaz, *et al.*,[3] based upon the labeling pattern in turn does not imply involvement of averufin. Therefore, a pathway different from either of the previously proposed pathways must actually be used in the biosynthesis of aflatoxin B_1.

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[9] R. Thomas, "Biogenesis of Antibiotic Substances," Z. Vanek and Z. Hestalek, Ed., Academic Press, New York, N. Y., 1965, p 155.

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Lithium Triethylborohydride. An Exceptionally Powerful Nucleophile in Displacement Reactions with Organic Halides

Sir:

Lithium triethylborohydride possesses enormous nucleophilic power in SN2 displacement reactions with alkyl and cycloalkyl halides (eq 1). Kinetic studies

$$\mathrm{LiEt_3BH + RX \longrightarrow RH + Et_3B + LiX} \tag{1}$$

reveal that the reagent is considerably more powerful than nucleophiles such as thiophenoxide and alkyl mercaptide, previously considered to be the most powerful simple nucleophiles available for SN2 displacements[1] (eq 2).

$$\begin{aligned} k_{\mathrm{Et_3BH^-}}/k_{\mathrm{C_6H_5S^-}} &= 20 \\ k_{\mathrm{Et_3BH^-}}/k_{\mathrm{NO_3^-}} &= 10^7 \end{aligned} \tag{2}$$

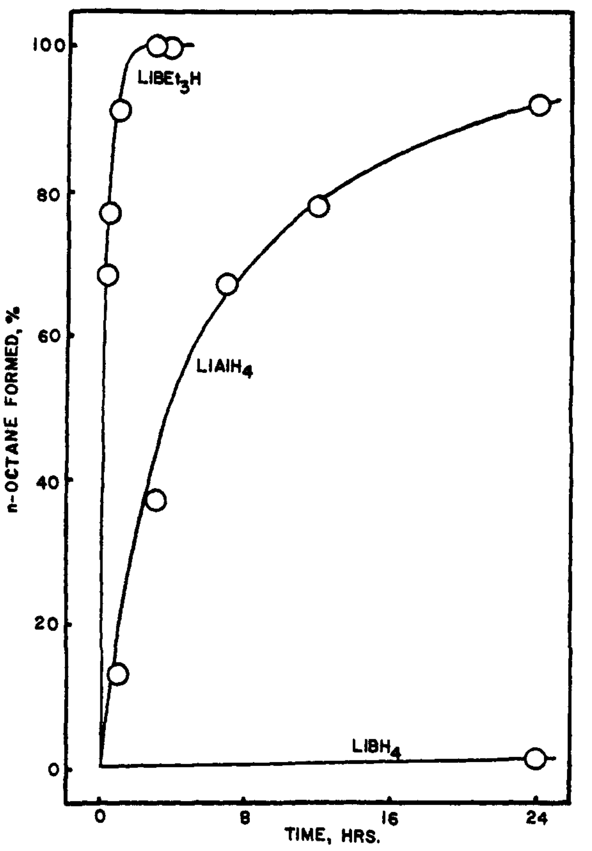

Figure 1. Rates of reduction of *n*-octyl chloride (0.25 *M*) with representative complex metal hydrides (0.5 *M*) in tetrahydrofuran at 25°.

Addition of triethylborane to THF solutions of lithium tri-*tert*-butoxyaluminohydride (LTBA) results in a rapid disappearance of hydride and the concurrent formation of 1-butanol.[2] It was established that this reductive cleavage proceeds through the formation of lithium triethylborohydride[3] and monomeric aluminum *tert*-butoxide.[4]

In the course of these investigations, certain observations suggested that lithium triethylborohydride must be an exceptionally powerful nucleophile. To test this possibility, lithium triethylborohydride was prepared in THF (eq 3) and treated with *n*-octyl chloride. Com-

$$\mathrm{LiH + BEt_3 \xrightarrow[25^\circ]{THF} LiEt_3BH} \tag{3}$$

parison of the rate of reduction with lithium aluminum hydride and lithium borohydride revealed the marked superiority of the new reagent (Figure 1).

These results persuaded us to undertake a quantitative comparison of the rates of reaction of lithium triethylborohydride and sodium thiophenoxide with *n*-octyl chloride under identical conditions. The results revealed that the reaction involving lithium triethylborohydride is far faster (Table I).

From these results, we calculated the nucleophilic reactivity of other nucleophiles using Streitwieser's nucleophilicity data:[1] $\mathrm{Et_3BH^-}$, 9,400,000; n-$\mathrm{C_4H_9S^-}$,

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[1] For a detailed review and discussions on the subject of nucleophilic reactivity see: (a) J. F. Bunnett, *Annu. Rev. Phys. Chem.*, **14**, 271 (1963); (b) A. Streitwieser, Jr., "Solvolytic Displacement Reactions," McGraw-Hill, New York, N. Y., 1962, pp 9-11; (c) J. O. Edwards and R. G. Pearson, *J. Amer. Chem. Soc.*, **84**, 16 (1962); (d) R. G. Pearson, H. Sobel, and J. Songstad, *ibid.*, **90**, 319 (1968).

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[4] H. C. Brown and S. Krishnamurthy, *J. Chem. Soc., Chem. Commun.*, 868 (1972).

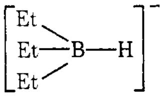
Table I. Second-Order Rate Constants for the Reaction of *n*-Octyl Chloride with Various Nucleophiles in Tetrahydrofuran at 25.00 ± 0.01° [a]

Reagent	Nucleophile	Rate constant k_2, l. mol^{-1} min^{-1}
Lithium triethylborohydride	Et_3BH^-	2.02×10^{-1}
Sodium thiophenoxide	$C_6H_5S^-$	1.05×10^{-2}
Lithium aluminum hydride	AlH_4^-	5.0×10^{-3}
Lithium borohydride	BH_4^-	2.11×10^{-5}

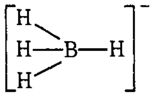
[a] All of the reactions were carried out in a thermostated bath under dry nitrogen and kinetics were followed by measuring the disappearance of *n*-octyl chloride or the appearance of *n*-octane with time by glpc using an internal standard. All of the reactions gave excellent second-order plots.

680,000; $C_6H_5S^-$, 470,000; AlH_4^-, 230,000; I^-, 3,700; $C_2H_5O^-$, 1,000; BH_4^-, 940; Br^-, 500; $C_6H_5O^-$, 400; NO_3^- 1.00. These results reveal that triethylborohydride is the most powerful nucleophile for SN2 displacement reactions now available.

Thus, replacement of three of the four hydrogen atoms in $LiBH_4$ enhances the nucleophilicity by a factor of 10,000! The enormously enhanced nucleophilic power of $LiEt_3BH$ presumably arises from the greater ease of transferring hydride ion from the weaker Lewis acid, triethylborane (I), than from the stronger Lewis acid, borane (II).



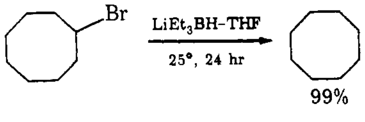
I



II

Encouraged by these results, we treated representative alkyl halides with this reagent at 25° in order to establish its effectiveness as a probe in nucleophilic reactions, including in the study derivatives such as neopentyl,[5] cyclohexyl, cyclooctyl, and *exo*-norbornyl bromides, structures which are highly resistant to SN2 displacements. Allylic and benzylic bromides are reduced almost instantly. Simple primary alkyl bromides, such as *n*-octyl bromide, are completely reduced in 2 min. Even the usually inert neopentyl bromide is reduced at a reasonable rate at 25°; under reflux the reaction is complete in 3 hr. A 96% yield of neopentane was obtained, free of isomeric alkanes.

With secondary cycloalkyl bromides the reactivity follows the order cyclopentyl > acyclic > cycloheptyl > cyclooctyl > cyclohexyl > *exo*-2-norbornyl, and all of these derivatives, including *exo*-2-bromonorbornane, which is highly resistant to SN2 substitution, can be reduced quantitatively to the corresponding alkanes[6,7] (eq 4 and 5).

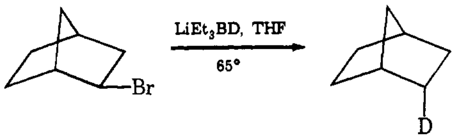


(4)

The reaction of tertiary alkyl bromides is slow and results predominantly in elimination.

Unlike lithium aluminum hydride,[8] the reagent is inert toward aryl halides and should therefore be valuable for the reduction of alkyl halides without simultaneous attack on aromatic halogen present in the system.

The corresponding deuterium derivative is easily synthesized from lithium deuteride (eq 3). Consequently, this provides a simple means of introducing deuterium into systems with clean stereochemical inversion at the substitution center[7] (eq 5).

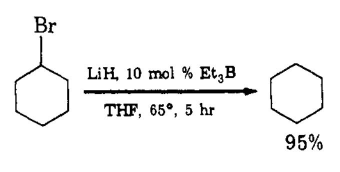


(5)

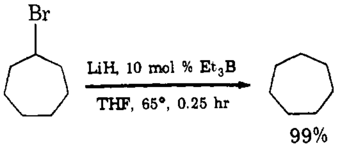
The product was identified as the pure endo *d* isomer by measuring the decrease in the intensity of the nmr signal (spectral measurements were carried out in Varian T-60 and Varian XL-100 spectrometers) at δ 1.13 (endo protons) using the intensity of bridgehead tertiary hydrogens (δ 2.28) as the standard.[7] While the relative intensity of exo protons (δ 1.43) to the bridgehead protons remained unchanged (4:2) as in the case of norbornane, the intensity of the signal due to the endo protons at δ 1.13 diminished by an amount corresponding to one proton in the deuterated product.

The following procedure for the reduction of cycloheptyl bromide is representative. An oven-dried 100-ml flask equipped with a side arm fitted with a Silicone rubber stopple, a magnetic stirring bar, and a reflux condenser connected to a mercury bubbler was cooled to room temperature under nitrogen. The flask was immersed in a water bath at 25°; then 10 ml of a 1.0 *M* solution in THF of $LiEt_3BH$ (10 mmol) was injected into the reaction flask, followed by 5 ml of a 1.0 *M* solution in THF of *n*-nonane (5 mmol) to serve as internal standard, followed by 5 ml of a 1.0 *M* solution in THF of cycloheptyl bromide (5 mmol). The reaction mixture was stirred vigorously. After 1 hr, 1 ml of the reaction mixture was withdrawn by a syringe, quenched with water, extracted with ether, and analyzed by glpc. The analysis revealed the presence of 75% cycloheptane. In 3 hr, a 99% yield of cycloheptane was realized.

The reactions (eq 1 and 3) suggest the possibility of achieving the reduction of alkyl halides with lithium hydride in the presence of a catalytic quantity of triethylborane. Indeed this proved to be quite feasible (eq 6 and 7).



(6)



(7)

In conclusion, it should be pointed out that lithium triethylborohydride possesses major advantages over other nucleophiles as a probe in the displacement reac-

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(5) Reductions of neopentyl halides or sulfonates are exceedingly difficult and frequently result in failure by conventional methods: see J. A. Marshall and R. A. Ryden, *J. Org. Chem.*, **36**, 594 (1971).

(6) S. J. Cristol and G. D. Brindell, *J. Amer. Chem. Soc.*, **76**, 5699 (1954).

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(8) H. C. Brown and S. Krishnamurthy, *J. Org. Chem.*, **34**, 3918 (1969).

tions. First, it possesses superior nucleophilic properties; second, it is easily prepared and the THF solutions of this reagent are stable indefinitely; and third, the products of the displacement reaction are simple alkanes and readily analyzed by simple techniques. Even more exciting is the discovery, after 25 years, of a nucleophilic reducing agent for alkyl halides far superior to lithium aluminum hydride. We have synthesized a wide range of trialkylborohydrides and all prove to be exceptionally active nucleophiles. Moreover, these derivatives possess extremely attractive properties for other reductions, such as the reduction of cyclic ketones with enzyme-like stereoselectivity.[9-11] We are currently exploring the utility of these new reagents in organic syntheses.[12]

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(11) E. J. Corey and R. K. Varma, *ibid.*, **93**, 7319 (1971).

(12) Research in progress with Dr. S. Krishnamurthy and S. C. Kim.

(13) Postdoctoral Research Associate on Grant No. DA 31-124 ARO(D) 453 supported by the U. S. Army Research Office (Durham).

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Absorption and Exciplex Emission Spectra of the Naphthalene–Anthracene Sandwich Pair

Sir:

The formation of fluorescent exciplexes by singlet excited aromatic hydrocarbons and other species which are usually easily classified as electron donors or acceptors is a well-known phenomenon. Such exciplexes are stabilized by charge-transfer interactions in contrast to the homopolar excimers which derive a considerable portion of their stabilization from exciton interaction. We have been able to prepare the anthracene–naphthalene sandwich pair in a rigid matrix, and we report the first study of a sandwich pair of two completely different aromatic hydrocarbons. This species exhibits exciplex fluorescence even though exciton interaction should be negligible and charge-transfer should not be particularly favorable. The absorption spectrum of the pair shows weak interaction in the ground-state geometry.

The discovery of the reversible intramolecular photoaddition of naphthalene to anthracene in 1-(9-anthryl)-3-(1-naphthyl)propane[1] suggested the possibility of generating the naphthalene–anthracene sandwich pair *via* the photodissociation of the adduct in a rigid matrix at low temperature. This has proved to be a useful technique for the study of hydrocarbon sandwich pairs. The adduct was prepared as a 2×10^{-5} *M* solution in methylcyclohexane, which was concentrated approximately threefold in order that the absorption spectrum could be measured easily in a 3-mm tube. It was broken by irradiation with 254-nm Hg light at 77°K in the usual manner.

The absorption spectra of the naphthalene–anthracent sandwich pair and the separated moieties formed after thawing and refreezing are given in Figure 1. The characteristic anthracene absorption system in the 320–380-nm region, which is not shown, was virtually the same in both configurations, and, because of the difficulties in measuring relatively weak absorption with high accuracy in our technique, no meaning is attributed to the slight differences.

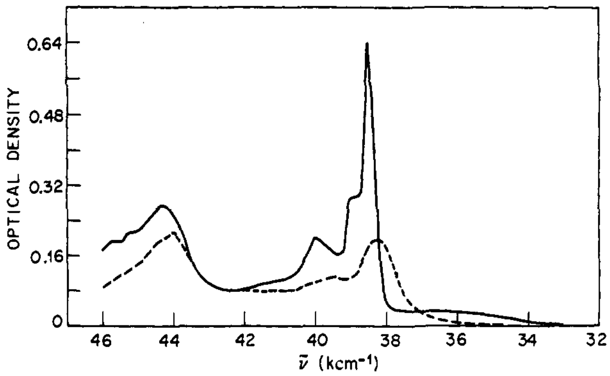

Figure 1. The absorption spectrum of the naphthalene–anthracene sandwich pair formed by photodissociation of the photoadduct (broken line) and the separated moieties obtained after thawing and refreezing (solid line).

Anthracene has an intense (ϵ $1.6 \times 10^5, f = 2.3$) long-axis polarized transition at 38.3 kcm^{-1}; naphthalene has a strong (ϵ $1.3 \times 10^5, f = 1.7$) long-axis polarized transition at 44.2 kcm^{-1}.[2] There does not appear to be any strong interaction between these two transitions in the sandwich pair, presumably a consequence of the substantial energy gap. This may be contrasted with the single transition observed[3] for the anthracene–9,10-dichloroanthracene pair in the same region where the individual transitions are separated by 1 kcm^{-1}. In the present case each absorption has been shifted to lower energy as might be expected to result from having a neighboring molecule of substantial polarizability in the proper orientation for interaction.[4] There is also considerable hypochromism, a more sensitive measure of interaction than a shift in energy. The corresponding effects on the much weaker first transition of anthracene would be much smaller.

The most interesting feature of the naphthalene–anthracene sandwich pair is its fluorescence spectrum. This is shown in Figure 2 along with the normal fluorescence of the methylanthracene moiety obtained after thawing and refreezing. The sandwich pair fluorescence is clearly not simply derived from the absorption spectrum, and it can be identified as an exciplex fluorescence. There appears to be a small amount of structure, whose frequency is about 1.4 kcm^{-1}, superimposed on a typical exciplex band. This is the characteristic vibrational frequency in the anthracene spectrum, but we cannot be sure that the structure is real.

The fluorescence maximum of the sandwich pair lies at 22.2 kcm^{-1}, 3.2 kcm^{-1} to the red of the 9-methylanthracene 0–0 band. This is much less than the normal 5.5-kcm^{-1} shift for the 9-methylanthracene excimer.[3] The excimer derived from 1,3-bis(1-naphthyl)propane is shifted 7 kcm^{-1} to the red of the mono-

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