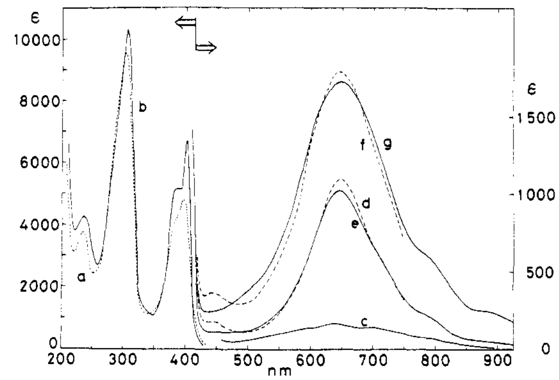

Figure 3. Absorption spectrum of 1-ethyl-4-methoxycarbonylpyridinyl in MTHF: (a) 5.5×10^{-3} *M*, at room temperature; (b, c) 6.9×10^{-3} *M*, at 77°K; (d) 2.9×10^{-2} *M*, at 77°K before irradiation; (e) after sufficient irradiation of d with a W-lamp; (f) 6.0×10^{-2} *M*, at 77°K before irradiation; (g) after irradiation of f.

pends on the radical concentration, the band is characteristic of the radical association and is presumably assigned to the second charge-transfer band in consideration of the appearance of two charge-transfer bands for some pyridinium salts.[5] The first band is almost certainly near 1.9 eV. It is thus assumed that the transformation of A_S into B_T occurred through the charge-transfer excitation of A_S, followed by the intersystem crossing to the triplet configuration. This sequence may include the dynamic reorientation of the radicals in a dimer to the positions capable of triplet transitions.

Spectral change seen in Figure 1 and the concentration dependences shown in Figure 2 may be explained by the transformation of A_S into B_T. However, the change in Figure 3 is different in intensity from that of Figure 1 for the region of 500–750 nm. This difference between two radicals will be caused by the fact that the absorptions in the 500–900-nm region originate in several kinds of species, such as radical monomer and singlet and triplet radical dimers. The monomer has an absorption due to the lowest excitation, $\Psi_g \rightarrow \Psi_1$,[2] in this region, which corresponds to the broad and weak absorption of the radical at room temperature.[6] The dimers would show the similar absorption due to the local excitation in a dimer. The radical association clearly leads to the appearance of other absorptions which are dependent on the radical concentration, as seen in Figure 2. It is thus difficult to interpret in detail the absorption intensity and the assignment for the 500–900-nm region. This region also bears relation to the π-mer formation[7] and the appearance of two charge-transfer bands demonstrated for some pyridinium salts.[5]

Further study on the transformation in the glassy state is in progress for the associations of analogous radicals.

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(4) When the radical was purified carefully by distillation, cooling of the radical solution did not bring about the significant change of the spectrum for the region shorter than 400 nm (Figure 1a and 1b), and the absorption intensity in 650-nm region at 77°K is smaller than that reported previously.[2] Addition of a metal halide to the solution sometimes results in an increase of the intensity at around 610 nm with the spectral change in the shorter region. For example, λ_{max} (ϵ) for **1a** in MTHF with lithium iodide at 77°K is 618 nm (4800) at the concentration of 4.7×10^{-3} *M*. This is explained by the complex formation of **1a** with lithium iodide.[1]
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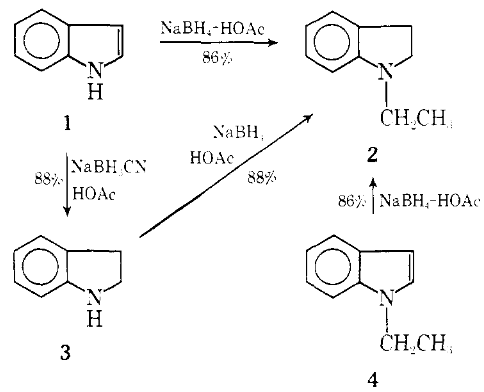
Reactions of Sodium Borohydride in Acidic Media. I. Reduction of Indoles and Alkylation of Aromatic Amines with Carboxylic Acids[1]

Sir:

We wish to report that sodium borohydride ($NaBH_4$) in neat carboxylic acids sequentially reduces the indole double bond and alkylates the nitrogen atom to give *N*-alkylindolines, *e.g.*, **1** → **2**, and that this combination of reagents conveniently alkylates primary and secondary aromatic amines, *e.g.*, **3** → **2** (Scheme I).

Scheme I. Transformations in Acetic Acid



Although the reduction of indoles to indolines has received considerable attention,[2] there is no general, efficient procedure for this transformation. Encouraged by the tendency of the indole ring to protonate at the 3-position[3,4] and by the observations that enamines can be reduced by $NaBH_4$ in acetic acid-tetrahydrofuran (HOAc-THF)[5] and sodium cyanoborohydride ($NaBH_3CN$),[6] we have examined the behavior of indoles with $NaBH_4$ in neat carboxylic acids.

Quite unexpectedly, the reaction of indole (**1**) with $NaBH_4$ in glacial HOAc gives *N*-ethylindoline (**2**) in 86% yield. Likewise, the reactions of indoline (**3**) and *N*-ethylindole (**4**) with $NaBH_4$-HOAc give **2** in high yield.

This unprecedented reduction–alkylation of indoles and reduction of *N*-alkylindoles[7] with $NaBH_4$ in liquid carboxylic acids appears to be a general transformation (Table I). However, the stronger acid, formic, produces indole dimers and other products in addition to *N*-methylindoline. Interestingly, the reaction of **1** with $NaBH_4$ in trifluoroacetic acid (CF_3CO_2H) gives indoline (**3**), the product of reduction without alkylation, in low yield. The yield of **3** can be increased to 88% when **1** is treated with $NaBH_3CN$-HOAc (Table I). This latter reaction permits a very convenient synthesis of **3**.

We believe that the reaction of **1** → **2** involves 3-protonation of indole,[4] followed by reduction of the resulting indolenium ion to give **3**,[8] which is subsequently alkylated (*vide infra*). The reduction of the indoloquinolizidine alkaloid **5**

Table I. Reaction of Indoles with $NaBH_4$–RCO_2H[a]

Substrate	Carboxylic acid	Product[b]	Yield,[c] %
1	HOAc	*N*-Ethylindoline	86
	HCO_2H	*N*-Methylindoline	53
	$CH_3CH_2CO_2H$	*N*-*n*-Propylindoline	69
	$(CH_3)_2CHCO_2H$	*N*-Isobutylindoline	49
	CF_3CO_2H	Indoline[d]	36
	HOAc–$NaBH_3CN$	Indoline	88
2-Methylindole	HOAc	1-Ethyl-2-methylindoline	84
3-Methylindole		1-Ethyl-3-methylindoline	45
2,3-Dimethylindole		1-Ethyl-2,3-dimethylindoline	60
Tetrahydrocarbazole		*N*-Ethylhexahydrocarbazole	77
7-Methylindole		1-Ethyl-7-methylindoline	90
N-Methylindole		*N*-Methylindoline	86
N-Ethylindole		*N*-Ethylindoline	86
1,2-Dimethylindole		1,2-Dimethylindoline	84

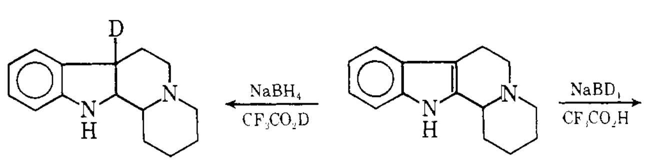
[a] Conditions are typically 0.005–0.02 mol of indole dissolved in 30–150 ml of dry carboxylic acid at 15–20° to which is slowly added 0.02–0.2 mol of $NaBH_4$ pellets (Alfa Inorganics, Inc., Beverly, Mass.). A brief heating period at 50–60° is sometimes necessary to complete the reaction. Reactions can be monitored by tlc or uv. [b] Identified by comparison with authentic material or by conversion to known derivatives (picrate, methiodide). All products exhibited satisfactory ir, nmr, and uv spectra. [c] Yields are for pure distilled material. In most cases starting indole was the only other material present in the reaction mixture. The reactions have not been optimized. [d] A small amount of *N*-trifluoroethylindoline is also formed.

Table II. Reaction of Aromatic Amines with $NaBH_4$–RCO_2H[a]

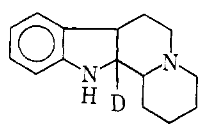
Substrate	Carboxylic acid	Product[b]	Yield,[c] %
Aniline	HOAc	N-Ethylaniline	88
	HOAc (50–60°)	*N*,*N*-Diethylaniline	74
	HOAc–Me_2CO	*N*-Isopropylaniline	68
	HOAc–Me_2CO (50–60°)	*N*-Ethyl-*N*-isopropylaniline	79
	HOAc–PhCHO (50–60°)[d]	*N*-Benzyl-*N*-ethylaniline	80
	$(CH_3)_3CCO_2H$[e]	*N*-Neopentylaniline	80
N-Methylaniline	HOAc	*N*-Ethyl-*N*-methylaniline	72
	HOAc–Me_2CO	*N*-Isopropyl-*N*-methylaniline	78
	HCO_2H	*N*,*N*-Dimethylaniline	77
	HOAc–$(HCHO)_n$–THF	*N*,*N*-Dimethylaniline	59
	$CH_3CH_2CO_2H$	*N*-Methyl-*N*-propylaniline	83
N-Ethylaniline	$CH_3CH_2CO_2H$	*N*-Ethyl-*N*-propylaniline	70
N-Isopropylaniline	HOAc	*N*-Ethyl-*N*-isopropylaniline	69
Indoline	HOAc	*N*-Ethylindoline	88
	CF_3CO_2H	*N*-Trifluoroethylindoline[f]	7[g]
Diphenylamine	HOAc	*N*-Ethyldiphenylamine	80
Carbazole	HOAc	*N*-Ethylcarbazole	92
5*H*-Dibenz[*b*,*f*]azepine	HOAc	9-Ethyl-5*H*-dibenz[*b*,*f*]azepine	72

[a–c] See corresponding footnotes in Table I. [d] *N*-Benzylaniline could be isolated from the 20° reaction. [e] This reaction was also run with diglyme as a cosolvent. [f] Indoline was recovered in 51% distilled yield. [g] From the pot residue there was isolated in 34% yield an indoline dimer containing three trifluoroethyl groups.

with $NaBH_4$–CF_3CO_2H proceeds without alkylation (72%) and the deuteration experiments, **5** → **6** and **5** → **7**, are in accord with our suggested mechanism.



6 **5**



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The combination $NaBH_4$–RCO_2H also provides for the facile alkylation of a variety of primary and secondary aromatic amines[9] (*e.g.*, **3** → **2**), and the reaction can be controlled to give mono- or dialkylation of primary amines. Thus, aniline with $NaBH_4$–HOAc at 20° gives *N*-ethylaniline, and further reaction at 60° gives *N*,*N*-diethylaniline (Table II).

This alkylation method is extended by our observation that aldehydes and especially ketones are reduced to alcohols relatively slowly by $NaBH_4$–RCO_2H,[10] so that unsymmetrical tertiary amines can be prepared from primary amines in one flask. Thus, aniline with $NaBH_4$–HOAc–acetone gives either *N*-isopropylaniline or *N*-ethyl-*N*-isopropylaniline, depending on the temperature (Table II). This versatility is not available with previous methods for reductive amination[6,11] of aldehydes and ketones (H_2,[11a,b] HCO_2H,[11c,d] $NaBH_3CN$,[6,11e] $NaBH_4$,[11f,g] $Fe(CO)_5$[11h]).

We view the amine alkylation as a stepwise process: (1) reduction of carboxylic acid to aldehyde[12] (or aldehyde equivalent), perhaps *via* one or more acyloxyborohydride species[13] and intra- or intermolecular hydride reduction of the carbonyl group; (2) reaction of the aldehyde with amine to form an iminium ion; and (3) hydride reduction[14] of the iminium ion to product amine.

Although amides are side products in some cases, they are very clearly not obligatory intermediates in the alkylation reaction. Thus, *N*-acetylindoline and *N*-acetylindole are recovered in 67 and 82% yield, respectively, after treatment with $NaBH_4$–HOAc, under conditions which convert indoline completely into *N*-ethylindoline. Likewise, it seems unlikely that diborane[7] is the reducing agent in the reaction, since externally generated gaseous diborane bubbled into amine–HOAc gives clean acylation and *not* alkylation of the amine.[15]

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(9) We have also been able to alkylate several aliphatic amines with $NaBH_4$/RCO_2H (*e.g.*, cyclohexylamine, benzylamine, dibenzylamine, piperidine, pyrrolidine) as part of a study which will be reported separately.
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(18) National Defense Education Act Predoctoral Fellow, 1968–1970.

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Stereochemistry of the Oxythallation of 1,2-Cyclononadiene

Sir:

Although a great many studies on the mechanism of the oxymercuration reaction have been disclosed,[1] there have been comparatively few studies on the analogous oxythallation reaction. The oxythallation reaction with alkenes has been shown to have many similarities to the oxymercuration reaction.[2] It has been suggested that rearrangement of a π complex to a σ-bonded oxythallation adduct is rate limiting.[2a] With Tl(III) acetate in aqueous acetic acid, the reaction was shown to be first order in alkene and thallic ion.[2a] A correlation of the rate of oxidation of alkenes by Tl^{3+} with Brown's σ^+ values ($\rho^+ = 2.2$)[2b] and Taft's σ^* values ($\rho^* = -3.2$)[2c] suggests that there is a high degree of positive charge delocalization in the transition state. In the latter study no kinetic evidence for a thallinium ion intermediate was found.

The most notable difference between the two oxymetalation reactions is the lack of solvolytic stability of the carbon–thallium bond resulting in dethallation of the organothallium intermediates. In fact, only a few oxythallation adducts of olefins have been isolated. The oxythallation products of styrene[3] and isobutylene[4] suggested that the reaction proceeds in the Markownikov sense. Because of the ease of heterolysis of the C–Tl bond, conclusive evidence for the stereochemistry of this electrophilic addition reaction is still lacking. Norbornene and norbornadiene have been shown to afford exo cis adducts on acetoxythallation.[5] An anti mode of addition to 4-*tert*-butylcyclohexene has been inferred on the basis of indirect evidence.[6]

We chose 1,2-cyclononadiene (**1**)[7] as a model compound to elucidate the stereochemistry of oxythallation since the vinyl thallium adducts[8] are readily isolated and characterized. Solvolysis of the C–Tl bond in **4** would afford a relatively unstable vinyl cation. This study also affords a direct comparison with the oxymercuration of **1** which has been thoroughly investigated.[9,10] The mechanism of the oxythallation of **1** is of particular interest since the oxymercuration of this cyclic allene proceeds by an anti mechanism[10] while the acetoxyplumbation occurs in a syn fashion.[10] We now report that oxythallation of optically active (**1**)[7] affords optically active products by an anti addition.

Treatment of **1** with an equivalent of thallic acetate in glacial acetic acid afforded the oxythallation adduct **4a** (84%).[11] Reduction of **4a** with basic $NaBH_4$ afforded *cis*-3-acetoxycyclononene (**5a**) (61%) that was identical in every respect to an authentic sample prepared by the acetoxymercuration–demercuration[10] of **1**. Acetoxythallation of optically active **1**, $[\alpha]^{25}D$ −15.6° afforded **4a** that had $[\alpha]^{25}D$ *ca.* −0.5° which on reduction with $NaBH_4$ afforded **5a**, $[\alpha]^{25}D$ +0.6°. The reaction of **1** with $Tl(OAc)_3$ in methanol also afforded a stable methoxythallation adduct **4b**[12] (76%). Demetalation with $NaBH_4$ gave *cis*-3-methoxycyclononene (**5b**)[10] (72%). The position of the diacetatothallium moiety was further established by treatment of **4b** with Br_2 in CCl_4 affording *cis*-2-bromo-3-methoxycyclononene (**6**)[10] (82%). Methoxy- and ethoxythallation–dethallation of optically active **1** also afforded optically active allylic ethers (*S*)-(+)-**5** (Table I).

The isolation of an optically active product from these reactions establishes that the planar allylic cation **3** cannot be the sole precursor to **4**. Thus, bridging due to π-complex formation is sufficient to prevent complete carbon–carbon bond rotation affording **3**. The oxythallation of (*S*)-(−)-1,2-cyclononadiene[10,13] to afford (*S*)-(+)-3-acetoxy- and alkoxycyclononene[14] must proceed by an anti mode of addition. Our data also show that the relative stereospecificity of the oxythallation reaction is comparable to that of the anti oxymercuration reaction but is considerably less than that observed for the syn- acetoxyplumbation of **1**.[15] The optical purity of **5b** and **5c** was further reduced when $Tl(NO_3)_3$ was used (Table I).[16]

We have also established that the oxythallation adducts **4b** and **4c** (X = OAc or NO_3) are not formed reversibly from either **2** or **3**. Thus, treatment of **4b** in EtOH solvent or **4c** in CH_3OH solvent in the presence of an equivalent of HNO_3 did not result in alkoxy exchange. Similarly, attempts to exchange alkenes by treatment of **4a** (X = NO_3) with 1-octene did not effect an alkene exchange. In contrast, reaction of the methoxymercurial of 1-octene (X =