retro-Diels-Alder elimination were identical with the hydrogenated product **3a**. The NMR spectrum ($CDCl_3$) of **3b** showed peaks at 2.54 (s, 3 H), 2.60–3.32 (m, 7 H), the aromatic protons appear at 7.00–7.76 (m, 7 H).

The voltammogram shows that the formation of **2** proceeds via two one-electron reduction steps. We suggest that the first electron uptake leads to the formation of a relatively stable radical **4** leading to the sequence **5** → **6** → **7** → **2a**.

We believe this to be the first demonstration of an intramolecular cathodic cyclization of a benzylisoquinolinium salt, involving the intermediacy of an aryl radical, generated from an aryl halide.

In order to evaluate the potential of this new aporphine synthesis for the preparation of methoxy-substituted aporphines, (±)-10,11-dimethoxyaporphine (**3c**) was prepared from **1b**. Thus 300 mg (0.55 mmol) of **1b** gave after electrolysis 120 mg (74%) of an oil **2b**: UV_{max}^{MeOH} (log ϵ) 238 (4.51), 269 (4.11), 278 (4.14), 340 (4.09), 353 (4.18), 395 (3.69), 417 (3.74), 445 (3.71); NMR ($CDCl_3$) 3.00 (s, 3 H), 3.76 (s, 3 H), 5.56 (d, 1 H), 5.97 (s, 1 H), 5.23 (d, 1 H), the aromatic protons appear at 6.76 (d, 1 H), 6.98–7.34 (m, 3 H), 8.92 (d, 1 H). Without further isolation, **2b** was converted directly to **3c** with PtO_2 (25 mg) in MeOH containing a few drops of concentrated hydrochloric acid. Two molar equivalents of hydrogen were rapidly absorbed. The product was converted to the free base, and also to the hydroiodide salt, mp 262 °C dec oil bath (lit.[17] 282 °C dec (dta)); UV, NMR, and mass spectrum were identical with those of (−)-apomorphine dimethyl ether hydroiodide.[17] The high-yield conversions of **1** → **3** constitute the most efficient direct route to aporphines reported to date.

Studies are currently underway to explore the scope and mechanism of the electroreductive cyclization of benzylisoquinolines to aporphines.

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(16) The principal fragmentation pathway of aporphines exhibits intense molecular ion peaks and fragments at $[M - 1]^+$, as the result of hydrogen loss at the C-6a position. Of particular importance in determining the presence of substituents in the C-5 position is the expulsion of a $CH_2{=}NCH_3$ moiety via a retro-Diels–Alder mechanism.[3]
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Oligomerization Stereochemistry of Vinyl Monomers. 2. Effect of Ion Pair Structure on the Methylation Stereochemistry of 1,3-Di(2-pyridyl)butane Anion

Sir:

There has been considerable interest in stereoselective alkylation reactions of Li compounds in recent years and much understanding of these reactions has been gained. However, a systematic investigation of the effect of cation on such reactions involving ionic species appears not to have been made. We now wish to report such a study dealing with the methylation stereochemistry of 1,3-di(2-pyridyl)butane[2] (**2′**) that shows dramatic and interesting effects of cation and its state of coordination.

Anion **2** was prepared by metalation of ethylpyridine using BuLi or alkali salts of α-methyl styrene tetramer[3] in THF followed by slow in vacuo distillation of vinyl pyridine onto a stirred solution of **1** at −78 °C (Scheme I). Methylation was similarly carried out by an in vacuo distillation of CH_3I onto a solution of **2** at temperatures below 0 °C. The methylation products, **3′**, were distilled (bp 102–106 °C (0.15 mm Hg)) after extraction and analyzed by NMR (*meso*-**3′**: δCH_2 1.77 and 2.25, J_{ab} = 13.3 Hz; δCH 2.80, $J_{ac} = J_{bc}$ = 7.1 Hz; δCH_3 1.25, J_{cd} = 6.7 Hz; *rac*-**3′**: δCH_3 = 1.19, J_{cd} = 7.0 Hz). Product ratios were determined by comparison of CH_3 doublet intensities of the meso compound and the racemic mixture. The results are shown in Table I and demonstrate the effect of cation size and coordination on the reaction stereochemistry. The methylation stereoselectivity shows a decrease with increasing cation size, the Li and Na salts being highly selective, while methylation of the Rb salt leads to approximately equal

Scheme I

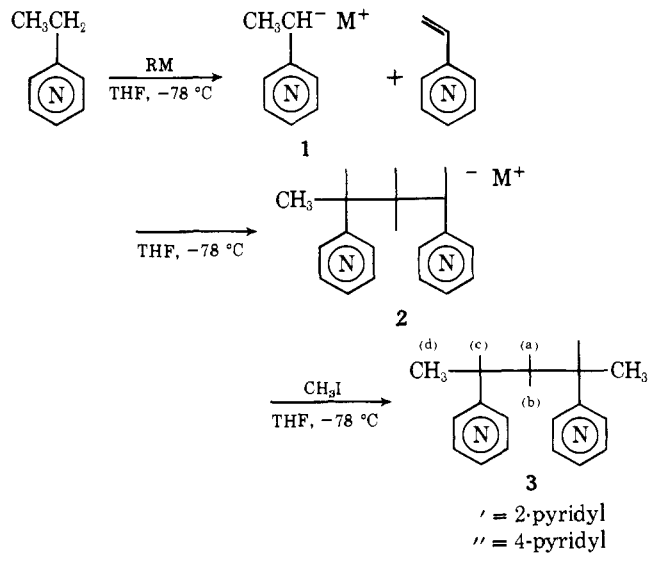


Table I

R^-M^+	Carbanion	Solvent	T, °C	% meso
n-BuLi	**2′**	THF	−78	>99
α-MeStLi[d]	**2′**	THF	−78	>99
n-BuLi	**2′**	THF	0	95
n-BuLi	**2′**	THF/Pyridine[b]	−78	83
α-MeStNa[d]	**2′**	THF	−78	96
α-MeSt(NaCE)[a,d]	**2′**	THF	−78	58
α-MeStK[d]	**2′**	THF	−78	65
α-MeStRb[d]	**2′**	THF	−78	57
$^-DD^-$, $2Li^+$[e]	**2″**	THF	−78	~50[c]

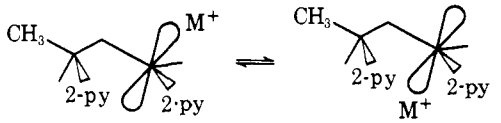
[a] 18-Crown-6 present in 10% excess. [b] 50% by volume. [c] Diastereomers not identified by NMR. [d] Prepared by reacting α-methylstyrene with the metal mirror in THF in vacuo (see ref 3). [e] $Li^+{}^-(Ph)_2C-(CH_2)_2-C(Ph)_2{}^-Li^+$, prepared by reacting 1,1-diphenylethylene with Li metal in THF, in vacuo.

quantities of the meso and racemic compound. Also, coordination of cation with strongly complexing molecules decreases the stereoselectivity. For instance, 18-crown-6 complexed Na salt is nonselectively methylated.[4]

The methylation stereochemistry of the Li salt of the corresponding 4-pyridyl derivative (**3″**) is also of interest. The methylation was not stereoselective in this case.

Epimerization studies on *meso*-**3′** in Me_2SO using *t*-BuOK as a catalyst indicate *meso*-**3′** and *rac*-**3′** to be of approximately equal stability, a result similar to that obtained by Flory and co-workers for the corresponding diphenylpentane.[5] Kinetic control of the reaction seems thus likely, a conclusion that is also supported by the very large differences in stereochemistry using different cations and coordinating agents.

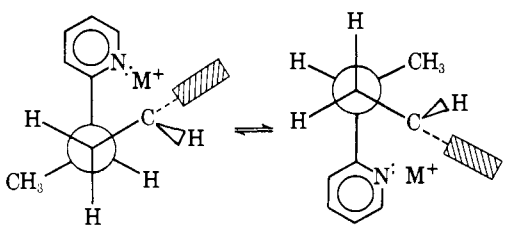
It is likely, on the basis of experimental results[6] and calculations[7] carried out on contact ion pairs[8] of these type of systems, that the counterion is present above (or below) the carbanion plane. Hence, two diastereomeric ion pairs should exist in principle, each of which may exist in several conformations. Barring greatly different reactivities of **4′a** and **4′b**



4′a **4′b**

the high methylation stereoselectivity of the Li (and Na) salt is consistent with the presence of either **4′a** or **4′b** and with either retention or inversion during methylation. Several recent reports on stereoselective alkylations of Li compounds indicate retention as the predominant mode of reaction.[1a-d] A cation side approach of electrophile seems reasonable, since anti approach would lead to an incipient product separated ion pair[9] in the transition state.[10]

It appears then that diastereomer **4′a** is favored for the Li salt of **2′**, while this is not the case for the corresponding salt



5′a **5′b**

4′a **4′b**

of **2″**. This is unusual and seems only possible if other than steric factors are involved. Cation complexation with penultimate 2-pyridine has been demonstrated[11,12] for an almost identical Na carbanion salt and is likely to exist here also. Schematic representations of such cation complexed conformations are shown below. Inspection of models leads one to expect that **5′a** may be more stable than **5′b** because of nonbonded CH_3-pyridine lone pair interactions and because of an additional unfavorable gauche interaction in **5′b**. The proposed mechanism is also consistent with the observation that the stereoselectivity decreases with increasing cation size and cation coordination. It is further supported by the lack of stereoselectivity of the methylation of **2″**, where intramolecular pyridine–cation coordination is not possible.

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A Chiral Synthesis of D-(+)-2,6-Dideoxystreptamine and Its Microbial Incorporation into Novel Antibiotics

Sir:

It has recently been shown[1-5] that suitable aminocyclitols can be converted microbiologically into antibiotics by mutants which lack the pathway for deoxystreptamine biosynthesis, but which when grown on a medium containing deoxystreptamine will form the appropriate antibiotic. For example a mutant of *S. fradiae* grown on a medium supplemented with deoxystreptamine biosynthesized neomycin. Analogues of deoxystreptamine such as streptamine and epistreptamine were also incorporated to give novel antibiotics.[1,2] This opens a route for