lamps at a distance of 42 mm. After irradiation, a solution containing 4.8×10^{-2} mmol of biphenyl was added. Quantitation of anisole, using biphenyl as the standard, indicated that 3 ± 0% (duplicate analyses) of the anisole had degraded during sample irradiation.

The presence of 3-(phenylthio)pyridine in reaction mixtures also was confirmed by GLC/mass spectrometric analysis.

Search for Deuterated Pyridine during Reduction. Substitution of 3-Iodopyridine in Methanol-*d*. Two samples were prepared. The first consisted of 0.32 M 3-iodopyridine, 1.1 M CH_3ONa, and 0.47 M C_6H_5SNa, the second being 0.32, 0.62, and 0.48 M, respectively, all in CH_3OD. The first was irradiated for 60 min and the second for 131 min. Both NMR tubes were irradiated with two sunlamps, each at a distance of 42 mm. Analysis by GLC/mass spectrometry on a carbowax column showed the presence of pyridine and some benzene probably arising from the degradation of 3-(phenylthio)pyridine. Multiple scans of the pyridine peak gave ratios ranging from m/z 100/5.5 to 100/5.8 for m/z 79/80 for the first sample and m/z 100/5.5 to 100/6.9 for the second. Authentic pyridine under the same conditions gave m/z 100/5.0 to 100/5.3 for the same mass ratio. Using the mass 80 peak as a measure of the amout of pyridine-*d*, the maximum amount present is 6.9 − 5.0 = 1.9%.

Registry No. **1**, 1120-90-7; **2**, 1532-97-4; **3**, 5332-24-1; sodium methoxide, 124-41-4; sodium thiophenoxide, 930-69-8; methanol, 67-56-1; 3-pyridyl, 29761-81-7; 4-isoquinolyl, 54978-42-6; 3-quinolyl, 54978-40-4; 3-bromopyridine, 626-55-1; 3-chloropyridine, 626-60-8; 1-bromonaphthalene, 90-11-9; iodobenzene, 591-50-4; 3-(phenylthio)quinoline, 87393-53-1.

The Effect of a Cyano Group on the Thermodynamic Ease of Electron Removal from Hydrazines

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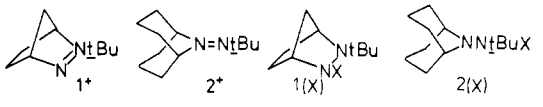
Formal oxidation potentials relative to SCE are reported for several cyano-substituted hydrazines and their analogues with the cyano group replaced by a methyl group. $\Delta E^{\circ\prime}$ was 0.83 V for 2-cyano- and 2-methyl-3-*tert*-butyl-2,3-diazabicycloheptane (**1**(CN) and **1**(Me)), 0.35 V for trimethyl(cyanomethyl)hydrazine and ethyltrimethylhydrazine (**3**(CN) and **3**(Me)), and 0.23 V for (β-cyanoethyl)trimethylhydrazine and propyltrimethylhydrazine (**4**(CN) and **4**(Me)). The ESR spectrum of **1**(CN)-d_2 has nitrogen splittings of 17.2 and 7.7 G. The significance of these results is discussed.

In this work we compare the thermodynamic ease of electron removal from tetraalkylhydrazines with that for related compounds in which a methyl group is replaced by a cyano group. For the most interesting case, that in which the cyano group is directly attached to nitrogen, we chose examples in which α-deprotonation of the radical cation is kinetically inhibited by having the α CH bonds held near the nodal plane of the p orbital at the adjacent nitrogen. We hoped that then the thermodynamically destabilized radical cation would prove to be long-lived under cyclic voltammetry (CV) conditions, so that the thermodynamically significant formal potential for electron removal ($E^{\circ\prime}$) could be measured. Stable diazenium salts[1,2] $\mathbf{1}^+\mathbf{BF}_4^-$ and $\mathbf{2}^+\mathbf{BF}_4^-$ were treated with methyllithium–



TMEDA[3] and potassium cyanide[4] to give the desired X = CH_3 and X = CN derivatives. Because a cation radical reduction wave as large as the oxidation wave was observed by CV, **1(CN)** gives a cation radical which is long-lived on the CV time scale. Cation decomposition could be detected in the CV of **2(CN)** at slow scan rates. Large oxidation,

Table I. Cyclic Voltammetry Data[a] for Some Tetraalkyl- and Trialkylcyanohydrazines

compd	$E^{\circ\prime}$, V	ΔE_p^{ox}, mV [electrode]
1(Me)	0.21	100 [Au]
1(CN)	ca. 1.04	210 [Pt]
2(Me)	0.11	62 [Au]
2(CN)	ca. 1.0	550 [Pt]
3(Me)	0.33	80 [Au]
3(CN)	0.64	80 [Pt]
4(Me)	0.32	88 [Au]
4(CN)[b]	ca. 0.55	240 [Au]

[a] Conditions: ca. 2 mM substrate in acetonitrile containing 0.1 M tetra-*n*-butylammonium perchlorate vs. SCE, 200 mV/s scan rate. [b] Data from ref 7.

reduction peak separations (ΔE_p) were observed, however, showing that heterogeneous electron transfer is quite slow. One factor is that platinum had to be used for the working electrode because of the high $E^{\circ\prime}$ values for these cyanohydrazines. Tetraalkylhydrazines are already known to show slower electron transfer (larger ΔE_p values) at platinum than at gold.[5] It is nevertheless clear, especially for **2(CN)**, that heterogeneous electron transfer is significantly slower than for tetraalkylhydrazines. We suspect that conformational effects are important in causing the large ΔE_p values, but will not return to this interesting point here. For the present purpose, determination of the effect of cyano substitution on the thermodynamics of electron loss, the large ΔE_p values observed are a distinct disad-

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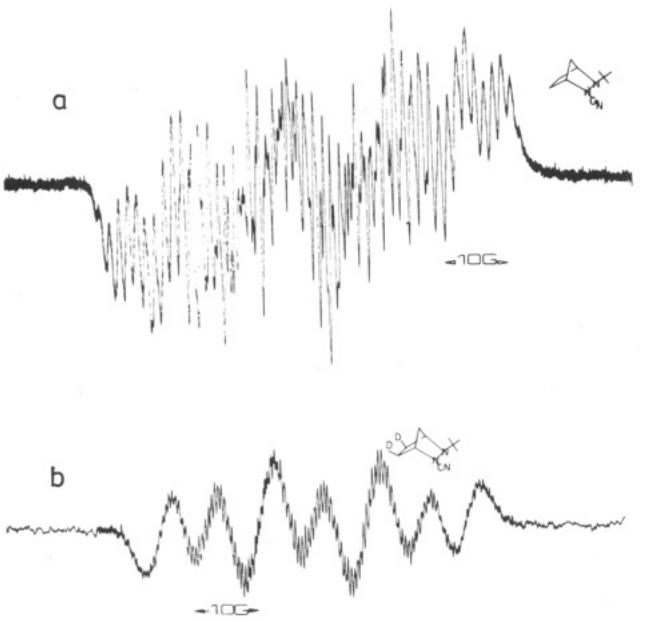


Figure 1. (a) ESR spectrum of **1(CN)**$^{+\cdot}$. (b) ESR spectrum of **1(CN)**-$d_2^{+\cdot}$. Samples were generated by electrolysis in butylnitrile at −40 °C.

vantage, for they limit the accuracy with which $E^{\circ\prime}$ is determined. When electron transfer is fast and ΔE_p is close to 57 mV, $E^{\circ\prime}$ is vanishingly close to the average of the oxidation and reduction peak potentials. As electron transfer becomes slower and ΔE_p increases, $E^{\circ\prime}$ can be significantly different from the average of the peak potentials if the heterogeneous transfer coefficient α differs significantly from 0.5. Because α is close to 0.5 for **1(CN)** from the observed wave shape, we report $E^{\circ\prime}$ as the peak potential average in Table I. The accuracy of this measurement is considerably less for **2(CN)**, because of the large ΔE_p observed.

One expects the presence of a cyano group to be considerably less cation destabilizing when methylene groups are inserted between the nitrogen and the cyano group, and this turns out to be the case. Trimethylhydrazines with one and two methylenes between the nitrogen and the cyano group, **3(CN)** and **4(CN)**, were prepared by

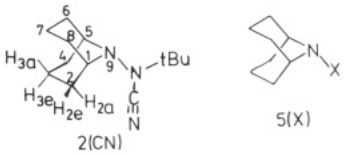
$Me_2NN(Me)CH_2X$ $Me_2NN(Me)CH_2CH_2X$ X = Me, CN
3(X) 4(X)

condensation of trimethylhydrazine with a mixture of formaldehyde and cyanide[6] and addition of it to acrylonitrile,[7] respectively. The CV data for **3** and **4** also appear in Table I.

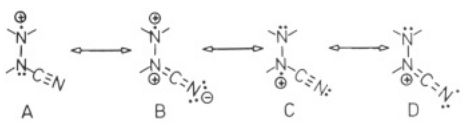
The ESR spectrum of **1(CN)**$^{+\cdot}$ proved to be extremely complex (Figure 1a), which is not surprising considering that there are 12 different magnetically active nuclei which could give a total of 15 552 lines. Luckily however, replacing the exo hydrogens at C_5 and C6 by deuterium (the dideuteriodiazenium salt was available from previous work[8]) led to considerable narrowing of the observed patterns, which could only result if the largest proton splittings were caused by these hydrogens, as would happen if there were significant π spin density at both N_2 and N_3. The spectrum of **(1(CN)-*d*$_2$)**$^{+\cdot}$, shown in Figure 1b, consists of an approximately 1:1:2:1:2:1:1 septet of ill-resolved multiplets, as expected if the splittings of the two nitrogens were in approximately a 2:1 ratio. Measurement of the total and outer separations gave a(N) values of 17.2 and 7.7 G, which we assigned to N_2 and N_3, although we have no way of determining which gives the larger splitting.

Discussion

Conformation of 2(NC). The NMR spectra of **2(CN)** are worthy of comment because they show unusual conformational effects. The ^{13}C NMR spectrum shows, in addition to the *N-tert*-butyl signals at δ 26.74 (Me) and 60.44 (C_8), five other carbons: 57.72 (C_1, C_4, CH), 33.10 (C_6, C_8, CH_2), 22.54 (C_2, C_4, CH_2) 19.59 (CH_2), and 19.41 (CH_2) (see **2(CN)** for the assignments; as for **1(CN)**, we



did not observe the nitrile carbon). The carbon spectrum is only consistent with "front–back" carbon interconversion in **2(CN)** ($C_1 \leftrightarrow C_5$, $C_2 \leftrightarrow C_4$, $C_6 \leftrightarrow C_8$) being fast on the NMR time scale, but "top–bottom" interconversion ($C_{2,4} \leftrightarrow C_{6,8}$, $C_3 \leftrightarrow C_7$) being slow. The amino-substituted nitrogen N_9 ought to be strongly nonplanar, but the nitrile substituted nitrogen should be planar or nearly so; the cyano group obviously must be that directed toward C_2,C_4 as indicated in A. Inversion at N_9 requires simultaneous



180° rotation about the NN bond to reach the equal energy conformation with CN directed toward $C_{6,8}$, and this process is clearly slow on the NMR time scale. The δ 22.5 and 33.1 chemical shifts of $C_{2,4}$ and $C_{6,8}$ of **2(CN)** should be compared with those of the same carbons in other examples of **5(X)** recorded at a temperature where N_9 inversion is slow: 21.3 and 32.2 for **5(CH)$_3$**,[9] 23.1 and 33.6 for **5(Cl)**,[10] 26.3 and 32.5 for **5(SMe)**.[11] The proton NMR of **2(CN)** is very complex but shows anomalous chemical shifts for both H_{2a} and H_{2e}. At 270 MHz, a 2-H signal at δ 1.38 appears as a doublet of doublets (J = 13.9, 6.6 Hz). We assign these protons at H_{2e} and H_{4e} because they are consistent with the splittings of H_{2e} of the model tetraalkylhydrazine **5(5)**, where the spectrum was fit by using $J_{2e,2a}$ = 12.9 $J_{2e,3a}$ = 4.9, $J_{2e,1}$ = −0.6, $J_{2e,3e}$ = 0.5 Hz, and δ H_{2e} = 1.45.[12] A second 2-H signal at δ 2.64 appears as a seven line pattern with separations of about 6.6 Hz, and relative intensities of about 1:2:3:4:3:2:1. We assign these hydrogens as H_{2a} and H_{4a}, once again on the basis of the spectrum of **5(5)**, which was fit with the above geminal coupling, $J_{2a,3a}$ = 13.7, $J_{2a,3e}$ = 5.7, $J_{2a,1}$ = 5.3, and δ H_{2a} = 2.06. The seven-line pattern is that expected for two large couplings of about the same size and two medium ones about half that size. This observed chemical shift of H_{2e} of **2(Cn)** is δ 0.07 upfield of that of **5(5)**, while the H_{2a} shift of **2(CN)** is δ 0.58 downfield. This seems consistent with

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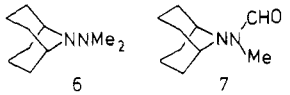
our assignmentbecause the H_{2a} hydrogens of **2(CN)** must be rather close to the nitrile carbon, and the position of H_{2a} in **5(5)** is averaged between syn and anti amino group conformations.

Ease of Oxidation. The replacement of Me by CN in going f rom **2(Me)** to **2(CN)** raises $E^{\circ\prime}$ by about 0.89 V (ca. 20.5 kcal/mol). A comparable increase in $E^{\circ\prime}$ was seen comparing **1(CN)** with **1(Me)**, 0.83 δ (19.1 kcal/mol) (Table I), and also upon replacing the methyl group of **6**



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by a formyl group to give **7**, 0.81 V (18.7 kcal/mol).[13] The differences in conformation between neutral **2(CN)** and **7** precludes a very detailed comparison of the $E^{\circ\prime}$ values, which are influenced by differences in steric interactions in both neutral and radical cationic states, but these data establish that direct attachment of a cyano group raises $E^{\circ\prime}$ by an amount comparable to that seen upon direct attachment of a carbonyl group.

The data of Table I establish that electron removal from cyano hydrazines becomes easier when saturated carbon atoms are placed between a nitrogen and the cyano group. This seems unsurprising, as it is what would be predicted on inductive grounds, but such behavior is in fact a great contrast with the effect of placing saturated carbon atoms between a carbonium ion center and a cyano group. Olan[14] and especially Gassman and co-workers[15] have shown that a cyano group directly attached to a carbon atom bearing a leaving group slows solvolysis much less that would be expected on inductive grounds. β-Cyano tosylates solvolyze more slowly than α-cyano tosylates. The powerful cation-destabilizing σ-electron-withdrawing effect of the cyano substituent appears to be nearly balanced by its π-electron-releasing effect.[16] From the Gassman group's solvolysis rates, $\Delta G^{\ddagger}$ is 2.2 kcal/mol higher for β-cyano-2-tosyladamantane than it is for α-cyano-2-tosyladamantane,[15c] and the corresponding increase for the 3-methyl-2-tosylbutane system is 3.1 kcal/mol. In contrast, the ground-state, product radical cation energy gap, ΔG_e°, shows the opposite trend for α- and β-cyano hydrazines. It is 9.2 kcal/mol thermodynamically more difficult to remove an electron from the α-cyanohydrazine **1(CN)** than it is from β-cyanohydrazine **3(CN)**. This is a striking qualitative difference in behavior.

To examine the effect of a cyano group on the ease of electron removal more quantitatively, we compare the difference in $E^{\circ\prime}$ between tetraalkylhydrazines and their analogous cyanohydrazines in which a methyl group is replaced by a cyano group in Figure 2. Because different alkyl groups, especially bicyclic ones, change the ease of oxidation of tetraalkylhydrazines, we make the comparison shown to damp out the effect of the bicyclic alkyl groups in **1(X)** for comparison with the acylic pairs **3(X)** and **4(X)**. The change in $E^{\circ\prime}$ for the cyano and methyl compound, $\Delta E^{\circ\prime}$, is plotted against the Taft σ_I value for CN, CH_2CN,

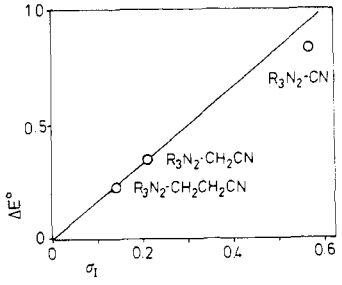

Figure 2. Plot of the difference in formal potentials for oxidation of cyano-substituted hydrazines and the compounds with cyano replaced by methyl vs. Taft's σ_I values for the cyano-containing substituent.

and CH_2CH_2CN (we employed 0.57, 0.21, and 0.14, respectively[17]). If only inductive effects were involved, we would expect a plot of $\Delta E^{\circ\prime}$ v s. σ_I to be a straight line going through the origin. As seen in Figure 2, the unconjugated examples, **3(X)** and **4(X)**, do give points that lie on a line through them and the origin, which we assume establishes the line for electron removal from nonconjugated cyano-substituted hydrazines, where the principal effect of the cyanoalkyl group should be of destabilizing the radical cation inductively. The point for the α-cyano compound **1(X)** lies 0.1 V (ca. 2.7 kcal/mol) below the line, showing that it is only slightly easier to oxidize **1(X)** than might have been expected on strictly inductive grounds.

We suggest that the principle reason for the qualitatively different behavior of α- and β-cyano substitution on the ease of solvolysis to give carbocations and on electron loss from hydrazines involves the difference in conjugation. In the α-cyano solvolysis case, only the product carbocation is conjugated with the cyano group, and charge delocalization into the cyano group will stabilize the cation, offsetting its strong inductive destabilization. In contrast, the α-cyanohydrazine has both neutral hydrazine and the hydrazine radical cation with the cyano group directly involved in conjugation. We suggest it is conjugative energy lowering in the neutral compound, which is the principal factor in the turnaround between α- and β-carbocation formation (where localization is 2–3 kcal/mol more difficult in the β-cyano case) and hydrazine radical cation formation (where electron removal is 12 kcal/mol easier in the β-cyano for methyl substitution case). The deviation of the α-cyanohydrazine point in Figure 2 from the β- and α-cyanohydrazine line does not have a simple interpretation, because both the neutral form and the radical cation have the α-cyano group conjugated with a nitrogen lone pair.

The question of what the π-electron distribution is in the α-cyanohydrazide radical cation is an interesting one. If NCN conjugation were powerful enough, the presence of the cyano group might tend to localize the spin on the dialkylamino nitrogen (A and B the predominate resonance forms), making the cation radical essentially an amine radical cation with a weakly interacting N(R)CN group. If hydrazine radical cation resonance stabilization were more important the NRCN interaction, A and C might predominant, making the species essentially a hydrazine radical cation with a weakly interacting cyano substituent. MNDO–UHF calculations[18] on planar $(H_2NNHCN)^{+\cdot}$ give essentially the latter situation, with five-electron, four heavy-atom p spin densities of 0.51 (NH_2), 0.44 (NHCN),

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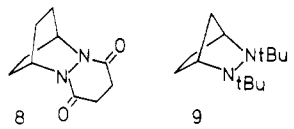
-0.09 (C≡N), and 0.13 (C≡N). A slightly bent form is calculated to be slightly stabler than the planar one. The experimental ESR spectrum suggests a much larger difference in nitrogen spin densities, since the a(N) values are in a 7:3 ratio. The ESR spectrum of $(8)^{+\cdot}$ has a(2N) = 9.6 G,[13] so the larger a(N) value for **1(CN)** should presumably be assigned to the *tert*-butylated nitrogen. The sum of the nitrogen splittings in $\mathbf{1(CN)}^{+\cdot}$ is 92% as large as the sum of them in the di-*tert*-butyl model $(9)^{+\cdot}$,[3] sug-



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gesting that the cyano substituent only perturbs the hydrazine radical cation group rather weakly, i.e., that A and C do predominate.

Conclusion

Electron removal from an α-cyanohydrazine is substantially more difficult than from a β- or γ-cyanohydrazine, but slightly less so than a $\Delta E^{\circ\prime}$ vs. σ_I plot would predict. The principal reason for the different behavior of cyano substitution on electron loss from a hydrazine and an ionization to give a carbocation is suggested to be conjugative stabilization of the neutral form of an α-cyanohydrazine. Most of the spin density in α-cyanohydrazine radical cation $\mathbf{1(CN)}^{+\cdot}$ appears to be in the hydrazine nitrogen p orbitals, and the nitrogen splitting constants were in a 7:3 ratio.

Experimental Section

2-Cyano-3-*tert*-butyl-1,2,3-diazabicyclo[2.2.1]heptane (1-(CN)) was prepared by the method of Snyder and co-workers.[4] A large excess of KCN in water was added to 0.25 g (1.04 mmol) of $1^+Br_4^-$ in CH_2Cl_2.[3] After 2 h of stirring the aqueous layer was separated and washed twice with CH_2Cl_2, and the combined organic layers were dried with sodium sulfate and evaporated to give **1(CN)** as a white solid: mp 60–61 °C; 0.13 g (70%): ^{1}H NMR ($CDCl_3$) δ 1.05 (s, 9 H), 1.36 (d, J = 10.1, 1 H), 1.45–1.60 (m, 1 H), 1.6–1.7 (m, 2 H), 1.82–1.92 (m, 1 H), 2.0–2.14 (m, 1 H), 3.63 (br, 1 H), 3.92 (br, 1 H); ^{13}C NMR ($CDCl_3$) δ 27.33, 27.92, 30.61, 35.84, 58.08, 59.50, 62.68 (cyano nitrogen not observed); empirical formula $C_{10}H_{17}N_3$ established by high-resolution mass spectroscopy; IR (CCl_4) 2960, 2190, 1360, 1220, 1070 cm^{-1}.

1,1-(1,5-Cyclooctyl)-2-*tert*-butyl-2-cyanohydrazine (2(CN)) was prepared from the corresponding diazenium salt[2] by the same method as **1(CN)** in 50% yield: mp 80–81 °C; ^{1}H NMR ($CDCl_3$) v 1.25 (s, 9 H), 1.38 (dd, J = 13.9, 6.6 Hz, 2 H (2e, 4e)), 1.48–1.82 (complex, 4 H (3e, 6e, 7e, 8e)), 1.87–2.18 (complex, 4 H (3a, 6a, 7a, 8a)), 2.64 (m, 2 H), (2a, 4a)), 3.17 (br t, 2 H, 1, 5)); ^{13}C NMR ($CDCl_3$, see text); empirical formula $C_{13}H_{23}N_3$ established by high-resolution mass spectroscopy; IR (CCl_4) 2980, 2930, 2180, 1460, 1370 cm^{-1}.

(Cyanomethyl)trimethylhydrazine (3(CN)) was prepared by treating trimethylhydrazine with formaldehyde and cyanide under the conditions of Hamilton, Harris, and Winter[6] and obtained as an oil in 39% yield; ^{1}H NMR (acetone-d_6) δ 2.30 (s, 6 H), 2.35 (s, 3 H), 3.0 (s, 2 H); empirical formula $C_5H_{11}N_3$ established by high-resolution mass spectroscopy; IR (CCl_4) 2960, 2930, 2820, 2220, 1460, 1120, 1040 cm^{-1}. The cyclic voltammetric and ESR experiments were performed as previously described.[3]

Acknowledgment. We thank the National Science Foundation for generous financial support of this work under Grants CHE 77-24627 and 80-26111. We thank Timothy Clark of the University of Erlangen—Nürnberg for helpful discussions and a copy of the MNDO program.

Registry No. **1(Me)**, 42842-99-9; **1(CN)**, 87207-04-3; $\mathbf{1(CN)}^{+\cdot}$, 87207-05-4; $\mathbf{1(CN)}$-$d_2^{+\cdot}$, 87207-06-5; **2(Me)**, 87226-19-5; **2(CN)**, 87207-07-6; **3(Me)**, 50599-41-2; **3(CN)**, 87207-08-7; **4(Me)**, 60678-65-1; **4(CN)**, 74773-78-7.

α-Amino Acids as Chiral Educts for Asymmetric Products. Chirally Specific Syntheses of Tylophorine and Cryptopleurine

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Chirally specific total syntheses of major representatives of the phenanthroindolizidine and phenanthroquinolizidine alkaloids have been completed from (*S*)-α-amino acids as educts. This was achieved in each case by utilizing a key intramolecular Friedel–Crafts acylation to produce both the tylophorine and cryptopleurine ring systems optically intact. The amido ketones resulting from these cyclizations were further elaborated to the desired natural product alkaloids in good overall yields. Both alkaloids, derived from (*S*)-α-amino acids, are dextrorotatory and exhibit positive CD curves. Assignments of absolute stereochemistry are made, and several discrepancies with prior assignments are discussed.

The phenanthroindolizidine and phenanthroquinolizidine alkaloids have been subjects of numerous biological and chemical studies. Several of these natural products are powerful vesicants,[1-3] often highly toxic,[4] and can modulate the growth of various normal and abnormal mammalian tissues.[5-7] Numerous comprehensive reviews[8-11] are available which summarize efforts to determine chemical structure and stereochemistry and to synthesize these interesting classes of heterocyclic compounds.

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