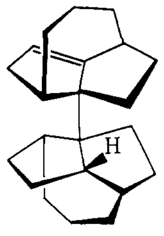
carbons present in **6**, thus confirming this structure for the diol and that (**5**) assigned to the diketone.

Of the methods investigated for transformation of the diol (**6**) into the olefin (**2**), the Corey–Winter reaction[15] proved most efficacious. Although **6** did not react with thiocarbonyldiimidazole, when the diol was first converted to the lithium salt and then heated at reflux in THF with this reagent, the thionocarbonate (**7**)[14] was obtained in 82% yield. Decomposition of **7** in refluxing triethyl phosphite, containing diphenylisobenzofuran as trapping agent, gave the Diels–Alder adduct of **2**[14] in 85% isolated yield. When diphenylisobenzofuran was omitted from the reaction, a hydrocarbon[14] was isolated in 85% yield. Its mass spectrum showed it to be a dimer of **2.** However, its ^{1}H NMR spectrum ($CDCl_3$) clearly indicated that it was not the formal product of a ${}_{\pi}2_{s} + {}_{\pi}2_{s}$ reaction, for a single olefinic proton appeared as a broad doublet at δ 5.48, $J = 5$ Hz. Among the 22 resonances in its ^{13}C NMR spectrum ($CDCl_3$) the two corresponding to the olefinic carbons appeared at δ 127.19 (d) and 162.02 (s). The structure of the hydrocarbon is, therefore, formulated as that (**8**)[16,17] expected from an ene reaction[19] between two molecules of **2.** Support for this structural assignment comes from the fragmentation of the hydrocarbon on electron impact; substantial peaks at the mass of olefin (**2**) ± 1 appear in the mass spectrum. Further evidence for structure **8** was obtained by hydrogenation (Pd/C, ethanol) of the hydrocarbon. The proton decoupled ^{13}C NMR spectrum of the crystalline hydrogenation product,[14] mp 131–132.5 °C, showed only 11 resonances, indicating that it possesses either a plane or twofold axis of symmetry.[16]



8

Although this is, to the best of our knowledge, the first example of a bridgehead olefin giving an ene type dimer, the formation of such a product finds precedent in the chemistry of a torsionally strained olefin with a sterically shielded double bond.[20] Further studies of the chemistry and trapping of **2** are in progress.

Acknowledgment. We thank Dr. William Kingsley for carrying out some preliminary experiments on the isocyanomethyllithium method of ring expansion and the National Science Foundation and the Eli Lilly Company for partial support of this work. Acknowledgment is also made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of the portion of this work that was carried out by T.R. and W.T.B. at Harvard.

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(14) This compound gave satisfactory analytical data—elemental analysis and/or exact mass.
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(16) Since **2** is chiral, it can in fact dimerize to give two different ene type products, only one of which is represented in structural formula **8.** From the ^{13}C NMR spectrum of the dimer and its hydrogenation product, it appears that only one is formed. We are trying to determine whether the dimer does, in fact, correspond to the one represented in **8.**
(17) It should be noted that **8** is itself a strained olefin, since it contains a bicyclo[3.3.0]oct-1(2)-ene moiety.[5,18] Indeed on prolonged refluxing (36 h) in triethyl phosphite, an isomer[14] of **8** becomes the major product isolated. The ^{1}H NMR spectrum of the isomer shows a two-proton multiplet centered at δ 5.68, and two olefinic carbons appear in the ^{13}C NMR spectrum at δ 132.38 (d) and 137.26 (d). The spectroscopic data and the fact that the isomer gives the same crystalline hydrocarbon as **8** on hydrogenation indicate that the isomer is the formal product of a 1,3 hydrogen shift, which releases the strain present in **8.**
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The Relationship between $^{15}N^{13}C$ Coupling Constants and Hybridization

Sir:

In a previous paper[1] we described semiempirical calculations of $^{13}C^{15}N$ spin-spin coupling constants which included the three contributing terms—Fermi contact (J^{Fc}), orbital (J^{o}) and spin dipolar (J^{sd}). The importance of such calculations is that they allow the evaluation of the latter "noncontact" terms, which are often invoked ad hoc when the observed one-bond coupling constant, $^1J_{CN}$, appears anomalous with respect to hybridization. It is now possible to explore a long-standing question in carbon–nitrogen coupling—why the relationship proposed by Binsch et al.[2]

$$|^1J_{^{13}C^{15}N}| = (80)^{-1}(\%S_C)(\%S_N) \qquad (1)$$

holds for some CN constants while failing badly for others? This issue is important because reference to eq 1 has appeared in most studies to date reporting CN coupling constants and because it represents an important conceptual framework for interpreting $^1J_{CN}$. An alternate approach, relating $^1J_{CN}$ linearly to the square of the density matrix element $P_{S_CS_N}$ of molecular orbital theory has met with similar difficulties.[3,4] Only when the nature of these deficiencies are clarified will it be possible to extract hybridizations with assurance from the observed $^1J_{CN}$.

To analyze this problem we have chosen to compute $(\%S_C)(\%S_N)$ from INDO localized orbitals (rather than use nominal hybridizations, e.g., sp, sp^2, sp^3), utilizing the formula

$$(\%S_C)(\%S_N) \approx (100P_{S_CS_N})^2 \qquad (2)$$

where the $P_{S_CS_N}$ is defined as $2\Sigma_j\, C_{jS_C}C_{jS_N}$, the sum running over products of $2S$ coefficients in the localized orbital(s) of the CN bond(s). Thus, for single bonds $P_{S_CS_N}$ is slightly larger than its delocalized counterpart,[5] since only orbitals contributing to the CN bond are included[6] and slightly smaller than the product percent s character, which is obtained by truncation to two centers. For the bent localized orbitals of multiple

Table I. Contributions ot ${}^1J_{^{13}C^{15}N}$ and CN Hybridizations

Molecule	J^{Fc}	J^{o}	J^{sd}	${}^1J^{total}$	Expt[a]	$(\%S_C)(\%S_N)$
(1) $(CH_3)_4N^+$	−5.9	0.1	−0.1	−5.9	(5.8)[b]	488
(2) CH_3NH_2	−2.7	0.2	−0.1	−2.0	−4.5[c]	628
(3) CH_3NO_2	−17.8	0.2	−0.1	−17.7	−10.5[d]	818
(4) CH_3NC(C–N)	−11.9	0.2	−0.1	−11.8	−10.7[e]	858
(5) Pyridine	−0.7	1.6	−0.3	0.6	0.6[f]	1020
(6) Pyrrole	−14.8	0.9	0.0	−13.9	−13.0[f]	1052
(7) Pyridinium ion	−13.5	1.2	−0.2	−12.5	−11.9[f]	1120
(8) Pyridine *N*-oxide	−18.3	1.2	−0.8	−17.9	−15.2[f]	1128
(9) PhC≡N	2.7	−9.5	−16.2	−23.0	−17.5[g]	3488
(10) PhC≡NO	−34.4	−23.0	−17.8	−75.2	(77.5)[h]	3600
(11) CH_3NC(N≡C)	19.3	−8.2	−13.9	−2.8	−8.9[i]	2674

[a] Experimental values in parentheses are of undetermined signs. [b] E. Bullock, D. G. Turk, and E. J. Woodhouse, *J. Chem. Phys.*, **38,** 2318 (1963). [c] L. Paolillo and E. D. Becker, *J. Magn. Reson.*, **3,** 200 (1970). [d] E. D. Becker and R. B. Bradley, cited in T. Axenrod, "Nitrogen NMR", G. Webb and M. Witanowski, Ed., Plenum Press, New York, N.Y., 1972, p 261. [e] I. Morishima, A. Mizuno, and T. Yonezawa, *Chem. Commun.*, 1321 (1970). [f] T. Bundegaard and H. J. Jakobsen, *J. Magn. Reson.*, **19,** 345 (1975). [g] W. McFarlane, *Mol. Phys.*, **10,** 603 (1966). This is the value for acetonitrile. [h] M. Christl, J. P. Warren, B. L. Hawkins, and J. D. Roberts, *J. Am. Chem. Soc.*, **95,** 4392 (1973). This is the value for the 2,4,6-trimethyl derivative. [i] W. McFarlane, *J. Chem. Soc. A*, 1660 (1967); N. J. Koole, D. Knol, and M. J. A. DeBie, *J. Magn. Reson.*, **21,** 499 (16).

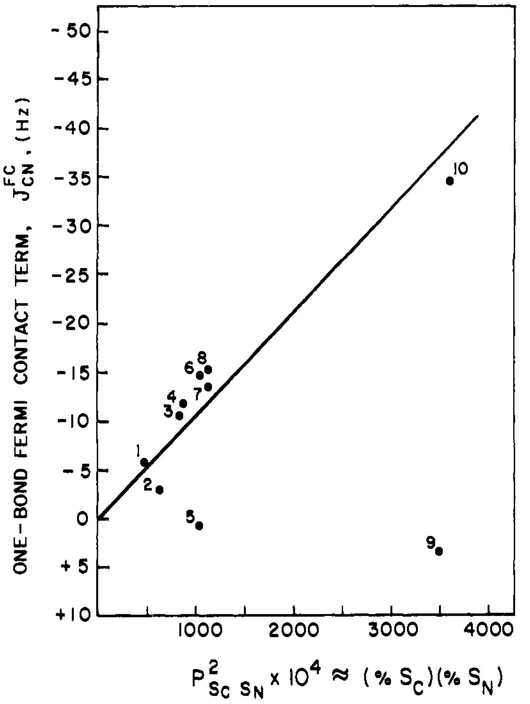

Figure 1. A plot of the Fermi contact term for ten CN coupling constants vs. $(\%S_C)(\%S_N)$ as defined in the text. The numbering is that of Table 1. For nitromethane and pyridine *N*-oxide the calculated J^{Fc} are somewhat too negative; more accurate values were obtained for each by subtracting the small orbital and dipolar terms from the experimental ${}^1J_{CN}$.

bonds, it appears to be an appropriate generalization of the concept of percent s character. In any event, the results described here are not contingent on this particular choice and future workers may prefer to use the more readily available delocalized $P_{S_C S_N}$ of INDO theory.[7]

Table I contains 11 representative coupling constants and their hybridizations. It can be seen that the orbital and dipolar contributions are large for the nitriles, isocyanide, and nitrile oxide "triple bonds" and clearly eq 1 will fail for these systems for the simple reason that J^{Fc} is only a small part of ${}^1J_{CN}$. We may consider, however, whether the calculated contact terms are linearly related to $(\%S_C)(\%S_N)$, since this would at least allow direct use to be made of the observed ${}^1J_{CN}$ for single and double bonds. For seven of the ten cases plotted in Figure 1, which span a range of −6 to −45 Hz, the answer is in the affirmative. In fact, the slope of $(94.1)^{-1}$ is similar, although slightly smaller than that of Binsch et al.[2] Just as interesting are the exceptions with positive deviations—methylamine, pyridine, and benzonitrile;[8] methylisocyanide has a deviation even larger due to its large positive J^{Fc}. Common to all of these molecules is a lone pair containing s character both on the atom on which it is situated and on adjacent atoms through its "orthogonality tail". An obvious interpretation is that the lone pair makes a contribution to ${}^1J_{CN}{}^{Fc}$ which, in part, offsets the usually dominant negative contributions of the CN localized bonding orbital(s), whose sign arises from the negative product of ^{15}N and ^{13}C gyromagnetic ratios. This argument is supported by (1) localized orbital calculations which explicitly demonstrate such contributions,[1] (2) the fact that the positive deviations from linearity increase monotonically (though greater than linearly) with $(\%S_C)(\%S_{\text{lone pair}})$,[9] and (3) that molecules such as methylamine and aniline obey eq 1 when the calculations are performed for planar nitrogens,[10] i.e., when $\%S_{\text{lone pair}} = 0$.[11] The duality in sign of ${}^1J_{CN}{}^{Fc}$ is thus seen to result from two opposing contributing terms, with the net contact term zero or positive for large values of $\%S_{\text{lone pair}}$, e.g., 42, 46, and 71% in pyridine, azirane, and methylisocyanide, respectively. Clearly, in terms of its effect on the adjacent CN coupling the lone pair is an extraordinary ligand and the *one-bond lone-pair effect* is an extremely large perturbation.

We may now formulate two simple rules for the validity of equations such as 1 to ${}^1J_{CN}$, the actual sign being negative: (1) the CN bond cannot be a nitrile, isocyanide, nitrile oxide, or isocyanate; (2) the single or double CN bond must have no s-containing lone pairs on C or N; pure p lone pairs, however are permitted. The first rule has been conjectured, in part, on several occasions, but has never been demonstrated by actual calculation. The second rule appears to be entirely new and it may have some application to other coupling constants as well, e.g., ${}^1J_{NH}$ and ${}^1J_{CP}$.

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orbitals. Either framework is, of course, sufficient, the point being to obtain the simplest heurlstic model.

(6) If all the occupled localized orbitals were included, $P_{S_C S_N}$ would be invariant under the localizing unitary transformation.

(7) For reference, the squared INDO density matrlx elements ($\times 10^4$) obtained from all the occupled orbítals, localízed *or* delocalized, are for couplings (1)–(11): 395, 473, 542, 725, 726, 705, 795, 710, 1191, 2079, and 829, respectively.

(8) The small posltive deviation for methylamine is large relative to its $^{1}\mathcal{J}^{c}$ (as is the case with pyrldine and benzonitrile). On the other hand, for benzonitrile oxide the positlve relative deviation is small and probably arises merely as a consequence of the least-squares fitting procedure, which requires both positive and negative deviations.

(9) For methyl isocyanide the corresponding expression would be $(\% S_N)(\% S_{\text{lone pair on carbon}})$.

(10) A similar observation was made in ref 4.

(11) For the above reasons we prefer this interpretation to the more general statement of a fallure of the average energy approximatlon. The latter may, however, be appropriate to one exception we have found to eq 1 and Figure 1. The molecule ^{15}N-methylphenylpropynylamine has recently been reported to have a $^{15}N—^{13}C\equiv C–$ $|^{1}J_{CN}|$ of 36.2 Hz (T. Bottin-Strzalko, M. J. Pouet, and M. P. Simonnin, *Org. Magn. Reson.*, **8**, 120 (1976)). For the model system, planar $H_2N—C\equiv CH$ we obtain $\mathcal{J}^{c} = -29.5$, $\mathcal{J}^{p} = 0.3$, and $J^{sd} = -0.03$ Hz, in reasonable agreement with experiment with only the contact term of consequence. The corresponding $(\% S_C)(\% S_N) = 1650$ places this $^{1}J_{CN}$ somewhat above the line in Figure 1. As wlth other systems, when the nitrogen is pyramidalized the positive lone-pair effect causes $^{1}J_{CN}$ to fall below the line.

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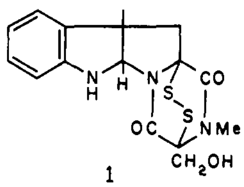
The Structure of Chetomin

Sir:



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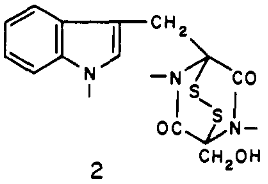

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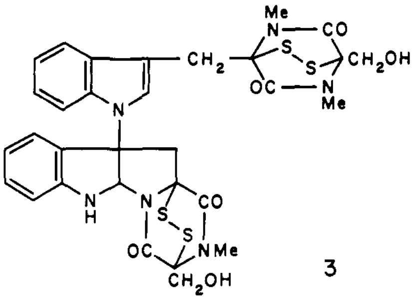

3

Chetomin, an antibiotic discovered more than 30 years ago,[1] is thought to be associated with poor growth in young ruminants.[2] Chemical degradation and spectroscopic studies,[3] suggested that the fragments **1** and **2** were present, linked by a bond between the quaternary β-indoline carbon of **1** and one of the three nitrogen atoms of **2**. The other nitrogen atoms of **2** bore methyl substituents. Evidence for the orientation of the substituents on the nitrogen atoms of **2** has now been obtained with the aid of ^{15}N labeling, and ^{15}N and ^{13}C NMR spectroscopy.

Chaetomium cocliodes (HLX 833)[3] was grown in shake flasks for 14 days at 25 °C on a medium containing (g/l.) glucose, 30; calcium carbonate, 3; potassium chloride, 0.5; magnesium sulfate, 0.5; dipotassium hydrogen phosphate, 1; trace metals;[4] and sodium nitrate, 2.44 (in the labeling experiments $Na^{15}NO_3$, 99 atom % was used). Chetomin ($[\alpha]^{20}D$ +257° (c, 0.1, $CHCl_3$), ϵ_{285nm} (MeOH) 11 800, 4 mg/l.) was isolated from extracts of the mycelium by partition chromatography.[3]

The broad band ^{1}H-decoupled ^{15}N NMR spectrum of ^{15}N enriched chetomin consisted of six resonances (δ_N 123.0, 117.4, 95.3, 91.1, 90.3, 51.0, referred externally to 4 M NH_4Cl in 2 N HCl). ^{13}C NMR spectra with ^{1}H broad band decoupling were recorded with concomitant single frequency irradiation ($\gamma H_2/2\pi$ 15–65 Hz) of each ^{15}N resonance. The ^{15}N resonance at δ_N 117.4 could be assigned to the indole nitrogen of **2**, for it was coupled ($^{1}J_{CN}$ = 13.8 Hz) to the carbon atom bearing a hydrogen substituent (δ_C 127.3, $^{1}J_{CH}$ = 186 ± 2 Hz)[3,5] in the five-membered indole ring. This nitrogen atom was also coupled to a quaternary aromatic carbon (δ_C 134.1, $^{1}J_{CN}$ = 14.5 Hz) and to the β-quaternary carbon atom of the five-membered ring of the indoline nucleus of 1 (δ_C 73.8, $^{1}J_{CN}$ = 11.9 Hz). This β-indoline quaternary carbon was long-range coupled to the pyrroline (δ_N 123.0, $^{2}J_{CN}$ = 3.7 ± 0.6 Hz) and indoline (δ_N 51.0, $^{1}J_{NH}$ = 87.7 Hz, $^{2}J_{CN}$ ~ 1 Hz) nitrogen atoms of the eserine system. The orientation **3** may therefore be assigned to chetomin, and this conclusion was confirmed by the following facts. The indoline nitrogen (δ_N 51.0) was coupled ($^{1}J_{CN}$ = 8.1 Hz) to a methine carbon (δ_C 80.2, $^{1}J_{CH}$ = 174 ± 1 Hz) which was also coupled ($^{1}J_{CN}$ = 5 ± 1 Hz) to the pyrroline nitrogen (δ_N 123.0). This pyrroline nitrogen atom was further coupled to a carbonyl carbon (δ_C 163.1, $^{1}J_{CN}$ = 14.6 Hz) and to two quaternary carbon atoms each bearing a sulfur substituent (δ_C 76.3, $^{2}J_{CN}$ = 6.2 Hz; δ_C 73.6, $^{1}J_{CN}$ = 5.0 Hz). The remaining three nitrogen atoms (δ_N 90.3, 91.1, 95.3) were coupled ($^{1}J_{CN}$ = 9.3 Hz) to methyl carbons (δ_C 27.5, 27.5, 28.3) and to ($^{1}J_{CN}$ = 13.7 Hz) carbonyl carbons (δ_C 165.6, 165.6, 166.8) and were therefore parts of amide systems as required by structure **3**. Other ^{15}N-^{13}C and ^{13}C-^{1}H couplings, not mentioned, were fully consistent with this structure.

This structural conclusion is of biosynthetic interest. In the ring closure reaction giving eserine metabolites a second tryptophan residue may be substituted at the β-position of its indole ring as in the chaetocin and verticillin groups[6] or at the ring nitrogen as in chetomin. A second ring closure does not occur in the latter case, thus providing an example in the same molecule of the two types of metabolite (gliotoxin[7] and hyalodendrin[8]) found in the phenylalanine series.

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