standard methods, L-valine was elaborated via optically pure aldehyde **16**[15] to stannyl carbamate **17** as a 1:1 mixture of diastereomers (Scheme IV).[16] Since we anticipated complications due to proton transfer and eliminative loss of the nitrogen substituent, the carbamate was deprotonated with KH prior to tin–lithium exchange.[17] The result, presumably dianion **18**, gave products **19** and **20** upon gradual warming to room temperature from which the desired β-lactam (**19**) could be isolated in yields of 30–35%. Although the mechanistic details of the conversion **17** → **19** await elucidation,[18] this preliminary example serves to illustrate a potentially useful strategy for the synthesis of optically active β-lactams from readily available α-amino acids.

The demonstration that nucleophilic α-alkoxy carbanions may be generated in the presence of mildly electrophilic acyl functionality through kinetically preferred tin–lithium exchange lays the groundwork for the design and execution of many new intramolecular processes. While the condensations in this study are functionally equivalent to the acyloin condensation, the present method is superior in its control over placement of the new carbon–carbon bond and its attendant oxygen substituents and allows the preparation of compounds that are inaccessible through acyloin methodology. Studies are under way to define the limits of functional group compatibility in intramolecular bond-forming processes and to utilize the carbon–tin bond directly in intramolecular acylations without the intermediacy of the organolithium species.

Acknowledgment is made to the National Institutes of Health for generous support of this work. We also thank J. Michael Williams for his assistance in obtaining and interpreting the NMR spectra for some of the compounds in this study.

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[15] Stanfield, C. F.; Parker, J. E.; Kanellis, P. *J. Org. Chem.* **1981**, *46*, 4797.

[16] Since the main objective of this experiment was to realize cyclization of 17, no attempt has been made to improve stereoselection in its preparation.

[17] Attempts to use excess *n*-BuLi without prior KH deprotonation under a variety of conditions failed to produce any of the desired β-lactam 19.

[18] Perhaps bearing on this question, an intramolecular attack at a deprotonated amide carbonyl has been suggested to explain a homoenolate rearrangement.[14a]

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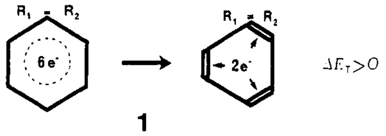
Is the Delocalized π-System of Benzene a Stable Electronic System?

Summary: Computational evidence is provided that the symmetric hexagonal structure of benzene is driven by the σ-framework alone. The π-system is found to favor a distorted and localized structure. Electronic (π) delocalization in benzene is thus forced by the σ-framework.

Sir: Why does benzene have a symmetric hexagonal geometry? According to common wisdom the tendency of the π-system to be delocalized (in "resonance") is the root cause of such a structural symmetry. This common notion has recently been questioned.[2] It was reasoned that π-delocalization cannot be the driving force for the structural features of benzene and that these features originate in the σ-framework alone, which prefers a symmetric hexagon and thereby forces the π-system to be delocalized. This communication presents computational evidence that the π-system of benzene is indeed not stable in a symmetric hexagon and that it is the σ-framework that determines the structural symmetry of benzene and forces π-delocalization.

The tendency of benzene to remain symmetric and delocalized is measured by the energy change, ΔE_T, that accompanies the localizing asymmetric distortion in **1**. It is well-known that such a distortion of benzene requires energy; i.e., $\Delta E_T > 0$ in **1**. This can be taken as evidence that the geometry and special stability of benzene are driven by the π-system that tends to cluster in a symmetric arrangement where delocalization ("resonance") of the "electronic sextet" does occur. However, while it is evident that the σ-framework, were it by itself, would favor a symmetric hexagon, there is no single proof that the π-electrons are a contributing driving force for symmetrization nor there is clear evidence that the π-system possesses an inherent tendency to be delocalized without the buttressing effect of the σ-skeleton. These tendencies must be proved or else falsified.



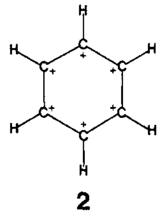
1

The total energy of benzene (at the SCF level) is expressed in eq 1. Here h_π and h_σ are the corresponding monoelectronic integrals of the π and σ MOs. The R terms

$$E_T = 2\sum_{\pi}^{\mathrm{occ}} h_\pi + R_{\pi,\pi} + R_{\sigma,\pi} + 2\sum_{\sigma}^{\mathrm{occ}} h_\sigma + R_{\sigma,\sigma} + V_{NN} \quad (1)$$

stand for electron–electron repulsion of a type that is specified by the subscript. The last term V_{NN} accounts for nuclear repulsion.

The first two terms in eq 1 describe the energy of the six π-electrons in the field of the bare nuclei of the C_6H_6 framework, i.e., in the field of $(C^{6+})_6(H^{1+})_6$. By adding the third term ($R_{\sigma,\pi}$) in eq 1 to the first two, the attraction of the six π-electrons to $(C^{6+})_6(H^{1+})_6$ will be partly counterbalanced by electron–electron repulsion with all the σ-type electrons (five e on each carbon and one e on each hydrogen). Therefore the first three therms in eq 1 describe the six π-electrons in the field of the σ-$(C^{1+})_6H_6$ framework which is shown in **2** and in which the charge effectively resides on the carbon atoms. Therefore the first three



2

terms of eq 1 represent the π-energy, E_π, of the six π-electrons in the field of the σ-framework which is shown in **2**. The rest of the terms in eq 1 naturally represent then

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[2] (a) Epiotis, N. D. *Nouv. J. Chim.* **1984**, *8*, 11. (b) Shaik, S. S.; Bar, R. *Nouv. J. Chim.* **1984**, *8*, 411. Shaik, S. S.; Hiberty, P. C. *J. Am. Chem. Soc.* **1985**, *107*, 3089.

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Table I. Energy Changes Accompanying an Asymmetric Distortion (1)[a,b]

entry	species	method	ΔE_σ	ΔE_π	ΔE_T
1	C_6H_6	STO-3G	+17.1	−11.9	+5.2
2	$(C_6H_6)^{6+}$	STO-3G[c]	+17.3		+17.3
3	C_6H_6	STO-3G +π-CI	+17.1	−11.2	+5.9
4	C_6H_6	6-31G	+16.3	−9.7	+6.6
5	C_6H_6 (π-septuplet)	STO-3G	+16.9		+16.9 (+18.1)[d]

[a] The distortion that conserves constant V_{NN} refers to 1 in the text where C_6H_6, $R_1 = R_2 = 1.400$ Å → C_6H_6, $R_1 = 1.34$ Å, $R_2 = 1.4627$ Å. [b] $\Delta E > 0$ means reluctance to distort, while $\Delta E < 0$ means that the distortion leads to stabilization. [c] $(C_6H_6)^{6+}$ contains no π-electron. [d] The value in parentheses includes the net π-repulsion which is described in the text.

the σ-energy, E_σ, of the σ-framework that is specified in **2**.

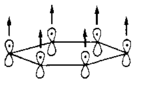
It should be noted that this definition of E_π and E_σ is the commonly used one in π-electron approximations.[3] What renders this definition inappropriate *for ab initio* calculations is the fact that V_{NN} cannot be partitioned into σ and π components. However, this problem can be avoided in the present case, since we are interested in energy *variations* rather than absolute energies. Then, if we perform an asymmetric distortion (see **1**), which conserves constant V_{NN} between carbons, then the energy change ΔE_T in **1** will involve only electronic effects that are due to π- and σ-electrons mutually in each other's field, i.e.,

$$\Delta E_T = \Delta E_\pi + \Delta E_\sigma \qquad (2)$$

The ΔE_σ value can be obtained independently by calculating the distortion energy for the σ-framework in **2** and comparing the result to ΔE_σ which obtains from the partition in eq 2. The partition at the STO-3G level yields $\Delta E_\pi = -11.9$ kcal/mol and $\Delta E_\sigma = +17.1$ kcal/mol, while the independent computation on **2** yields $\Delta E_\sigma = +17.3$ kcal/mol. The correspondence of the two results shows that the energy partition in eq 2 is self-consistent and that at the STO-3G level the π-system wishes to distort to a localized structure ($\Delta E_\pi = -11.9$ kcal/mol),[4] but this tendency is quenched by the σ-framework ($\Delta E_\sigma = +17.1$ kcal/mol). Further improvement of the value of ΔE_π can be obtained at the level of full π-space configuration interaction (CI) which will change the value of ΔE_π, while leaving ΔE_σ unchanged.

The results on various levels of computation are collected in entries 1–4 of Table I. As can be seen, on all levels, the resistance of benzene toward a nonsymmetric distortion is dominated by the σ-framework, while the π-system is stabilized by the distortion. It is therefore concluded that the π-system of benzene prefers a structure with three localized π-bonds rather than a delocalized "aromatic sextet", at least at the levels of computations presented in Table I.

To further check this result the ΔE_π and ΔE_σ quantities have been computed in a different way. The π-electrons were unpaired into a septuplet state as shown in **3**. We a priori know that in such a species the π-electrons are only very slightly sensitive to an asymmetric distortion.[5] The septuplet species was thus subjected to the same asymmetric distortion as in eq 1. The reluctance of this species to an asymmetric distortion was found at the STO-3G level to be 18.1 kcal/mol. A small part of this resistance results from the repulsions between the π-electrons whose spins are identical. This π-contribution was determined as 1.2 kcal/mol by summing up the π-orbital energies of the septuplet species and substracting the bielectronic terms (to avoid counting them twice). The resulting species is a σ-framework in a field of "nonresonating" π-electrons. When π-delocalization was thus "turned off", the resistance of the σ-frame to an asymmetric distortion was found to be 16.9 kcal/mol (entry 5 in Table I). This resistance is seen (from ΔE_T in entries 1, 3) to diminish to 5.9 kcal/mol as π-delocalization is "turned on". We are aware that a much higher quality computation should decrease the absolute magnitude of ΔE_π, but even then the minor importance of the π-system, as a driving force for delocalization, will be an inescapable conclusion.[6] Thus from whichever direction we approach the problem we reach the same conclusion: π-Delocalization in benzene is a phenomenon "forced" by the σ-system which prefers a symmetric skeleton. As has been shown previously, the reluctance of the π-system to be delocalized is due to the cost of electronic reorganization,[2b] which originates in the the strength of the localized π-bond.[2] Thus the π-system of benzene and the unstable H_6 hexagon[7] obey the same basic rule.



3 (SEPTUPLET)

In summation, the symmetric hexagonal geometry of benzene is established not because of but in spite of the π-electrons.[2] In fact there is no theoretical level that opposes this conclusion, and even at the Hückel level (with variable β), it can be shown that an hexagonal π-system prefers to distort to a localized structure. This qualitative result has been obtained in the framework of the second-order Jahn–Teller effect,[8] and further studies along these lines have recently been pursued on allylic-type resonance.[9] In any case, however, a σ–π separation, like the one described above, for example, is necessary to draw any conclusion regarding the π-system. Thus, the often quoted theoretical Hückel theory basis for the delocalization propensity of the "electronic sextet" is entirely fragile. It is only within the constraints of a symmetric hexagonal σ-framework that the π-electrons tend to delocalize. Our conceptual thinking must then adapt itself to this new

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(3) Bishop, D. M. "Group Theory and Chemistry"; Clarendon Press: Oxford, 1973; p 204.

(4) Noteworthily, the sum of π-orbital energies ($2\sum_\pi^{occ} E_\pi^{SCF}$) is also lowered by the distortion.

(5) An upper limit of this π-contribution can be determined from the isoelectronic H_6 hexagon. The septuplet H_6 (with $r_{HH} = r_{CC}$ in C_6H_6) resists the asymmetric distortion by 2.2 kcal/mol. This resistance is due only to the interaction of electrons of the same spins in the septuplet state.

(6) The same result was obtained for allyl radical, at the higher level of triple-ζ basis set + σ- and π-CI, see: Shaik, S. S.; Hiberty, P. C.; Lefour, J. M.; Ohanessian, G. *Nouv. J. Chim.* **1985**, *9*, 385. At the level of STO-3G + π-CI we obtained $\Delta E_\pi = -3.2$ kcal/mol. This π-instability persisted ($\Delta E_\pi = -0.35$ kcal/mol) at the very high level of 6-311G + σ- and π-correlation (involving more than 5×10^6 determinants). CI was carried out with the CIPSI algorithm: Huron, B.; Malrieu, J. P.; Rancurel, P. *J. Chem. Phys.* **1973**, *58*, 5745. See also: Evangelisti, S.; Daudey, J. P.; Malrieu, J. P. *Chem. Phys.* **1983**, *75*, 91. Considering the fact that there are six partial π-bonds in benzene relative to only two in allyl, one could project that for benzene ΔE_π would be approximately −1 kcal/mol (3 times −0.35 kcal/mol). This is a lower limit of instability as may be judged by comparing the H_3 and H_6 analogues ($E(H_3) = -20$ kcal/mol and $E(H_6) = -109$ kcal/mol at the level of STO-3G + CI).

(7) Haddon, R. C.; Raghavachari, K.; Whangbo, M. H. *J. Am. Chem. Soc.* **1984**, *106*, 5364. Ichikawa, H. *J. Am. Chem. Soc.* **1983**, *105*, 7467; **1984**, *106*, 6249.

(8) See: Salem, L. "The Molecular Orbital Theory of Conjugated Systems"; W. A. Benjamin: Reading, MA, 1972; pp 494–505.

(9) Feller, D.; Davidson, E. R.; Borden, W. T. *J. Am. Chem. Soc.* **1983**, *105*, 3347; **1984**, *106*, 2513.

interpretation of the "aromatic stability" of benzene.

A detailed treatment of electronic delocalization in conjugated π-systems and their isoelectronic species will follow in a future publication.

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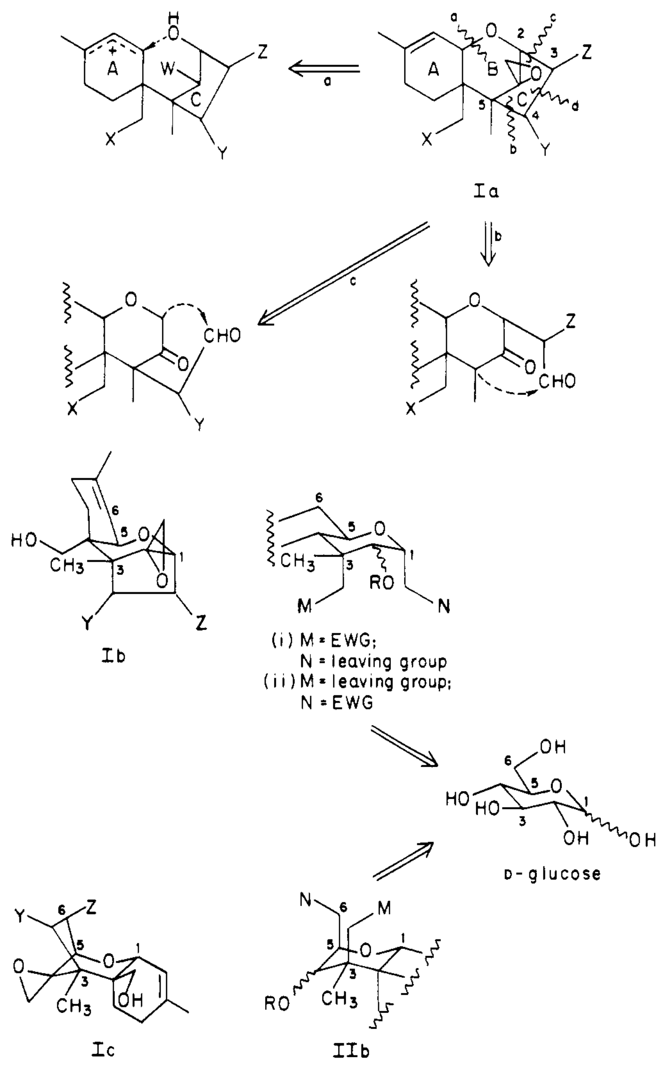
A Route to Optically Active Trichothecane Skeleton by Bisannulation of a Pyranose Derivative[1,2]

Summary: A process has been developed for bisannulation of a pyranose ring to produce the trichothecene skeleton in which (a) the cyclohexeno (A) ring is connected at C1/C2 of the sugar, (b) an Eschenmoser–Claisen rearrangement is applied at C3 to generate an equatorially oriented acetamido unit, and (c) the activated methylene group is used to displace a sulfonate at C6 of the original sugar in a process that forms the C ring.

Sir: Most recent syntheses[4,5b–f] of the trichothecane system Ia have relied upon variations of the biogenetic process[6] (path a, Scheme I) in which the pyran ring is formed by the intramolecular addition of a hydroxyl group on ring C to a ring A electrophilic center.[7] In connection with our longstanding interest in these substances,[8,9] we have been concerned with the development of routes to the optically active sesquiterpene core, and we describe herein some pertinent results.

We were mindful of the seminal studies of the Raphael group which culminated in the first synthesis of a trichothecene, trichodermol.[5a] This achievement, which employed a bond b disconnection (Scheme I) was difficult, and could not be extended to a synthesis of verrucarol.[10] Goldsmith[7d] and Kraus[5g] have utilized a bond c disconnection via an intramolecular aldol condensation, this being particularly convenient since their target molecules were hydroxylated at C3 (Z = OH).

Scheme I



Formation of bond d remained an unexplored possibility, and the conformational representations depicted in Ib and Ic revealed two independent approaches, via the counterparts IIa and IIb, both of which emanate from D-glucose. Theoretically, IIa offered two options, i and ii, (Scheme I), depending on how the activated and leaving groups are positioned. Option ii was rejected since such activated *C*-glycopyranosides undergo ready based-catalyzed $\alpha \rightarrow \beta$ "anomerization" initiated by a retro-Michael reaction.[11] The other possibility, option i, would require the preparation of a precursor bearing a one-carbon, electrophilic substituent at C1 of the pyranose ring in an α-D orientation. The equivalent precursor, IIb, seemed considerably more attractive, since the one-carbon electrophile would already be present in the guise of C6 of glucose.

The ring closure arising from IIb is reminiscent of the formation of a 3,6-anhydro sugar[12] in which the pyranoside ring is also required to adopt the unfavorable $^1C_4$ confor-

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[1] This project was supported by a grant from the Public Health Service (GM 32569).

[2] Portions of this work were presented at the 14th International Symposium on the Chemistry of National Products, Poznan, Poland, July, 1984.

[3] Taken from the Ph.D. Thesis of R.T., Duke University, 1985.

[4] For a recent comprehensive review: McDougal, P. G.; Schmuff, N. R. *Fortschr. Chem. Org. Naturst.* **1985**, *47*, 153.

[5] For some recent syntheses of the noted compounds, see the following. Trichodermol: (a) Colvin, E. W.; Malchenko, S.; Raphael, R. A.; Roberts, J. S. *J. Chem. Soc., Perkin Trans 1* **1973**, 1989. (b) Still, W. C.; Tsai, M. Y. *J. Am. Chem. Soc.* **1980**, *102*, 3654. Verrucarol: (c) Schlessinger, R. H.; Nugent, R. A. *J. Am. Chem. Soc.* **1982**, *104*, 1116. (d) Trost, B. M.; McDougal, P. G.; Haller, K. J. *J. Am. Chem. Soc.* **1984**, *106*, 383. (e) Roush, W. R.; D'Ambra, T. E. *J. Am. Chem. Soc.* **1983**, *105*, 1058. (f) For the only route to optically active systems: Brooks, D. W.; Grothaus, P. G.; Mazdiyasni, H. *J. Am. Chem. Soc.* **1983**, *105*, 4472. Calonectrin: (g) Kraus, G. A.; Roth, B.; Frazier, K.; Shimagaki, M. *J. Am. Chem. Soc.* **1982**, *104*, 1114.

[6] (a) Machida, Y.; Nozoe, S. *Tetrahedron* **1972**, *28*, 5113. (b) Masuoka, N.; Kamikawa, T.; Kubota, T. *Chem. Lett.* **1974**, 751. (c) Masuoka, N.; Kamikawa, T. *Tetrahedron Lett.* **1976**, 1691.

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[8] Tulshian, D. B.; Fraser-Reid, B. *Tetrahedron Lett.* **1980**, *21*, 4549.

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[10] Colvin, E. W.; Malchenko, S.; Raphael, R. A.; Roberts, J. S. *J. Chem. Soc., Perkin Trans. 1* **1978**, 658.

[11] Dawe, R. D.; Fraser-Reid, B. *J. Org. Chem.* **1984**, *49*, 522.

[12] Peat, S. *Adv. Carbohydr. Chem.* **1945**, *2*, 37.

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