with care to avoid direct light. The thick yellow oil was chromatographed on silica gel (2% EtOAc, balance petroleum ether). The yellow band was collected and concentrated in vacuo: ^{1}H NMR ($CDCl_3$) δ 6.58 (m, 1), 6.56 (m, 1), 6.41 (m, 1), 6.36 (m, 1), 2.62 (q, 2, J = 7.5 Hz), 1.26 (t, 3, J = 7.5 Hz), 1.03 (s, 9), 0.27 (s, 6); ^{13}C NMR ($CDCl_3$) δ 166.2, 128.7, 127.9, 127.2, 121.3, 118.9, 28.5, 25.6, 24.0, 13.3, -4.0; IR (neat) 2957, 2861, 1626, 1472, 1464, 1370, 1333, 1276, 1192, 1084 cm^{-1}; MS, m/e 236, 207, 179, 151, 105, 73; exact mass calcd for $C_{14}H_{24}OSi$ 236.1596, found 236.1586. Anal. Calcd for $C_{14}H_{24}OSi$: C, 71.12; H, 10.39. Found: C, 70.93; H, 10.39.

6-[(*tert*-Butyldimethylsilyl)oxy]-6-methylfulvene: ^{1}H NMR ($CDCl_3$) δ 6.67 (m, 1), 6.55 (m, 1), 6.42 (m, 2), 2.35 (s, 3), 1.07 (s, 9), 0.33 (s, 6); ^{13}C NMR ($CDCl_3$) δ 160.9, 129.3, 127.6, 127.1, 121.5, 118.6, 25.5, 21.3, 18.3, -3.7; IR (neat) 2945, 2861, 1633, 1471, 1464, 1257, 1197 cm^{-1}; MS, m/e 222, 207, 165, 151, 91, 73; exact mass calcd for $C_{13}H_{22}OSi$ 222.1442, found 222.14224.

6-[(*tert*-Butyldimethylsilyl)oxy]-6-(2-propyl)fulvene: ^{1}H NMR ($CDCl_3$) δ 6.63 (m, 1) 6.56 (m, 1), 6.40 (m, 1), 6.33 (m, 1), 3.32 (m, 1, J = 6.9 Hz), 1.22 (d, 6, J = 6.9), 1.05 (s, 9), 0.33 (s, 6); ^{13}C NMR ($CDCl_3$) δ 169.6, 128.2, 127.7, 126.4, 121.8, 119.2, 33.7, 25.9, 23.9, 20.7, 19.0, -3.6; IR (neat) 2958, 2861, 1612, 1471, 1466, 1374, 1320, 1196, 1085 cm^{-1}; UV ($CHCl_3$) λ 294 nm (ϵ 11 400); MS, m/e 250, 207, 193, 151, 119, 105, 91; exact mass calcd for $C_{15}H_{26}OSi$ 250.1721, found 250.1728. Anal. Calcd for $C_{15}H_{26}OSi$: C, 71.99; H, 10.41. Found: C, 71.93; H, 10.46.

6-[(*tert*-Butyldimethylsilyl)oxy]-6-*tert*-butylfulvene: ^{1}H NMR ($CDCl_3$) δ 6.78 (m, 1), 6.52 (m, 1), 6.36 (m, 1), 6.27 (m, 1) 1.41 (s, 9), 1.06 (s, 9), 0.28 (s, 6); ^{13}C NMR ($CDCl_3$) δ 173.1, 128.2, 127.1, 125.0, 121.8, 121.6, 40.0, 31.3, 26.2, 19.2, -2.7; IR (neat) 2958, 2861, 1586, 1472, 1464, 1371, 1272, 1175, 873 cm^{-1}; MS, m/e 264, 249, 207, 192, 177, 151, 133, 105; exact mass calcd for $C_{16}H_{28}OSi$ 264.1909, found 264.1898.

6-[(*tert*-Butyldimethylsilyl)oxy]-6-phenylfulvene: ^{1}H NMR ($CDCl_3$) δ 7.28 (m, 2), 7.49 (m, 3), 6.77 (m, 1), 6.50 (m, 1), 6.41 (m, 1), 6.29 (m, 1), 1.02 (s, 9), -0.02 (s, 6); ^{13}C NMR ($CDCl_3$) δ 169 (?), 134.4, 127.1, 126.9, 126.1, 125.8, 125.2, 121.6, 117.4, 28.3, 0.1; IR (neat) 2960, 2860, 1613, 1471, 1463, 1367, 1328, 1291, 1279, 1255, 1164, 1073, 996 cm^{-1}; UV ($CHCl_3$) λ 310 nm (ϵ 20 400); MS, m/e 284, 227, 179, 135, 105, 91; exact mass calcd for $C_{18}H_{24}OSi$ 284.1597, found 284.1615.

***syn*-2-Methyl-3-[(*tert*-butyldimethylsilyl)oxy]-6-(benzyloxy)hexanoic acid**: ^{1}H NMR ($CDCl_3$) δ 7.32 (m, 5), 4.49 (s, 2), 3.99 (m, 1, J = 4.4, 8.9 Hz), 3.45 (m, 2), 2.61 (m, 1, J = 4.4, 6.9 Hz), 1.57 (m, 4), 1.12 (d, 3, J = 6.9 Hz), 0.89 (s, 9), 0.09 (s, 3), 0.07 (s, 3); ^{13}C NMR ($CDCl_3$) δ 179.7, 138.3, 129.1, 128.3, 127.6, 127.5, 106.7, 73.2, 73.0, 70.1, 44.4, 31.0, 25.7, 25.6, 17.9, 10.8, -4.4, -4.8; IR (neat) 2957, 2900, 1709, 1472, 1462, 1361, 1253, 1096 cm^{-1}; MS, m/e 366, 320, 259, 257, 217, 201, 181, 157, 143, 127, 105, 91; MS (CI, CH_4), m/e 367 (M + 1), 349, 309, 201, 127, 105, 91; exact mass calcd for $C_{20}H_{34}O_4Si$ (M + 1) 367.2304, found 367.22845.

***syn*-2-Methyl-3-[(*tert*-butyldimethylsilyl)oxy]-6-(benzyloxy)hexanoyl Chloride.** The silyloxy acid (800 mg, 2.17 mmol) was dissolved in benzene (5 mL). The solution was cooled in an ice bath until the benzene began to freeze, and oxalyl chloride (0.38 mL, 4.3 mmol) was added. A drop of DMF was then added, and the mixture began to foam. The ice bath was removed, and foaming increased. The foaming ceased after 15 min at room temperature. The mixture was stirred for 1 h and concentrated in vacuo (0.10 mm). The crude acid chloride was used immediately for the formation of the fulvene: ^{1}H NMR ($CDCl_3$) δ 7.23 (m, 5), 4.41 (s, 2), 4.22 (m, 1), 3.40 (m, 2), 2.85 (m, 1), 1.4-1.6 (m, 4), 1.11 (d, 3, J = 7.2 Hz), 0.77 (s, 9), -0.03 (s, 3), -0.04 (s, 3).

6-[(*tert*-Butyldimethylsilyl)oxy]-6-[*syn*-1-methyl-2-[(*tert*-butyldimethylsilyl)oxy]-5-(benzyloxy)pentyl]fulvene. The crude 2-methyl-3-[(*tert*-butyldimethylsilyl)oxy]-6-(benzyloxy)hexanoyl chloride was used as described in the general procedure above to provide the fulvene in 44% yield for the two steps from the acid: ^{1}H NMR ($CDCl_3$) δ 7.26 (m, 5), 6.53 (m, 1), 6.47 (m, 1), 6.38 (m, 1), 6.30 (m, 1), 4.35 (s, 2), 3.93 (m, 1, J = 3.9, 9.4 Hz), 3.34 (t, 2, J = 6.5 Hz), 3.15 (m, 1, J = 9.4, 6.8 Hz), 1.66 (m, 2, J = 7.5 Hz), 1.52 (m, 2), 1.23 (d, 3, J = 6.8 Hz), 1.00 (s, 9), 0.90 (s, 9), 0.31 (s, 3), 0.28 (s, 3), 0.06 (s, 3), 0.05 (s, 3); ^{13}C NMR ($CDCl_3$) δ 166.5, 138.7, 128.1, 127.6, 127.4, 126.8, 122.4, 118.9, 73.6, 72.0, 70.5, 44.8, 31.7, 25.9, 25.8, 23.1, 18.9, 18.1, 17.3, -3.7, -3.8, -4.1, -4.4; IR (neat) 2958, 2860, 1612, 1472, 1463, 1373, 1362, 1273, 1260, 1191, 1105 cm^{-1}; MS (CI, CH_4), m/e 528, 503, 471, 422, 326, 293, 187, 145; exact mass calcd for $C_{31}H_{52}O_3Si_2$ 528.3454, found 528.3434.

General Procedure for the Preparation of 6-(Acyloxy)-6-alkylfulvenes. 6-(Propionyloxy)-6-ethylfulvene. To a solution of cyclopentadiene (0.5 mL) in THF (20 mL) at 0 °C was added $KN(TMS)_2$ (4.0 mL, 2.0 mmol, 0.5 M solution in toluene). The gray slurry was cooled to -78 °C, and HMPA (0.7 mL, 4 mmol, distilled from BuLi) was added. After 10 min, the addition of propionyl chloride (0.34 mL, 4.0 mmol) in THF (2 mL) was begun. The slurry became yellow within 5 min. After addition was complete, the solution was slowly warmed to room temperature for 10 min, and saturated NH_4Cl was added. Petroleum ether was added, and the organic material was transferred to a separatory funnel. The bright yellow organic layer was washed three times with water and then brine. The crude solution was concentrated in vacuo at room temperature with care to avoid direct light. The thick yellow oil was chromatographed on silica gel (5% EtOAc, balance petroleum ether). The yellow band was collected and concentrated in vacuo to give the fulvene (339 mg, 95%): ^{1}H NMR ($CDCl_3$) δ 6.45 (m, 3), 6.30 (m, 1), 2.78 (q, 2, J = 7.5 Hz), 2.57 (q, 2, J = 7.5 Hz), 1.27 (t, 3, J = 7.5 Hz), 1.18 (t, 3 J = 7.5 Hz); ^{13}C NMR ($CDCl_3$) δ 171.9, 158.3, 134.1, 131.6, 131.4, 121.2, 119.3, 27.4, 25.6, 11.9, 9.0; IR (neat) 2979, 1759, 1661, 1462, 1422, 1367, 1154 cm^{-1}; MS, m/e 178, 149, 122, 93, 71, 57; exact mass calcd for $C_{11}H_{14}O_2$ 178.100, found 178.0993.

6-(Acetyloxy)-6-methylfulvene: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.43 (m, 3), 6.36 (m, 1), 2.37 (s, 3), 2.25 (s, 3); ^{13}C NMR ($CDCl_3$) δ 167.9, 153.1, 134.4, 131.5, 131.0, 121.2, 118.7, 20.4, 18.3; IR (neat) 2982, 1748, 1675, 1373, 1194, 1016 cm^{-1}; MS, m/e 150, 108, 93, 77, 65; exact mass calcd for $C_9H_{10}O_2$ 150.0680, found 150.0692.

6-[(Trimethylacetyl)oxy]-6-*tert*-butylfulvene: ^{1}H NMR ($CDCl_3$) δ 6.73 (m, 1), 6.46 (m, 1), 6.35 (m, 1), 6.13 (m, 1), 1.39 (s, 9), 1.38 (s, 9); ^{13}C NMR ($CDCl_3$) δ 176.6, 164.5, 134.0, 132.2, 129.7, 121.7, 121.3, 39.5, 39.0, 30.3, 27.4; IR (neat) 2982, 1747, 1629, 1479, 1369, 1114 cm^{-1}; MS, m/e 234, 150, 135, 108, 107, 85, 57; exact mass calcd for $C_{15}H_{22}O_2$ 234.1619, found 234.1608.

6-(Hexanoyloxy)-6-pentylfulvene: ^{1}H NMR ($CDCl_3$) δ 6.43 (m, 3), 6.31 (m, 1), 2.74 (t, 2, J = 7.5 Hz), 2.52 (t, 2, J = 7.5 Hz), 1.75 (m, 2, J = 7.5 Hz), 1.58 (m, 2, J = 7.5 Hz), 1.35 (m, 8), 0.92 (m, 6); ^{13}C NMR ($CDCl_3$) δ 173.7, 159.9, 137.2, 133.9, 133.8, 123.8, 121.7, 36.6, 34.7, 33.7, 33.6, 29.3, 27.0, 24.7, 24.6, 16.2 (2 C); IR (neat) 2956, 2856, 1761, 1661, 1465, 1367, 1137, 1101 cm^{-1} MS, m/e 262, 164, 121, 108, 99, 92, 71; exact mass calcd for $C_{17}H_{26}O_2$ 262.1953, found 262.19038.

Acknowledgment. This work was supported by the National Institutes of Health (National Cancer Institute Grant No. CA21144).

Registry No. **3** (R = C_2H_5), 114837-46-6; **3** (R = CH_3), 701-12-2; **3** (R = t-C_4H_9), 114837-47-7; **3** (R = n-C_5H_{11}), 114837-48-8; **4** (R = C_2H_5), 114837-38-6; **4** (R = CH_3), 114837-39-7; **4** (R = i-C_6H_7), 114837-40-0; **4** (R = t-C_4H_9), 114837-41-1; **4** (R = C_6H_5), 114837-42-2; **5**, 114837-43-3; **6** (isomer 1), 114837-45-5; **6** (isomer 2), 114860-78-5; TBDMS-Cl, 18162-48-6; C_5H_5COCl, 79-03-8; CH_3COCl, 75-36-5; i-C_3H_7COCl, 79-30-1; t-C_4H_9COCl, 3282-30-2; C_6H_5COCl, 98-88-4; n-$C_5H_{11}COCl$, 142-61-0; *syn*-2-methyl-3-[(*tert*-butyldimethylsilyl)oxy]-6-(benzyloxy)hexanoyl chloride, 114837-44-4; cyclopentadiene, 542-92-7; oxalyl chloride, 79-37-8.

The Quest for a Neutral Homoaromatic Hydrocarbon. A Study of Pentacyclo[7.2.1.0^{4,11}.0^{6,9}.0^{6,10}]dodeca-1,4-diene, an Annelated Semibullvalene Derivative

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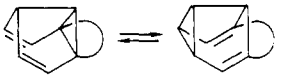
Received February 2, 1988

The concept of homoaromaticity was first proposed by Doering[1] over three decades ago. The idea was generalized

and the term "Homoaromaticity" was introduced three years later by Winstein.[2] Since that time there has been extensive interest in this area.[3] The phenomenon of homoaromaticity is well accepted for charged systems.[3,4] Although many neutral molecules have been prepared where there is appreciable homoconjugative interaction,[5,6] there is much debate as to whether this interaction (in an appropriate cyclic array involving $4n + 2$ electrons) is stabilizing[7] (homoaromatic) or destabilizing.[8] The semibullvalene nucleus has long been recognized as an ideal probe for homoaromaticity. It has been suggested that semibullvalene, which undergoes degenerate Cope rearrangements through a "homoaromatic" transition state with extremely low activation energy,[9] is "the system most closely approaching the realization of homoaromatic six-electron cyclic delocalization".[5] Therefore, it appeared reasonable to study semibullvalene derivatives in the search for a neutral hydrocarbon with an authentic homoaromatic ground state. Indeed several theoretical studies have been carried out on semibullvalene and its derivatives.[10,11] This has led to the suggestion that appropriate substitution with electron-withdrawing groups will stabilize the symmetrical (homoaromatic?) structure. Several such derivatives have been prepared[12] and although the activation barrier to the Cope rearrangement has been lowered, the localized structures still appear to be the ground state. More recently, a fully substituted derivative has been prepared[13] and it is possible that this molecule may constitute the first example of a neutral homoaromatic.

The effect of a single annelation across the terminus of the semibullvalene nucleus with medium to large rings has been examined experimentally.[14] In these cases the equilibrium **1a** ⇄ **1b** is finely balanced with the low-temperature localized geometry depending upon the length and substitution pattern of the annelating chain. This localization can be rationalized by assuming the additional ring strain in **1a** or the anti-Bredt nature of **1b** dominates.

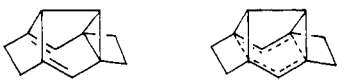


1a **1b**

Annelation onto the ethano bridge as in **2** has also been investigated theoretically[11] and in the case of the three-membered-ring species **2a**, a completely delocalized symmetrical ground state was proposed.

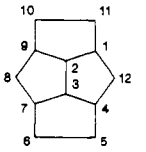
2 **2a**, $n=1$

In this study we have carried out a theoretical investigation of the effects of small-ring annelation at the termini of the semibullvalene nucleus. Specifically the potential energy surface of compound **3** was examined. It was felt that the bisannelated semibullvalene **3** was the perfect candidate for a homoaromatic ground state. In this case, for the localized geometry (e.g., 3a) considerable destabilization is predicted. One annelating ethano bridge forms a four-membered ring fused to a three-membered ring, obviously an extremely strained situation, while the other ethano bridge forces two double bonds to occur at a bridgehead that suffers a similar *anti*-Bredt destabilization to that mentioned above. In the symmetrical (delocalized) form **3b** these destabilizing interactions should be minimized.



3a **3b**

Table I. Symmetric Geometries



atom pair	dist, Å	bond order	two-center energy, eV
		MNDO Results	
1, 12	1.4087	1.4361	−20.127
1, 11	1.5111	0.9704	−15.250
1, 2	1.5294	0.9597	−14.448
2, 3	1.5454	0.9652	−14.230
10, 11	1.5753	0.9668	−14.013
1, 9	2.4990	0.2682	−0.697
		AM1 Results	
1, 12	1.3998	1.4337	−19.432
1, 11	1.4920	0.9783	−14.552
1, 2	1.5234	0.9556	−13.718
2, 3	1.5378	0.9663	−13.624
10, 11	1.5619	0.9754	−13.523
1, 9	2.2677	0.2514	−0.783

Methods

The MOPAC semiempirical electronic structure program[15] was used to carry out both MNDO[16] and AM1[17] calculations on **3**. Geometrical optimization of all internal coordinates was performed to locate the structures **3a** and **3b**. As was shown for the parent semibullvalene mole-

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Table II. Localized MNDO Geometry

atom pair[a]	dist, Å	bond order	two-center energy, eV
1, 12	1.4743	1.0477	-16.698
4, 12	1.3722	1.8111	-22.867
1, 11	1.5231	0.9631	-14.717
4, 5	1.5143	0.9697	-15.200
1, 2	1.5345	0.9430	-13.012
3, 4	1.5447	0.9515	-14.114
2, 3	1.5402	0.9737	-14.641
10, 11	1.5653	0.9744	-13.875
5, 6	1.5806	0.9587	-13.841
1, 9	1.6969	0.8128	-8.143
4, 7	2.1814	0.0458	+0.254

[a] For atom numbering, see Table I.

cule,[11] SCF theory is not capable of giving an accurate description of the delocalized form and at least a simple 2 × 2 configuration interaction (CI) involving the highest occupied (HOMO) and lowest unoccupied (LUMO) molecular orbitals is necessary.

Results

Initial MNDO–SCF calculations on compounds **3** indicated that only the localized structures are minima on the potential energy surface. The delocalized structure **3b** was only optimized by imposing the necessary symmetry constraints. This structure is a transition structure between the two localized forms and is 3.22 kcal/mol higher in energy. The MNDO-based 2 × 2 CI results also give the localized forms as minima but now the symmetric form is also a minimum. The calculated ΔH_f was 108.245 kcal/mol for the localized form and 98.877 kcal/mol for the symmetric form. More importantly, the symmetric form is 10.37 kcal/mol *lower* in energy than the localized forms. The geometries of the CI-optimized structures are given in Tables I and II.

Like the MNDO calculations the AM1–CI results indicated the symmetric form as the minimum-energy form. However, neither the AM1–SCF method nor the AM1 2 × 2–CI method was able to find a stable localized structure. The geometry of the AM1 results is given in Table I and the calculated ΔH_f is 117.049 kcal/mol. As a test of the AM1 procedure and for comparison with experimental results, calculations were done on semibullvalene itself. These results indicate the localized forms (ΔH_f(AM1) = 83.303 kcal/mol) are the minimum-energy forms with the symmetric geometry (ΔH_f(AM1) = 87.470 kcal/mol) being a transition structure. The AM1 barrier of 4.17 kcal agrees well with the previous MNDO calculation of 5.7 kcal and the experimental results of 4.8 kcal.[11]

The question that remains is whether or not the predicted symmetric double-annelated semibullvalene is homoaromatic. It is true that the ring strain and anti-Bredt character of the localized geometries will cause them to be of high energy. However, there must be some interaction causing the molecule to adopt a symmetric geometry and this may be homoaromatic stabilization. The degree of stabilization (or destabilization) associated with a particular interaction can be indicated by using the energy partitioning from the MOPAC program into one-center (atomic) and two-center (bond) terms.[18] As can be seen (Tables I and II) typical stabilizations associated with the semibullvalene type single bonds (e.g., 2–3) are approximtely −14 eV. Although the 1–9 and 4–7 interactions are much weaker it is apparent that in the symmetric (homoaromatic) system **3b** they are a stabilizing effect. For the localized form found in the MNDO calculations the 1–9 interaction is very stabilizing (corresponding to a single bond) and the 4–7 interaction is now destabilizing. It should be pointed out that the computed bond orders also indicate a favorable 1–9 and 4–7 interaction in the symmetric molecule. We, therefore, conclude that not only does the bisannelated semibullvalene **3** display appreciable homoconjugation but also that this homoconjugation is energy lowering and, therefore, **3** joins the elite ranks as a rare example of a neutral homoaromatic (ground state) hydrocarbon.

The disagreement between the MNDO and AM1 methods on the existence of a stable localized structure for the double-annelated semibullvalene **3a** is of some concern. To answer this question properly would require a more complete search of the potential energy surface in order to locate transition structures and other possible minima. Currently, this is not feasible with our version of the MOPAC program. We are, however, interested in exploring the differences between AM1 and MNDO and continuing our studies in this area by encorporating new searching routines in the MOPAC program.

Further studies are also under way using ab initio methods. It has been shown previously that to get qualitative information on other homoaromatic systems via ab inito methods, it may be necessary to use very good basis sets (including polarization function) and also to include electron correlation.[19,20] The inclusion of correlation at the second-order Moller–Plessett (MP2) level has been shown to have a dramatic effect on systems of this type.

Acknowledgment. We acknowledge computer support for this work provided by the Center for Earthquake Research and Information at Memphis State University.

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A Stereospecific Synthesis of 3-Aminodeoxystatine[1]

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Received February 2, 1988

Pepstatin (**1**), first isolated by Umezawa and co-workers in 1970,[2] is a pentapeptide that exhibits extremely potent inhibitory activity with a majority of the enzymatic family of aspartyl proteinases (for example, a K_i of 4.6×10^{-11} M vs pepsin[3]). Mechanistically, **1** derives its activity from

Iva-Val-Val-Sta-Ala-Sta-OH
1

the unusual amino acid statine (**2**), (3*S*,4*S*)-4-amino-3-hydroxy-6-methylheptanoic acid, which functions either as a "transition state"[4] or "collected substrate"[5] insert

(1) Presented, in part, at the 20th National Medicinal Chemistry Symposium, Chapel Hill, NC, June 18, 1986, Abstract #34.

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