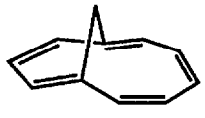
Tetrahedron Letters, Vol.30, No.3, pp 305-308, 1989 0040-4039/89 $3.00 + .00
Printed in Great Britain Pergamon Press plc

HOMOAZULENE ELECTROPHILIC AROMATIC SUBSTITUTION REACTIONS. PARALLELS TO THE CHEMISTRY OF AZULENE

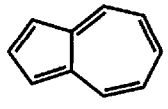
Lawrence T. Scott,* Chris A. Sumpter, Mitsunori Oda, and Ihsan Erden
Department of Chemistry and Center for Advanced Study
University of Nevada, Reno, Nevada 89557

Abstract: Homoazulene (**1**), like azulene (**2**), undergoes Friedel-Crafts acylation under exceptionally mild conditions (no Lewis acid) and exhibits the same site-selectivity as azulene; sequential disubstitution takes place exclusively at the α- and α'-positions in the smaller ring.

Homoazulene (1,5-methano[10]annulene, **1**)[1] differs constitutionally from azulene (**2**) by the formal replacement of a transannular bond with a bridging methylene group. From ^{1}H NMR spectroscopy,[1] one can see that the 10-electron cyclic π system in **1** supports a large induced diamagnetic ring current, despite the fact that it suffers significant distortion from planarity.[2] The resonance energy of **1** has also been determined from heats of hydrogenation measurements and found to be 25% of the value for benzene.[3] Thus, homoazulene can be regarded as "aromatic" on both spectroscopic and thermodynamic grounds. In fact, many of the electronic properties of homoazulene parallel the distinctive electronic properties of the prototypical nonalternate molecule, azulene, presumably as a consequence of transannular homoconjugation in **1**.[1,4] Herein we report the first chemical reactions of homoazulene and note that the parallels between **1** and **2** extend now even to the chemistry of the two systems.



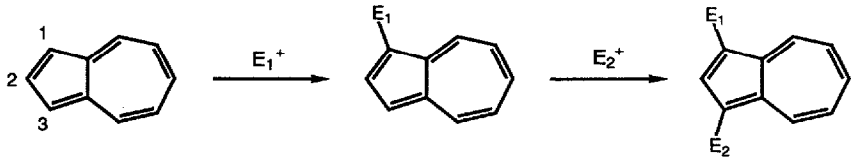
1



2

Azulene undergoes electrophilic aromatic substitution at the α-position in the smaller ring with a wide range of reagents under exceptionally mild conditions (no Lewis acid required).[5] Further substitution introduces a second group more slowly at the α'-position in the same ring to give 1,3-disubstituted azulenes (eq 1).[5] These results are fully consistent with theoretical calculations and

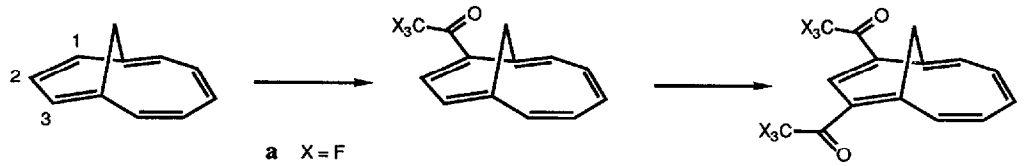
with the known polarization of azulene, which concentrates electron density in the five-membered ring.[6]



(1)

$E^+ = (CF_3CO)_2O$, $(CCl_3CO)_2O$, $C(NO_2)_4$, PhN_2^+, NBS, NCS, etc

Exposure of homoazulene to 4-5 eq of trifluoroacetic anhydride and 8-10 eq of triethylamine in methylene chloride at 0 °C for 6 min produces 1-trifluoroacetylhomoazulene **3a** as a viscous red oil in 91-95% yield.[7] As an indication of the electronic properties of the homoazulene ring system, it should be noted that the carbonyl stretching band in the infrared spectrum of **3a** appears at 1668 cm^{-1}, which is considerably lower than that for trifluoroacetylbenzene (1720 cm^{-1}), though not as low as that for trifluoroacetylazulene (1645 cm^{-1}).[5d] Trichloroacetyl chloride likewise reacts exothermically with homoazulene at 0 °C in the presence of excess triethylamine to give the corresponding 1-trichloroacetylhomoazulene **3b** as an orange-red solid in 75-89% yield.[7] In both cases, triethylamine serves to prevent the acid-catalyzed polymerization of unsubstituted homoazulene (**1**). Such rapid Friedel-Crafts acylations *under basic conditions* attest to the high susceptibility of homoazulene to electrophilic attack.



a X = F
b X = Cl

3 **4**

(2)

In comparison with the parent hydrocarbon, these acylated homoazulenes **3a** and **3b** exhibit greatly reduced sensitivity to acid and electrophiles and, unlike **1**, survive normal chromatography on silica gel. Indeed, the substitution reactions described above stop after introduction of the first trihaloacetyl group, even when excess reagent is employed. Under more forcing conditions, however, a second Friedel-Crafts acylation can be induced. Thus, 1,3-*bis*-trifluoroacetylhomoazulene (**4a**)[7] has been prepared in 40-56% yield by treatment of **3a** with trifluoroacetic anhydride and boron trifluoride etherate in ether at room temperature for several hours; the presence of polyvinylpyridine in the reaction mixture aids reproducibility.

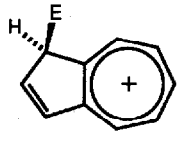
A one-pot synthesis of 1,3-*bis*-trichloroacetylhomoazulene (**4b**) directly from homoazulene has been accomplished by first acylating **1** at 0 °C in methylene chloride with 4 eq of trichloroacetyl

chloride in the presence of 2.2 eq of pyridine and then refluxing the reaction mixture for 15 h. In this manner, the doubly acylated homoazulene **4b**[7] can be obtained in 62% yield as a dark red solid, together with a 16% yield of the monoacylated homoazulene **4a**.

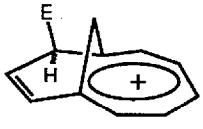
These doubly acylated homoazulenes, especially **4a**, exhibit an unexpected sensitivity toward base and water. Though protected by the electron withdrawing substituents from attack by acids and electrophiles, the π systems in **4a** and **4b** appear to be activated toward Michael addition.

Attempts to broaden the range of these electrophilic substitution reactions has so far been thwarted by the acid sensitivity of unsubstituted homoazulene (**1**). Acetic anhydride and trichloroacetic anhydride fail to react with **1** under neutral or basic conditions, but the addition of Lewis acids (*e.g.*, $SnCl_4$) simply destroys the homoazulene. N-Bromosuccinimide, nitronium tetrafluoroborate, and nitrosonium tetrafluoroborate all react uncontrollably with **1** even at -78 °C to give unidentified olefinic products.

The high reactivity and site selectivity of aromatic substitution in azulene is commonly explained by the exceptional stability of a Wheland intermediate that contains a tropylium ion (**5**).[8] The intermediacy of a homotropylium ion (**6**) in aromatic substitutions on homoazulene would explain the correspondingly high reactivity and site selectivity reported here for **1**. Direct support for this explanation was obtained by dissolving homoazulene in neat trifluoroacetic acid. An NMR spectrum of the resulting solution clearly indicated that quantitative protonation had occurred to produce homotropylium ion **6** (E = H).[9] Quenching the acid solution regenerated homoazulene. The extraordinary speed of these proton transfer reactions presumably accounts for the minimal polymerization of homoazulene in this experiment. Azulene can likewise be protonated to give tropylium ion **5** (E = H), but much stronger acids are required, *e.g.*, conc H_2SO_4 or 85% H_3PO_4.[10]



5



6

We conclude that, contrary to previous claims,[11] homoazulene does indeed undergo electrophilic aromatic substitution reactions and note that the parallels between **1** and **2** extend now even to the chemistry of the two systems.

Acknowledgment

We thank the National Science Foundation for financial support of this work.

References and Notes

1. (a) Masamune, S.; Brooks, D. W. ; Morio, K.; Sobczak, R. L. *J. Am. Chem. Soc.* **1976**, *98*, 8277.
   (b) Masamune, S.; Brooks, D. W. *Tetrahedron Lett.* **1977**, 3239.
   (c) Scott, L. T.; Brunsvold, W. R.; Kirms, M. A.; Erden, I. *J. Am. Chem. Soc.* **1981**, *103*, 5216.

2. Haddon, R. C.; Scott, L. T. *Pure Appl. Chem.* **1986**, *58*, 137.

3. Roth, W. R.; Böhm, M.; Lennartz, H.-W.; Vogel, E. *Angew. Chem. Internat. Edit. Engl.* **1983**, *22*, 1007.

4. (a) Scott, L. T.; Kirms, M. A. *J. Am. Chem. Soc.* **1982**, *104*, 3530.
   (b) Scott, L. T.; Oda, M.; Erden, I. *J. Am. Chem. Soc.* **1985**, *107*, 7213.
   (c) Scott, L. T.; Oda, M. *Tetrahedron Lett.* **1986**, *27*, 779.
   (d) Gerson, F.; Knobel, J.; Metzger, A.; Scott, L. T.; Kirms, M. A.; Oda, M.; Sumpter, C. A. *J. Am. Chem. Soc.* **1986**, *108*, 7920.

5. (a) Anderson, A. G., Jr.; Nelson, J. A.; Tazuma, J. J. *J. Am. Chem. Soc.* **1953**, *75*, 4980-4989.
   (b) Anderson, A. G., Jr.; Scotoni, R., Jr.; Cowles, E. J.; Fritz, C. G. *J. Org. Chem.* **1957**, *22*, 1193-1196.
   (c) Anderson, A. G., Jr.; Anderson, R. G.; Replogle, L. L. *Proc. Chem. Soc.* **1960**, 72.
   (d) Anderson, A. G., Jr.; Anderson, R. G. *J. Org. Chem.* **1962**, *27*, 3578-3581.
   (e) Mathias, L. J.; Overberger, C. G. *J. Org. Chem.* **1980**, *45*, 1701-1703.

6. The earliest work on this subject is reported by Brown, R. D. *Trans. Faraday Soc.* **1948**, *44*, 984.

7. All new compounds reported herein have been characterized by ^{1}H NMR, ^{13}C NMR, IR, UV, and either high resolution mass spectroscopy or combustion analysis; the ^{1}H NMR data are included here for reference purposes (ppm downfield from tetramethylsilane, $CDCl_3$ solutions): **3a** (300 MHz) δ 8.81 (d, 1H, J = 7.5 Hz), 8.22 (dd, 1H, J = 7.5, 1.7 Hz), 7.71 (dd, 1H, J = 7.4, 1.8 Hz), 7.62-7.46 (m, 3H), 7.37 (d, 1H, J = 7.4 Hz), 0.11 (d, 1H, J = 9.8 Hz), -1.04 (dd, 1H, J = 9.8, 1.7 Hz); **3b** (300 MHz) δ 8.85 (d, 1H, J = 7.7 Hz), 8.17 (dd, 1H, J = 7.7, 1.2 Hz), 8.09 (dd, 1H, J = 7.5, 1.7 Hz), 7.62-7.45 (m, 3H), 7.36 (d, 1H, J = 7.5 Hz), 0.13 (d, 1H, J = 9.8 Hz), -1.03 (dd, 1H, J = 9.8, 1.2 Hz); **4a** (60 MHz) δ 9.13 (d, 2H, J = 8.4 Hz), 8.45 (s, 1H), 7.8-7.3 (m, 3H), 0.87 (d, 1H, J = 9.8 Hz), -0.97 (d, 1H, J = 9.8 Hz); **4b** (300 MHz) δ 9.29 (s, 1H), 9.09 (d, 2H, J = 10.2 Hz), 7.84 (dd, 2H, J = 10.9, 10.2 Hz), 7.67 (t, 1H, J = 10.9 Hz), 0.88 (d, 1H, J = 9.8 Hz), -0.92 (d, 1H, J = 9.8 Hz).

8. Heilbronner, E. In "Nonbenzenoid Aromatic Compounds"; Ginsburg, D., Ed.; Interscience Publishers, Inc., New York, **1959**, Chapt 5.

9. ^{1}H NMR of **6** (E = H) in TFA (100 MHz): δ 8.77-8.35 (m, 5H, large ring hydrogens), 7.92 (d, 1H, J = 8.6 Hz, vinyl hydrogen), 7.61 (dd, 1H, J = 8.6, 1.7 Hz, vinyl hydrogen), 4.73 (d, 1H, J = 6.6 Hz, *anti* bridge hydrogen), 4.16 (d, 1H, J = 20 Hz, allylic hydrogen), 3.47 (dd, 1H, J = 20, 1.7 Hz, allylic hydrogen), 0.16 (d, 1H, J = 6.6 Hz, *endo* bridge hydrogen).

10. (a) Plattner, P. A.; Heilbronner, E.; Weber, S. *Helv. Chim. Acta* **1949**, *32*, 574-585,
    (b) Plattner, P. A.; Heilbronner, E.; Weber, S. *Helv. Chim. Acta* **1950**, *33*, 1663-1673.
    (c) Schulze, J.; Long, F. A. *J. Am. Chem. Soc.* **1964**, *86*, 322-326.
    (d) Long, F. A.; Schulze, J. *J. Am. Chem. Soc.* **1964**, *86*, 327-331.

11. Roth, W. R.; Sustmann, R. *Chem. Ber.* **1986**, *119*, 751-753.

(Received in USA 8 November 1988)