Communications to the Editor

Cyclopropabenzynes: Generation and Trapping[1]

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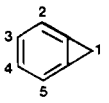
The study of strained organic molecules[2] continues[3] to provide an ever-increasing range of fascinating structural types to which we now wish to add the *o*-cyclopropabenzynes **7** and **8**.[4]

Cyclopropabenzene (**1**) and its lower homologue benzyne (**2**) constitute the most highly strained members of the ortho-bridged aromatic series of compounds. While **2** exists as a reactive



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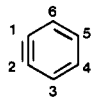


2

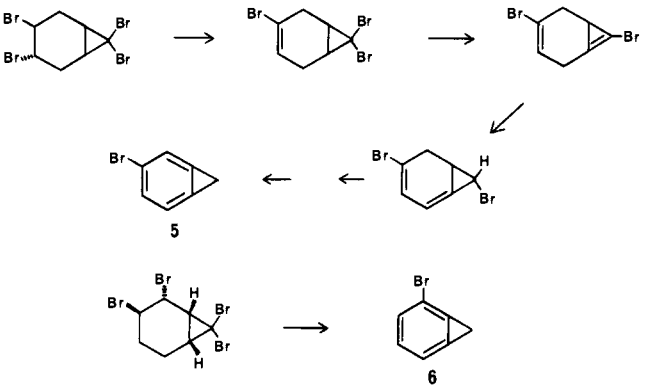
3

4

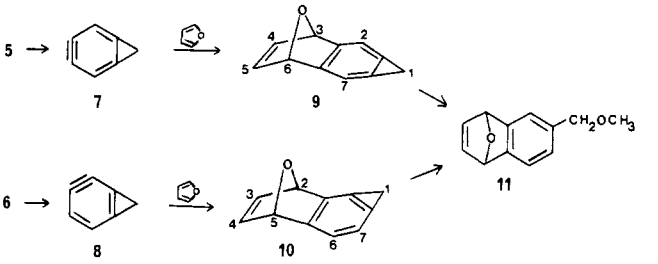
intermediate in solution[5] and has been characterized by matrix infrared studies,[6] **1** and its derivatives are surprisingly stable species[7] with strain energies[8] of approximately 68 kcal mol^{-1}. Despite many advances in the understanding of the stress, strain, and distortion that can be imposed upon the benzenoid framework, the limits to which these features can be taken have yet to be established. We have now addressed the question as to whether **1** can be strained even further and deliver didehydro derivatives capable of transient existence.

Of the strained dehydroaromatics the *o*-cyclobutabenzynes **3** and **4** have both been generated recently from *o*-bromoiodo aromatics and trapped with furan in high yields.[9] Analogous substrates are currently unavailable[7] to allow for a comparable approach to the more strained lower homologues **7** and **8**. However, 3-halocyclopropabenzenes, e.g., **5**, in Scheme I, have been known for some time[10] and their 2-isomers, e.g., **6**, have now been prepared[11] so that a potential route to the cyclopropabenzynes

Scheme I



Scheme II



7 and **8** exists by 1,2-dehydrobromination. When the classical[5] method of amide ion in liquid ammonia is employed, substrate **6** is consumed, but it is not clear whether **8** is formed since attempted trapping with furan fails to provide characterizable material.

In the search for milder and more controllable conditions the complex base *t*-BuO$^-$/NH$_2^-$ utilized by Bartsch for syn dehydrohalogenation,[12] but developed by Caubere[13a] and used by him for benzyne generation from aryl halides,[13b] appeared ideally suited to substrates **5** and **6**. In the event, treatment of **5** with the complex base at ambient temperature and in the presence of furan leads to adduct **9** (44%)[14] as an unstable oil together with unchanged starting material (29%) (Scheme II). The presence of a symmetry plane in **9** is evident from the appearance of only six resonances in the ^{13}C NMR spectrum and from the presence of a two-proton singlet (δ 7.10, H2 and H7) in the ^{1}H spectrum;[14] the Cl protons appear as an AB system (J = 2.0 Hz) in the usual[7] region of the spectrum. Ag^I-catalyzed methanolysis cleaves the three-membered ring of **9** and delivers the anticipated[7,8] epoxynaphthalene **11**,[15] whose structure has been confirmed by independent synthesis from 4-bromotoluene via 4-(methoxymethyl)benzyne.

Treatment of bromide **6** with the complex base under the same conditions leads to adduct **10** (10%),[16] which is less stable than

(1) Studies in the Cycloproparene Series. For the previous part see: Halton, B.; Officer, D. L. *Aust. J. Chem.* in press.

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(3) See, for example: Schlüter, A.-D.; Belzner, J.; Heywang, U.; Szeimies, G. *Tetrahedron Lett.* **1983**, 891-895. Gilbert, J. C.; Bage, M. E. *J. Am. Chem. Soc.* **1983**, *105*, 664-665. Gassman, P. G.; Bonser, S. M. *Ibid.* **1983**, *105*, 667-669. Wright, B. B.; Platz, M. S. *Ibid.* **1983**, *105*, 628-630.

(4) Compound **7** may also be named as bicyclo[4.1.0]hepta-1,5-dien-3-yne and compound **8** as bicyclo[4.1.0]hepta-1(6),2-dien-4-yne since "fusion" nomenclature requires cyclopropabenzene (**1**) to be named as bicyclo[4.1.0]-hepta-1,3,5-triene.

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(6) Chapman, O. L.; Mattes, M.; McIntosh, C. L.; Pacansky, J.; Calder, G. V.; Orr, G. *J. Am. Chem. Soc.* **1973**, *95*, 6134-6135. Chapman, O. L.; Chang, C.-C.; Kole, J.; Rosenquist, N. R.; Tomioka, H. *Ibid.* **1975**, *97*, 6586-6588.

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(11) Halton, B.; Randall, C. J. *Tetrahedron Lett.* **1982**, 5591-5594.

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(13) (a) Caubere, P. *Top. Curr. Chem.* **1978**, *1*, 49-124; *Acc. Chem. Res.* **1974**, *7*, 301-308. (b) Bachelet, J.-P.; Caubere, P. *J. Org. Chem.* **1982**, *47*, 234-238.

(14) Compound **9** may be named as 3,6-epoxy-3,6-dihydro-1*H*-cyclopropa[*b*]naphthalene: ^{1}H NMR δ 3.18 (d, J = 2.0 Hz, anti-Hl), 3.32 (d, J = 2.0 Hz, syn-Hl), 5.62 (t, J = 1.0 Hz, H3,6), 6.97 (t, J = 1.0 Hz, H4,5), 7.10 (s, H2,7); ^{13}C NMR δ 24.2 (Cl), 82.1 (C3.6), 109.6 (C2,7), 124.6 (Cla,7a), 143.4 (C4,5), 152.0 (C2a,6a).

(15) Compound **11** may be named as 1,4-epoxy-6-(methoxymethyl)-1,4-dihydronaphthalene. Anal. ($C_{12}H_{12}O_2$) C, H.

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9. The lack of symmetry in **10** is evidenced by the presence of 11 distinct carbon resonances and by an AB system (J_{ortho} = 6.1 Hz) in the aromatic proton region for H6 and H7.[16] Ag^{I}-catalyzed methanolysis of **10** proceeds in an apparently regiospecific manner to deliver the *same* ether, **11** (Scheme II), as is obtained from **9** and as expected on the basis of electrophilic substitution involving attack at a σ-bond.[17]

The formation of **10** from **6** must involve initial 1,2-dehydrobromination and intervention of the "angular" cyclopropabenzyne, **8**. On the other hand, the appearance of adduct **9** requires an effective and highly regioselective[18] generation of the "linear" benzyne **7** from **5**. This is in no way untoward. The bond length and angle deformations present in the cyclopropabenzenes (C1a–C5a < C1a–C2 < C3–C4 ≲ C2–C3; ∠C1a23 ~ ∠C455a ~ 110°; ∠C234 ~ ∠C21a5a ~ 126°)[7,19] and those predicted[20] for **2** (short C1–C2 bond, ∠C123 widened) complement one another in the "linear" benzyne, **7**, but not in its "angular" isomer, **8**. We take this to imply that the distortions present in **1** are accentuated further in **7** but that serious structural modification is likely in order to accommodate the "angular" isomer, **8**.

Acknowledgment. We are grateful to Professor R. A. Bartsch for helpful comment and to the New Zealand Universities Grants Committee for equipment grants.

Registry No. 5, 63370-07-0; **6**, 60040-77-9; **7**, 86921-89-3; **8**, 86921-90-6; **9**, 86921-91-7; **10**, 86921-92-8; **11**, 573-57-9.

(16) Compound **10** may be named as 2,5-epoxy-2,5-dihydro-1*H*-cyclopropa[*a*]naphthalene: ^{1}H NMR δ 3.19 (t, J = 5 Hz, CH_AH_B), 5.70 (t, J = 1.0 Hz, H2,5), 6.78 (d, J = 6.1 Hz, H7), 6.99 (t, J = 1.0 Hz, H3,4), 7.13 (d, J = 6.1 Hz, H6); ^{13}C NMR δ 18.4 (C1), 79.9/81.8 (C2/C5), 109.0 (C7), 115.0 (C1a), 120.2 (C6), 122.5 (C7a), 136.0 (C1b), 141.5/143.3 (C3/C4), 151.4 (C5a).

(17) Bee, L. K.; Garratt, P. J.; Mansuri, M. M. *J. Am. Chem. Soc.* **1980**, *102*, 7076–7079.

(18) Analysis of the ^{13}C NMR spectrum of the product mixture indicates that adduct **10** is present to an extent of ca. 2%.

(19) Allen, F. H. *Acta Crystallogr., Sect. B* **1981**, *B37*, 900–906.

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Structure of Carzinophilin. 3.[1] Structure Elucidation by Nuclear Magnetic Resonance Spectroscopy. 1

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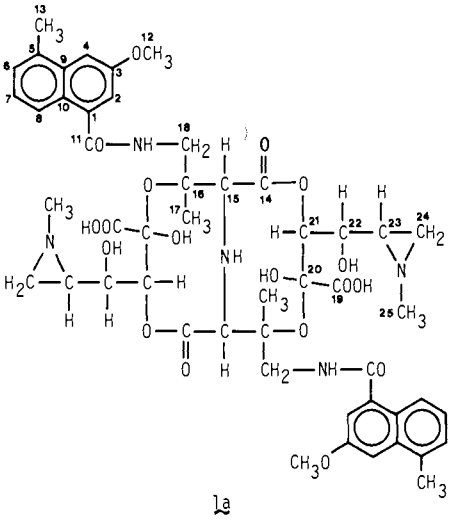
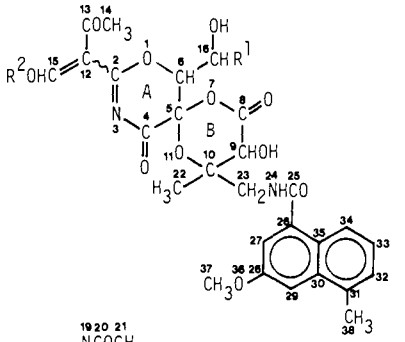
Carzinophilin (CZ, **1**) is an antitumor antibiotic isolated from *Streptomyces sahachiroi*.[2] Its molecular formula was given as $C_{60}H_{60}N_6O_{21}$,[3] which was later revised to be $C_{50}H_{58}N_5O_{18}$[4] or $C_{33}H_{35}N_3O_{12}$.[5] These formulas were based on the molecular weights obtained by Rast's method using camphor as solvent. It was therefore suspected that these scattered results were unreliable and that they might be responsible for thermal instability and low solubility of **1** in camphor. The molecular weight of **1** could not be obtained by conventional mass spectrometry. However, the molecular secondary-ion mass spectrum of dihydrocarzinophilin *p*-bromobenzoate using glycerol matrix provided the precise molecular weight[6] corresponding to $C_{31}H_{33}N_3O_{12}$ for **1**.[7] These findings suggested that the structure (**1a**) of CZ presented by Lown et al.[8] assuming the molecular formula to be $C_{50}H_{58}N_5O_{18}$ must be revised. We now report a revised structure (**1b**) for CZ.



1a

CZ (**1**) is an acidic compound. It afforded neutral carzinophilin *p*-bromobenzoate (**2**) on treatment with *p*-bromobenzoyl chloride. Hydrogenation of **1** over a platinum catalyst in dioxane afforded dihydrocarzinophilin (**3**), which provided neutral dihydrocarzinophilin *p*-bromobenzoate (**4**). The 100-MHz ^{1}H and 25.2-MHz ^{13}C NMR spectra of **1** showed 33 protons including 4 protons exchangeable with deuterium oxide and 31 carbons, respectively, which were consistent with the molecular formula

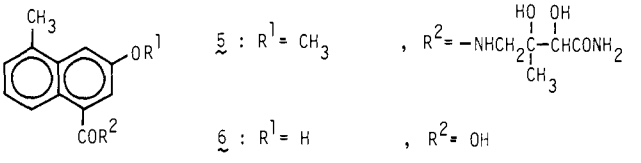


1b: R^1 = –CH(17)–CH$_2$(18)–NCOCH$_3$(19,20,21), R^2 = H

2: R^1 = –CH–CH$_2$–NCOCH$_3$, R^2 = *p*-BrC_6H_4CO–

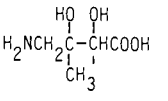
3: R^1 = –CH(17)NHCOCH$_3$(19,20,21) (CH$_3$ at 18), R^2 = H

4: R^1 = –CHNHCOCH$_3$ (CH$_3$ at 18), R^2 = *p*-BrC_6H_4CO–



5: R^1 = CH_3, R^2 = –NHCH$_2$C(HO, CH$_3$)–CHCONH$_2$(OH)

6: R^1 = H, R^2 = OH



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(1) Part 2: Onda, M.; Konda, Y.; Ōmura, S.; Hata, T. *Chem. Pharm. Bull.* **1971**, *19*, 2013.

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(3) Unpublished observation by Dr. T. Hata at The Kitasato Institute.

(4) Tanaka, M.; Kishi, T.; Maruta, Y. *J. Antibiot., Ser. B* **1959**, *12*, 361.

(5) Unpublished observation by Prof. S. Shibata at University of Tokyo.

(6) Molecular weight was obtained from *m/z* (M + Na)$^+$ 846 and 848 for $C_{38}H_{38}N_3O_{13}Br$.

(7) This formula was in accordance with elementary analysis data for CZ.

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