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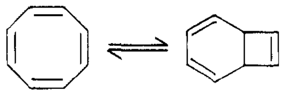
Trapping of 1,3,5,7-Cyclooctatetraene Valence Tautomers. Thermodynamic Stability of Bicyclo[4.2.0]octa-2,4,7-triene

Summary: High-temperature equilibrium constants of trapped mixtures of 1,3,5,7-cyclooctatetraene and its valence tautomer bicyclo[4.2.0]octa-2,4,7-triene were obtained by using a high-temperature thermal trapping technique and gave values for the thermodynamic parameters $\Delta S°$ and $\Delta H°$ of −4.3 ± 0.7 eu and 5.5 ± 0.6 kcal/mol, respectively.

Sir: [8]Annulene, or 1,3,5,7-cyclooctatetraene (COT) (I), because of its conjugated cyclic structure and possible antiaromatic characteristics has been the center of many theoretical and experimental studies.[1] One especially important property of COT is the chemistry of its valence tautomer bicyclo[4.2.0]octa-2,4,7-triene (II). It is through this equilibrium tautomer that much of the chemistry involving COT proceeds. Despite this extensive chemistry, the energetics of the monocyclic ⇄ bicyclic equilibrium is not well-known. While the rate of conversion of the bicyclic isomer back to COT is fairly well established ($\Delta G^\ddagger$ = 18.7 kcal/mol[2]), to date a study done by Huisgen[3] supplies the only existing information available on the energy difference between I and II. By use of an indirect method, a value of 0.01% was estimated for the equilibrium concentration at 100 °C which corresponds to $\Delta G°$ of 6.8 kcal/mol.[3] No direct experimental information is available for the enthalpy and entropy differences between these two species.[4]



I II

The extremely small equilibrium concentration of the bicyclic form has prevented direct measurement of the equilibrium constant. We would now like to report the first direct observation of high-temperature equilibrium ratios of I and II as well as the enthalpy and entropy for this equilibrium. We have used a thermal trapping technique which isolates high-temperature equilibrium mixtures at liquid nitrogen temperatures.[5] Samples thus prepared can be examined spectroscopically and equilibrium constants can be obtained directly by integration of the minor form and major form peaks.

The high-temperature equilibrium samples are obtained by passing COT vapor through an oven composed of a quartz tube (3-mm i.d.) heated over the bottom 4 cm with a tantalum resistance wire. A 10-mm tube fused at the bottom to a 5-mm NMR tube is placed around this oven such that the bottom of the oven is 2 cm from the 10–5-mm junction. The fused tube assembly and oven are connected to a vacuum system and immersed in liquid nitrogen to a level well above the top of the oven. The vapor is drawn through the oven and heated, and the high-temperature equilibrium mixture thus established is trapped on the cooled sides of the 10-mm tube. Since the pressure at the oven terminus is kept below 1 × 10^{-5} torr, no thermal reequilibration occurs before the molecules hit the sides of the tube. The oven temperature, which was measured by a chromel–alumel thermocouple positioned at the center of the oven region, was varied by 50-deg increments from 400 to 700 °C for the different thermal equilibrium runs.

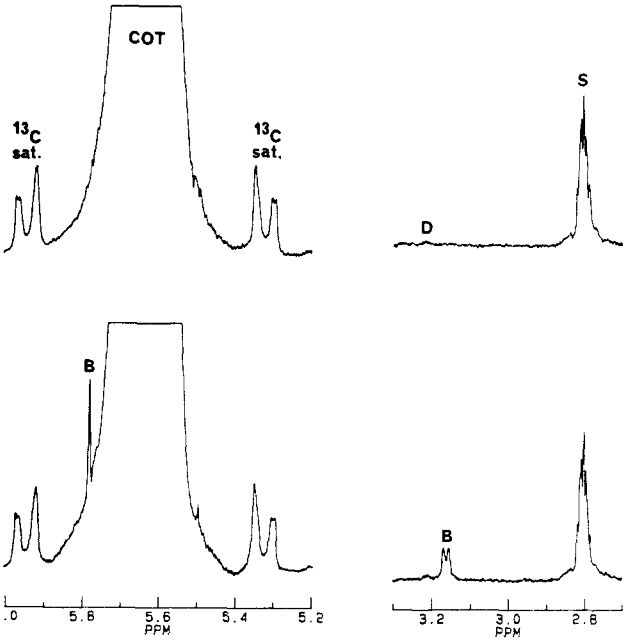


Figure 1. Bottom: ^{1}H NMR spectrum at −40 °C of COT deposited from 600 °C; resonances labeled B are due to the bicyclic tautomer. Top: Spectrum of same sample warmed to 20 °C and recooled to −40 °C. The small resonance at 3.21 ppm labeled D is due to a small amount of 1,2-dihydropentalene produced at this temperature, while the larger peak at 2.80 ppm labeled S represents a semibullvalene resonance. The other resonances of 1,2-dihydropentalene and semibullvalene are not shown.

GC-purified COT (11 mg) treated with alumina was deposited with an inlet pressure of 0.250 torr over a 2-h period. The oven was turned off and the 10–5-mm tube was warmed to −78 °C with a dry ice bath. Toluene-d_8 was slowly condensed onto the upper portion of the 10-mm tubing and rinsed the deposited COT down into the 5-mm NMR tube. The NMR tube was then cut off, capped, and stored in dry ice at −80 °C. The temperature of the tube was always kept well below −30 °C, the temperature at which the decay back to the major monocyclic form has a half-life of 2.5 h.[2,6]

Proton spectra of the thermally trapped samples were taken on a Bruker WM 250 NMR at −40 °C. Resonances due to both the monocyclic and bicyclic forms of COT were observable, as well as those due to other thermolysis products, semibullvalene, and dihydropentalene (Figure 1). Subsequent warming of the sample to room temperature caused rapid disappearance of the bicyclic form peaks. The sample was recooled to −40 °C, and a spectrum of the warmed sample was obtained (Figure 1).

Direct comparison of the trapped and warmed spectra confirm the presence of the bicyclic minor form. The observed chemical shifts correspond within expected solvent shift ranges to those observed by Vogel et al. in the original ^{1}H NMR identification.[2] The vinyl protons from the conjugated diene system are somewhat masked by the large COT resonance, but both the cyclobutene and

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(1) For reviews, see: (a) Paquette, L. A. *Tetrahedron* **1975**, *31*, 2855–2883. (b) Fray, G. I.; Saxton, R. G. *The Chemistry of Cyclo-octatetraene and Its Derivatives*, Cambridge University: Cambridge, 1978.

(2) Vogel, E.; Kiefer, H.; Roth, W. R. *Angew. Chem., Int. Ed. Engl.* **1964**, *3*, 442–443.

(3) Huisgen, R.; Mietzsch, C. F. *Angew. Chem., Int. Ed. Engl.* **1964**, *3*, 83–85.

(4) Huisgen, R.; Mietzch, F.; Boche, G.; Seidl, H. *Organic Reaction Mechanisms*; Special Publication 19; The Chemical Society: London, 1965; pp 3–20.

(5) (a) Anet, F. A. L.; Squillacote, M. E. *J. Am. Chem. Soc.* **1975**, *97*, 3243–3244. (b) Squillacote, M. E.; Semple, T. C.; Mui, P. W. *J. Am. Chem. Soc.* **1985**, *107*, 6842–6846. (c) Squillacote, M. E., Neth, J. M. *J. Am. Chem. Soc.*, in press.

(6) Olsen, H.; Snyder, J. P. *J. Am. Chem. Soc.* **1977**, *99*, 1524–1536.

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bridgehead protons are clearly observable at 5.78 and 3.15 ppm respectively. The equilibrium constant was determined at each temperature by integration of the unobscured bicyclic form doublet at 3.15 ppm (S:N > 10:1) relative to both the ^{13}C satellites of COT[7] and COT itself. As the equilibrium constants measured by integration are on the order of 10^{-3}, we are well within the dynamic range limit of the spectrometer. Integration of ^{13}C satellites served as an internal check on the accuracy of the COT integration and we found all COT–^{13}C satellite ratios to be within 5% of the naturally occurring isotope ratio, so no saturation of the COT resonance occurred. Given the 16-ms residence time for our system, the maximum free energy of activation required for equilibrium is calculated to be 45 and 31 kcal/mol at 700 and 400 °C, respectively. Both of these values are substantially higer than the reported activation energy for the COT equilibration process,[2,3,8] so complete equilibration occurs in the oven. The trapping process involves an intermolecular vibrational energy transfer at the cold surface which is known to occur with a rate of 10^{12} sec^{-1}.[9] Because this rate is considerably faster than the reequilibration rate, the trapping efficiency should be essentially unity. In fact, we have previously shown that complete trapping occurs at 20 K with a conformational mixture which reequilibrates at 45 K.[5b]

A van't Hoff plot of K_{eq} over the temperature range 400–700 °C yielded values of 5.5 ± 0.6 kcal/mol for ΔH° and -4.3 ± 0.7 eu for ΔS°. Extrapolation of our data to 100 °C yields a ΔG° value of 7.1 kcal/mol, which is in good agreement with Huisgen's indirect estimate. The relatively large entropy difference between I and II can be attributed to the different flexibilities of the two species.[10] Semibullvalene has been found to be 3.02 eu less entropically favorable than COT.[11] However, because semibullvalene can undergo a very facile Cope rearrangement[12] it would be expected to be entropically more favorable than the rigid II. Our value for ΔS° bears this out.

Also observed from our pyrolysis of COT were resonances due to both dihydropentalene and semibullvalene in amounts which varied with temperature. Semibullvalene had not been detected in previous COT flash pyrolytic studies;[13,14] however, the detection methods used in those studies (GC and IR) would not adequately resolve the expected small amounts of semibullvalene from COT. It has recently been suggested that semibullvalene is not produced directly from COT but rather through the bicyclo[3.3.0]octa-2,6-diene-4,8-diyl biradical which can also produce dihydropentalene.[12] Our results agree with these authors in that dihydropentalene must be produced via a much higher energy transition state than semibullvalene since we trap approximately 5-fold less dihydropentalene than semibullvalene. Direct production of semibullvalene from COT[15,16] is, however, not ruled out by either set of experiments. The COT ⇄ semibullvalene equilibrium may not be completely established with our system, but we see 5.0% semibullvalene, which substantially agrees with the results of Martin et al.[11] Our results establish the usefulness of this trapping technique and, due to the strong entropic contribution to ΔG°, show that temperature effects will be quite important in the synthetic chemistry of the COT system.

Registry No. I, 629-20-9; II, 4011-16-9; dihydropentalene, 91981-09-8; semibullvalene, 6909-37-1.

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[7] Anet, F. A. L. *J. Am. Chem. Soc.* **1962**, *84*, 671–672.

[8] Schröder, G.; Oth, J. M. F.; Merényi, R. *Angew. Chem., Int. Ed. Engl.* **1965**, *4*, 752–761.

[9] (a) Turro, N. J. *Modern Molecular Photochemistry*; Benjamin/Cummings: London, 1978; Chapter 6. (b) Chan, S. C.; Rabinovitch, B. S.; Bryant, J. T.; Spicer, L. D.; Fujimoto, T.; Lin, Y. N.; Pavlou, S. P. *J. Phys. Chem.* **1970**, *74*, 3160–3176.

[10] The rotational contribution to the entropy for species I and II favors II by R ln 4 due to symmetry; however, the flexibility of I compared to the extremely constrained nature of II will create a large and predominant vibrational contribution to the entropy favoring I. This contribution must also predominate for the COT–semibullvalene equilibrium.

[11] Martin, H.-D.; Urbanek, T.; Walsh, R. *J. Am. Chem. Soc.* **1985**, *107*, 5532–5534.

[12] Cheng, A. K.; Anet, F. A. L.; Mioduski, J.; Meinwald, J. *J. Am. Chem. Soc.* **1974**, *96*, 2887–2891.

[13] Jones, M.; Schwab, C. *J. Am. Chem. Soc.* **1968**, *90*, 6549–6550.

[14] Dudek, D.; Glänzer, K.; Troe, J. *Ber. Bunsenges. Phys. Chem.* **1979**, *83*, 776–788.

[15] Criegee, R.; Askani, R. *Angew. Chem., Int. Ed. Chem.* **1968**, *7*, 537.

[16] Zimmerman, H. E.; Iwamura, H. *J. Am. Chem. Soc.* **1970**, *92*, 2015–2022.

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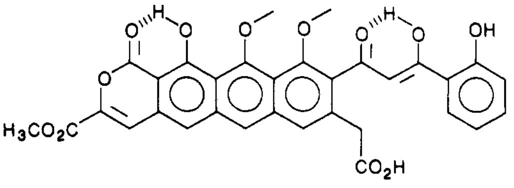
Thermorubin. 3. Synthesis of Novel Tetralone and Isocoumarin Synthons as C–D Ring Precursors to Thermorubin: An Unmasking Procedure for a Latent α-Pyrone Ring

Summary: Novel tetralone and isocoumarin synthons have been developed as C–D ring precursors to thermorubin.

Sir: Thermorubin,[1] a potent antibiotic substance of unique structure[2] (1) produced by the thermophilic fungus Thermoactinomyces antibioticus, shows selective toxicity toward procaryotic cells. Its mechanism of action involves the inhibition of protein synthesis at the level of translation, whereas DNA and RNA synthesis are unaffected.[3,4] Unlike the related tetracyclines and anthracyclines virtually all of the oxygen atoms of this achiral compound are contiguous along one edge of the molecule. This combination of unique pharmacological behavior and unusual structure has led us to investigate synthetic routes to 1.



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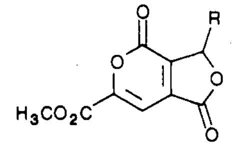

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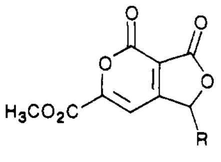

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[1] Craveri, R.; Coronelli, C.; Pagani, H.; Sensi, P. *Clin. Med.* **1964**, *71*, 511.

[2] Johnson, F.; Chandra, B.; Iden, C. R.; Naiksatam, P.; Kahen, R.; Okaya, Y.; Lin, S. Y. *J. Am. Chem. Soc.* **1980**, *102*, 5580.

[3] Pirali, G.; Somma, S.; Lancini, G. C.; Sala, F. *Biochim. Biophys. Acta* **1974**, *366*, 310.

[4] (a) Lin, F. L.; Wishnia, A. *Biochemistry* **1982**, *21*, 477. (b) Lin, F. L.; Wishnia, A. *Biochemistry* **1982**, *21*, 484.