into the known ketone **13**[11] as indicated in Scheme III. Since the latter compound has been converted into Vindorosine,[12] the present synthesis constitutes a formal route to this compound. Most important, however, is the general character of the present approach which may serve to construct a variety of indole alkaloids. Of added practical interest is the fact that the novel intermediate **11** can be prepared in three simple steps on a large scale in an acceptable yield. Studies aimed at alternative applications of the 1,5-electrocyclization/α-acyliminium route are in progress.

Acknowledgment. We express our appreciation to Professor S. Takano for sending us an authentic sample of **17**. The present investigation was carried out under the auspices of the Netherlands Foundation for Chemical Research (SON) and with financial support from the Netherlands Organization for Advancement of Pure Research (ZWO).

(10) Selected ^{1}H NMR values include the following. **8**: ^{1}H NMR ($CDCl_3$) δ 4.63 (1 H, s), 4.43 (1 H, t, J = 5 Hz), 3.06 (2 H, d, J = 5 Hz), 2.82 and 2.68 (2 H, AB, J = 17 Hz), 2.33 (3 H, s). **9**: ^{1}H NMR ($CDCl_3$) δ 8.25 (1 H, d, J = 8 Hz), 4.65 (2 H, s), 4.37 (1 H, d of d, J = 3.5 and 12.5 Hz), 3.22 and 2.82 (2 H, AB, J = 18.5 Hz), 2.77 (3 H, s). **10**: ^{1}H NMR ($CDCl_3$, 60 °C) δ 7.87 (1 H, br d, J = 7 Hz), 5.01 (1 H, d of d, J = 5 and 11.5 Hz), 3.95 (4 H, m), 3.20 (3 H, s). **11**: ^{1}H NMR ($CDCl_3$) δ 12.45 (1 H, br s), 4.72 (1 H, s), 4.19 (1 H, br), 3.84 (1 H, br, NH), 3.49 (3 H, s), 3.20 and 2.69 (2 H, AB, J = 19 Hz). **12**: ^{1}H NMR ($CDCl_3$) δ 3.88 (4 H, s), 3.53 (1 H, d of d, J = 5 and 6.5 Hz), 3.37 (1 H, t, J = 4.3 Hz), 2.65 (5 H, s).

(11) S. Takano, K. Shishido, J. Matsuzaka, M. Sato, and K. Ogasawara, *Heterocycles*, **13**, 307 (1979).

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The Spiro[2.5]oct-4-yl Cation, a Long-Lived Secondary Cyclohexyl Cation[1]

George A. Olah,* Alexander P. Fung, Tarik N. Rawdah,[1b] and G. K. Surya Prakash

Hydrocarbon Research Institute and Department of Chemistry University of Southern California Los Angeles, California 90007

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Tertiary cycloalkyl cations such as the 1-methyl-1-cyclopentyl cation show high stability in strong acid solutions and can be prepared from a variety of precursors.[2,3] While the secondary cyclopentyl cation was observed as a rapidly equilibrating degenerate ion,[4] no secondary cyclohexyl cation has yet been observed in superacid solution.[4,5] In continuation of our studies on cycloalkyl cations,[6] we wish now to report the preparation and ^{13}C NMR spectroscopic study of the spiro[2.5]oct-4-yl cation (**1**), a long-lived secondary cyclohexyl cation.

The ^{13}C NMR spectrum of the solution obtained upon ionization of spiro[2.5]octan-4-ol[7] (**2**) in SbF_5/SO_2ClF at −78 °C (Figure 1) consists of seven signals[8] at δ 201.1 (d, J_{C-H} = 170.5 Hz), 95.0 (s), 51.5 (t, J_{C-H} = 178.1 Hz), 34.9 (t), 29.3 (t), 21.0 (t), and 19.2 (t) (multiplicities are based on the proton coupled spectrum). On the basis of the observed chemical shifts and multiplicities, the spectrum is readily assigned to the spiro[2.5]oct-4-yl cation (**1**). Interestingly the same ion was obtained upon ionization of *trans*-bicyclo[4.2.0]octan-1-ol[9] (**3**) and bicyclo[4.1.0]hept-1-ylcarbinol[10] (**4**) in SbF_5/SO_2ClF at −78 or −130 °C. These results are in agreement with the solvolytic studies on spiro[2.5]oct-4-yl 3,5-dinitrobenzoate and *cis*- or *trans*-bicyclo[4.2.0]oct-1-yl 3,5-dinitrobenzoate in aqueous acetone[9] wherein ion **1** has been postulated as an intermediate. The intermediacy of the ion [1] has been assumed in the acetolysis of *cis*-bicyclo[4.2.0]oct-7-yl tosylate.[11]

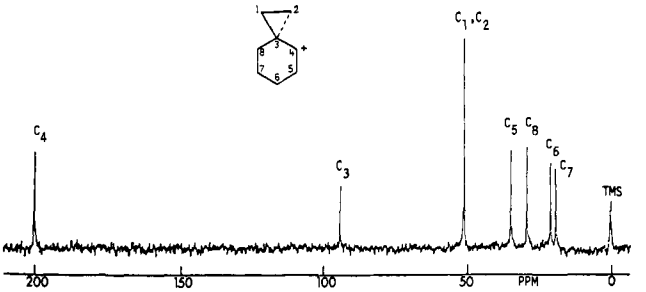
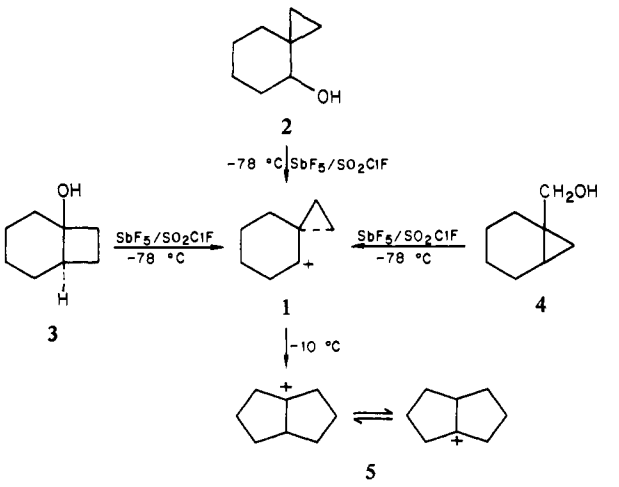


Figure 1. Proton-decoupled ^{13}C NMR spectrum of the spiro[2.5]oct-4-yl cation in SbF_5/SO_2ClF at −80 °C.



In ion **1**, the positive charge is significantly delocalized into the adjacent spiro cyclopropane ring, and correspondingly, the C-3 spiro carbon and C-1 and C-2 methylene carbons are substantially deshielded (^{13}C NMR δ 95.0 and 51.5, respectively). The equivalence of the methylene carbons (although expected in a spiro skeleton) is in accordance with a bisected geometry of the cyclopropane ring with the empty p orbital of the cationic center. The carbocationic center is also highly shielded (^{13}C NMR δ 201.1) for a static secondary carbocation. These trends are, however, in agreement with previous observations on related secondary cyclopropyl carbinyl cations.[6,12] It is also of interest to compare the ^{13}C NMR chemical shifts of cation **1** with those of the phenonium ion **6**[13] as well as the benzonortricyclyl cation **7**.[14] In the latter two cations the positive charge is, however, delocalized into the 4-π framework in addition to the spiro cyclopropane conjugation.

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(3) G. A. Olah and J. Lukas, *J. Am. Chem. Soc.*, **90**, 933-938 (1968).

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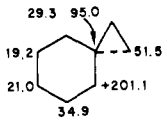

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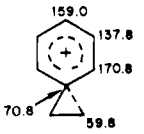

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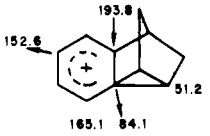

7

The secondary spiro cation **1** upon warming to −10 °C irreversibly rearranges to the thermodynamically more stable, well characterized,[15] rapidly equilibrating bicyclo[3.3.0] oct-1-yl cation (**5**). We are continuing our studies on the effect of a spiro cyclopropane ring adjacent to a carbocationic center in various medium and small sized rings.

Acknowledgment. Support of our work by the National Science Foundation is gratefully acknowledged.

(15) G. A. Olah, G. Liang, and P. W. Westerman, *J. Org. Chem.*, **39**, 367–369 (1974).

Preparation of Lactone Systems. Total Synthesis of (±)-Quadrone

Walter K. Bornack, Shripad S. Bhagwat, John Ponton, and Paul Helquist*

Department of Chemistry, State University of New York Stony Brook, New York 11794

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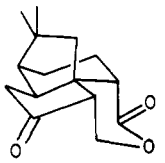
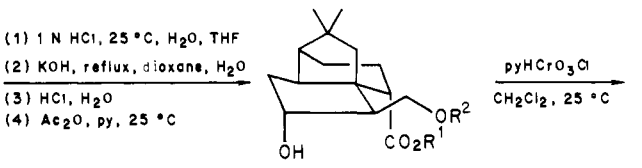
A few years ago, quadrone (**1**) was obtained as a metabolite of the fungus *Aspergillus terreus* and was found to display significant in vitro activity against KB human epidermoid carcinoma of the nasopharynx (ED_{50} 1.3 μg) and in vivo activity against P388 lymphocytic leukemia in mice. The structure of **1** was determined definitively by single-crystal X-ray diffraction, although the absolute configuration of the compound was not demonstrated.[1]



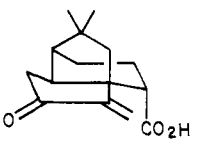
1

Because of its biological activity and the intriguing nature of its tetracyclic ring system, which includes a δ-valerolactone moiety, quadrone appeared to be an attractive synthetic target for the application of our recently developed methodology for the construction of various types of six-membered lactone ring systems.[2] However, while we were nearing the completion of our work, a synthesis was reported by Professor Danishefsky.[3] Although the basic strategy of our approach to quadrone overlaps considerably with that of the earlier synthesis, key elements of the methodology employed in the two routes are quite different. Most importantly, the use of our lactone annulation procedure[2] permits us to avoid the serious regiochemical difficulties encountered by Danishefsky in the introduction of the lactone ring of the natural product.

The starting material, 5,5-dimethylcyclopenten-3-one (**2**),[4] is subjected to copper-catalyzed 1,4-addition of vinylmagnesium bromide,[5] and the resulting enolate is trapped[6] as the trimethylsilyl enol ether **3** (Scheme I). Subsequent application of the cyclopentenone annulation procedure recently developed by Piers[7] affords the bicyclic enone **4**[8,9] in 37% overall yield for the four-step transformation (enolate regeneration, alkylation, enol ether hydrolysis, and intramolecular Horner–Emmons reaction). Through use of our approach to δ-valerolactone systems,[2] we planned next to fuse the lactone ring of quadrone onto **4**. Because of the highly folded nature of bicyclo[3.3.0]octane systems, we assumed that the overall process of 1,4-addition of the lithium enolate of methyl phenylmercaptoacetate and formaldehyde condensation would occur in a syn fashion on the convex face of the ring system. When this sequence is employed, a β-hydroxy ketone is indeed obtained in 68% yield, but lactonization with the acetate group fails to occur under the usual conditions. Instead the hydroxy ketone undergoes facile dehydration to an unstable α-methylene ketone. These findings led us to hypothesize that the 1,4-addition/condensation sequence occurs with anti stereochemistry, as confirmed by X-ray analysis of a later intermediate (vide infra). To offset these difficulties, the initially obtained hydroxy ketone, without purification, is reduced with sodium borohydride to a diol which is then protected as the acetonide to give **5**[9,10] in an overall yield of 47% from **4**. Desulfurization with lithium in liquid ammonia yields the olefinic ester **6**[9] which is modified for intramolecular alkylation by hydroboration with 9-borabicyclo[3.3.1]nonane (9-BBN),[11] tosylation of the resulting alcohol **7**,[9] and conversion of the crude tosylate into the iodo ester **8**.[9] Alkylative cyclization of the lithium enolate of **8** efficiently produces **9**,[9] having the desired α orientation of the carbomethoxy group[12] as indicated most clearly by the later X-ray analysis. Acid-catalyzed hydrolysis of the acetonide gives the dihydroxy ester **10** which may then be



10, $R^1 = CH_3$; R^2 = H (70%)
11, $R^1 = R^2$ = H (100%)
12, R^1 = H; R^2 = Ac (95%)



13 (67%)

saponified to the acid **11**. In order to confirm the stereochemical assignments made on the basis of spectroscopic data and chemical

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(7) Piers, E.; Abeysekera, B.; Scheffer, J. R. *Tetrahedron Lett.* **1979**, 3279–3282. See also: Begley, M. J.; Cooper, K.; Pattenden, G. *Ibid.* **1981**, *22*, 257–260. Klipa, D. K.; Hart, H. *J. Org. Chem.* **1981**, *46*, 2815–2816.

(8) The stereochemistry of this compound was ultimately assigned on the basis of the X-ray analysis of the later intermediate **11** but was initially inferred from the stereochemical outcome of 1,4-addition/alkylation sequences of related systems. See: Mitra, A. "The Synthesis of Prostaglandins"; Wiley: New York, 1977; pp 247–266.

(9) This compound was fully characterized spectroscopically, and the molecular composition was confirmed by elemental analysis and/or high-resolution mass spectrometry.

(10) This compound was obtained as a 1.5:1 mixture (^1H NMR) of diastereomers with respect to the relative configuration of the carbon atoms bearing the phenylthio substituent.

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(12) Although the reasons for this stereochemical result are obscure, an analogous observation was made by Professor Danishefsky.[3] If the carbomethoxy group had been introduced in the equatorial β position, we had planned to epimerize this center at a later stage in which the lactone ring had been constructed and for which the desired configuration would clearly be the more stable orientation.

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