Communications to the Editor

Valence Isomer of 4-Methoxyazulene. Synthesis of 6-Methoxytetracyclo[5.3.0.0^{2,4}.0^{3,5}]deca-6,8,10-triene

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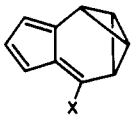
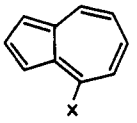
Although the synthesis and the ground- and excited-state reactions of the valence isomers[1] of benzenoid hydrocarbons have been extensively examined,[2] little attention has been paid to the chemistry of the valence isomers of nonalternant hydrocarbons. Notable early examples of such isomers were naphtho[1,8]tricyclo[4.1.0.0^{2,7}]heptene[3] and naphtho[1,8]bicyclo[3.2.0]heptene,[4] both of which are valence isomers of pleiadiene.[5] Subsequent studies of the thermal,[3b] photochemical,[3b] and transition-metal promoted reactions[3a,6] of these species have had an important influence on the development of current interest on both the electronic structures[7] and the mechanism of thermal and photochemical isomerizations.[8]

In this regard the synthesis of tetracyclo[5.3.0.0^{2,4}.0^{3,5}]deca-6,8,10-triene (**1a**),[9] a valence isomer of a representative nonalternant hydrocarbon azulene (**2a**), is of particular interest.



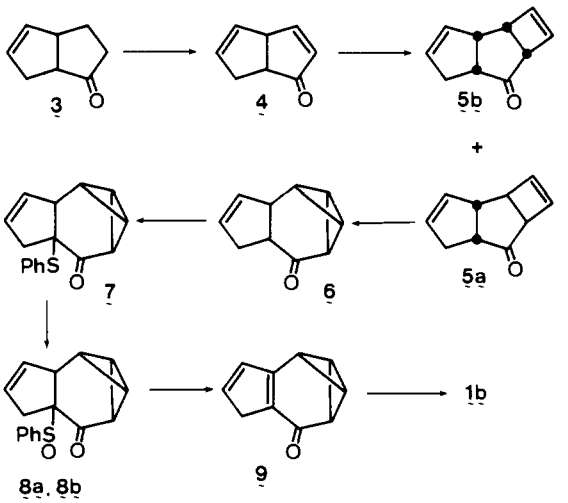
1a, X = H
1b, X = OCH_3



2a, X = H
2b, X = OCH_3

As far as the synthetic method for the valene-type isomers of cyclic conjugated systems is concerned, the utility of Katz reaction,[10] which possesses an advantage over routine construction of bicyclobutane skeleton,[11] has been well appreciated by the successful synthesis of benzvalene,[10] naphthovalene,[10] anthracenovalene,[12] naphtho[1,8]tricyclo[4.1.0.0^{2,7}]heptene,[3] and some heterocyclic systems.[13] Unfortunately, the Katz method cannot be used for the synthesis of **1** because of inaccessibility of the suitable precursor. We now report, for the first time, the realization of this goal as applied to the methoxy derivative **1b**. We envisioned early stage construction of the required bicyclobutane skeleton via oxa-di-π-methane rearrangement[14] of an appropriately designed tricyclic ketone **5a**,[15] which in turn was anticipated to be readily available via [2 + 2] photocycloaddition of the element of acetylene to bicyclo[3.0]octa-3,6-dien-2-one (**4**). Interestingly, the bicyclobutane skeleton in **9** survived without aromatization[16] to the more stable 4-methoxyazulene (**2b**) in the final synthetic step.

Scheme I



Our synthetic route is outlined in the Scheme I.[17] Introduction of an α,β-unsaturation in **3**[18] was effected with NaH and methyl *p*-toluenesulfinate in DME[20] followed by thermal elimination in refluxing benzene (68% yield). Irradiation of **4** thus obtained in 1,2-dichloroethylene (mixture of isomers) with a 450-W high-pressure Hg lamp through Pyrex afforded after 3 h to tricyclic dichloride which after column chromatography was readily converted to the desired precursor **5** in three steps [(i) ketalization (ethylene glycol/TsOH/benzene), (ii) reductive elimination of the vicinal chlorides (Na/liquid NH_3), and (iii) hydrolysis (2 N HCl/ether/8 h)]. Tricyclic ketone **5** proved to be a 9:1 mixture of stereoisomers (by ^{1}H NMR) which could be separated by column chromatography on silica gel. The major isomer (pre-

(1) For a review, see: Greenberg, A.; Liebman, J. F. "Strained Organic Molecules"; Academic Press: New York, 1978.

(2) (a) For degenerate photoinduced valence isomerizations and quantum chain processes: Renner, C. A.; Katz, T. J.; Pouliquen, J.; Turro, N. J.; Waddel, W. H. *J. Am. Chem. Soc.* **1975**, *97*, 2586. (b) For adiabatic photoreactions, see: Turro, N. J.; McVey, J.; Ramamurthy, V.; Lechtken, P. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 572. (c) For chemoexcitations, see: Lechtken, P.; Breslow, R.; Schmidt, A. H.; Turro, N. J. *J. Am. Chem. Soc.*, **1973**, *95*, 3025.

(3) (a) Murata, I.; Nakasuji, K. *Tetrahedron Lett.* **1973**, 47. (b) Pagni, R. M.; Watson, C. R., Jr. *Ibid.* **1973**, 59. (c) For the benzo analogue, see: Pagni, R. M. Burnett, K.; Hasell, A. C. *Ibid.* **1977**, 163; *J. Org. Chem.* **1978**, *43*, 2750.

(4) Meinwald, J.; Samuelson, G. E.; Ikeda, M. *J. Am. Chem. Soc.* **1970**, *92*, 7604.

(5) Boekelheide, V.; Vick, G. K. *J. Am. Chem. Soc.* **1956**, *78*, 653.

(6) Murata, I.; Nakasuji, K.; Kume, H. *Tetrahedron Lett.* **1973**, 3401, 3405.

(7) Gleiter, R.; Haider, R.; Murata, I.; Pagni, R. M. *J. Chem. Res., Synop.* **1979**, 72.

(8) (a) Watson, R., Jr.; Pagni, R. M.; Dodd, J. R.; Bloor, J. E. *J. Am. Chem. Soc.* **1976**, *98*, 2551. (b) Turro, N. J.; Ramamurthy, V.: Pagni, R. M.; Butcher, J. A., Jr. *J. Org. Chem.* **1977**, *42*, 92.

(9) We propose a trivial name "azulvalene" for **1a**.

(10) Katz, T. J.; Wang, E. J.; Acton, N. *J. Am. Chem. Soc.* **1971**, *93*, 3782. For a review on the lithium organic synthesis of benzvalene and a series of closely related compounds, see: Burger, U. *Chimia* **1979**, *33*, 147.

(11) For example: (a) Wiberg, K. B.; Ciula, R. P. *J. Am. Chem. Soc.* **1959**, *81*, 5261. (b) Moore, W. R.; Ward, H. R.; Merritt, R. F. *Ibid.* **1961**, *83*, 2019. (c) Lemal, D. M.; Menger, F.; Clark, G. W. *Ibid.* **1963**, *85*, 2529. (d) Wiberg, K. B.; Lampman, G. M. *Tetrahedron Lett.* **1963**, 2173. (e) Srinivasan, R. *J. Am. Chem. Soc.* **1963**, *85*, 4045.

(12) Gandillon, G.; Bianco, B.; Burger, U. *Tetrahedron Lett.* **1981**, *22*, 51.

(13) (a) For an isomer of 1-benzothiepin, see: Murata, I.; Tatsuoka, T.; Sugihara, Y. *Tetrahedron Lett.* **1973**, 4261. (b) For an isomer of indolizine, see: Burger, U.; Dreier, F. *Helv. Chim. Acta* **1979**, *62*, 540.

(14) Ipaktschi, J. *Chem. Ber.* **1972**, *105*, 1996. For a review, see: Houk, K. N. *Chem. Rev.*, **1976**, *76*, 1.

(15) Since an β,γ-unsaturated ketone is known to be active for photoreaction, a double bond in the cyclopentene ring must be located between 8- and 9-positions as shown in **5a** in order to effect the desired photoisomerization.

(16) Masamune, S.; Fukumoto, K.; Yasunari, Y.; Darwish, D. *Tetrahedron Lett.* **1966**, 193.

(17) All new compounds possessed satisfactory spectral data and correct analytical data by combustion or high-resolution mass spectral analysis.

(18) We have used the procedure for preparation of **3** by a modified version of that described in the following literatures: Roberts, J. D.; Gorham, W. F. *J. Am. Chem. Soc.* **1952**, *74*, 2278; Nee, M.; Roberts, J. D. *J. Org. Chem.* **1981**, *46*, 67. Thus, **3** could conveniently be prepared in 64% overall yield from bicyclo[3.2.0]hept-2-en-6-one[19] in three steps [(i) CHN_2CO_2Et/BF_3 ether, (ii) K_2CO_3/dioxane-H_2O/reflux, and (iii) separation of **3**, bp 60–64 °C (8 torr), from the isomeric bicyclo[3.3.0]oct-6-en-3-one by distillation using a spinning band column.

(19) Grieco, P. A. *J. Org. Chem.* **1972**, *37*, 2363.

(20) Coates, R. M.; Pigott, H. D. *Synthesis* **1975**, 319.

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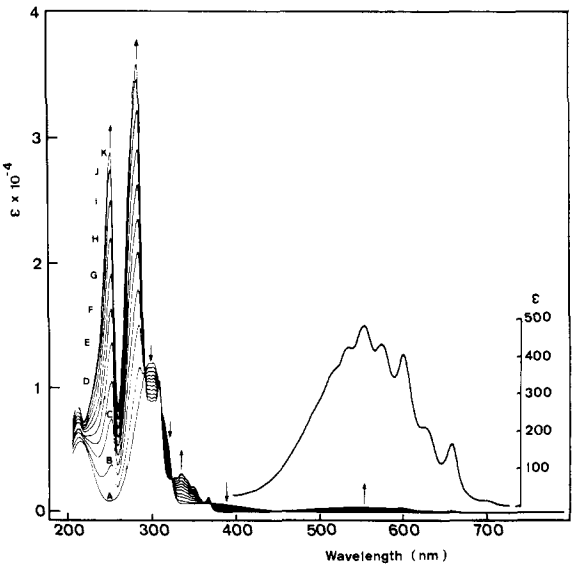

Figure 1. UV and visible spectral changes accompanying irradiation of a 4 × 10^{-5} M solution of 6-methoxytetracyclo[5.3.0.$0^{2,4}$.$0^{3,5}$]deca-6,8,10-triene (**1b**) in hexane. Features with an arrow pointing up and down are associated with the 4-methoxyazulene (**2b**) that is formed. Spectra A–K correspond to 0, 5.0, 10.5, 16.5, 23.0, 30.5, 39.5, 50.5, 65.5, 85.5, and 235.0-min irradiations.

sumably cis-anti-cis, **5a**) could be converted to bicyclobutane **6** by way of oxa-di-π-methane rearrangement (dry acetone/450-W high-pressure Hg lamp/3 h)[15,21] in 20–25% yield. Treatment of **6** with LDA at −35 °C followed by quenching at 0 °C with diphenyl disulfide[21c,d,22] afforded **7** in 73% yield. Oxidation of **7** (MCPBA/CH_2Cl_2/−78 °C) gave a 6:4 diastereomeric mixture of sulfoxide, **8a** and **8b**, quantitatively. Although the stereochemistry of each isomer was not fully characterized, the major one **8a**[23] suffers smooth elimination (CCl_4/45 °C/30 min) to afford **9** as a labile colorless liquid. With this efficient approach to the key intermediate **9** available, the stage was set to explore the crucial enol fixation. To our dismay, several usual attempts to effect O-alkylation, acylation, and silylation to the desired azulvalene[9] skeleton met with failure.[24] Success was finally achieved under very strictly controlled conditions (KO-*t*-Bu/HMPA + benzene/CH_3OFSO_2/0 °C).[25]

4-Methoxyazulvalene **1b** showed the following characteristics: air and acid-sensitive yellow plates, mp 71–73 °C (sealed capillary); MS, *m/e* 158 (M^+, 57%), 128 ($M^+ - CH_2O$, azulene cation, 100%), 115 (indenium ion, 93%); ^1H NMR (100 MHz, in $CDCl_3$ at 0 °C) δ 6.39–6.26 (m, 2 H, H-8,9), 6.10 (dd, 1 H, *J* = 2.2, 1.5 Hz, H-10), 4.08 (s, 3 H, OCH_3), 3.46 (t, 2 H, *J* = 2.5 Hz, H-3,4), 3.09 (dtd, 1 H, *J* = 4.0, 2.5, and 0.5 Hz, H-2), and 2.52 (dt, 1 H, *J* = 4.0, 2.5 Hz, H-5); UV (in hexane) λ_{max} 300 nm (ε 12 000) and 367 (689);[26] stable at room temperature under argon atmosphere.

On irradiation (100-W Hg lamp/hexane) at room temperature **1b** undergoes clean isomerization with six sharp isosbestic points (Figure 1) to 4-methoxyazulene (**2b**).[27]

In a preliminary experiment, the thermolysis of **1b** in isooctane at 110 °C was also found to produce **2b** as the final product with half-life of ca. 80 h. Whether the corresponding cyclobutene isomer is actually involved in the thermal isomerization of **1b** to **2b** as an intermediate or not could not be determined at the present stage. Further study on the detailed thermal and chemical behavior of **1b** as well as the independent synthesis of a cyclobutene isomer are being actively pursued.[28]

The preparation of a valence isomer of 4-methoxyazulene presents a new way to investigate the chemical and physical properties of this interesting molecule. The parent azulvalene **1a**, we believe, might be prepared from **1b** by way of hydride reduction, and studies are currently under way with the goal of achieving this transformation.

(21) (a) Sugihara, Y.; Morokoshi, N.; Murata, I. *Tetrahedron Lett.* **1977**, 3887. (b) *Chem. Lett.* **1979**, 745. (c) Sugihara, Y.; Sugimura, T.; Murata, I. *Ibid.* **1980**, 1103. (d) Sugihara, Y.; Yamato, A.; Murata, I. *Tetrahedron Lett.* **1981**, 3257.

(22) Trost, B. M.; Salzman, T. N.; Hiroi, K. *J. Am. Chem. Soc.* **1976**, *98*, 4887.

(23) Because of easy crystallization, the major isomer could readily be separated from the minor isomer by trituration with carbon tetrachloride.

(24) We examined here LDA/THF/Me_2SO_4, LDA/THF/$MeOFSO_2$, LDA/THF/TMSiCl, LDA/THF/CH_3COCl, and $Bu_4N^+F^-$/$Me_3SiCH_2CO_2CH_3$/THF, all to no avail.

(25) Cf.: Press, J. B.; Shechter, H. *Tetrahedron Lett.* **1972**, 2677. All solvents used are deoxygenated by bubbling with argon before use. For a typical run, to a stirred ice cooled solution of KO-*t*-Bu (purified by sublimation, 53.5 mg, 0.478 mmol) in dry HMPA (3 mL) under argon a solution of **9** (prepared from 119 mg of **8a**) in dry benzene (0.7 mL) was slowly added. After 5 min of stirring, the resulting deep yellow solution of the enolate was treated with freshly distilled methyl fluorosulfonate (ca. 0.1 mL) for 2 min. The reaction mixture was quenched with water, extracted rapidly with hexane, washed with water, and then dried ($MgSO_4$); the solvent was then removed. The residue was separated by chromatography on a short column of alumina (deactivated with 10% H_2O, 0.6 × 1 cm) with hexane into four 0.5-mL fractions. The second and third fraction afforded ~10 mg of yellow crystals which on recrystallization from hexane gave pure **1b**.

(26) 6,6-Diethoxyfulvene showed an intense absorption at 293 nm (log ε 4.26), and no band corresponding to the weak, long wavelength maximum of fulvene, which may be submerged under the long wavelength slope of the high-intensity maximum, has been reported. Hafner, K.; Schulz, G.; Wagner, K. *Justus Liebigs Ann. Chem.* **1964**, *678*, 39.

(27) Reid, D. H.; Stafford, W. H.; Ward, J. P. *J. Chem. Soc.* **1958**, 1100. Shani, A. *Isr. J. Chem.* **1975**, *13*, 53. Very recently, 4-methoxyazulene (**2b**) has been synthesized via an unambiguous method by Takase and Yasunami. We are grateful to Professors K. Takase and M. Yasunami, Tohoku University, for communicating their results prior to publication.

(28) **Note Added in Proof**: After submittion of this paper we have prepared the corresponding cyclobutene isomer of **1b** starting from **5a** through the bromination (NBS in CCl_4/azobis(isobutyronitrile)), dehydrobromination-enolate formation (2 equiv of KO-*t*-Bu in HMPA + benzene), and methylation (CH_3OFSO_2 in HMPA + benzene/0 °C) sequence. Since the cyclobutene isomer was found to be thermally stable up to 120 °C for 48 h, the intervention of this compound during the thermal isomerization of **1b** to **2b** could be ruled out.

Chirally Selective Synthesis of Sugar Moiety of Nucleosides by Chemicoenzymatic Approach: L- and D-Riboses, Showdomycin, and Cordycepin

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Naturally occurring *C*-nucleosides have attracted a great deal of synthetic study because of their unique structures of C-glycosylated heterocycles and interesting biological properties such as antibiotic, antiviral, and antitumor activity.[1] Most of the synthetic approaches have been based on the utilization of natural carbohydrate precursors.[1a] Recent progress of the synthetic approaches starting from noncarbohydrate reactants or readily available meso compounds is noteworthy in the stereocontrolled approach to the sugar moiety of nucleosides.[2] However, they require a conventional optical resolution step, and recycling of the undesired enantiomer is required in a chirally economic synthesis.[2c,3] A chirally selective approach is indeed required for

(1) (a) Hanessian, S.; Pernet, A. G. *Adv. Carbohydr. Chem. Biochem.* **1976**, *33*, 111. (b) Ohno, M. "Anticancer Agents based on Natural Product Models"; Cassady, J. M.; Douros, J. D., Eds.; Academic Press: New York, 1980; pp 73–130.

(2) (2) Noyori, R.; Sato, T.; Hayakawa, Y. *J. Am. Chem. Soc.* **1978**, *100*, 2561. (b) Just, G.; Liak, T. J.; Lim, M.-L.; Potvin, P.; Tsantrizos, Y. S. *Can. J. Chem.* **1980**, *58*, 2024 and references cited therein. (c) Schmidt, R. R.; Lieberknecht, A. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 769. (d) Gensler, W. J.; Chau, S.; Ball, D. B. *J. Am. Chem. Soc.* **1975**, *97*, 436.

0002-7863/81/1503-6739$01.25/0