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# SYNTHESIS OF THE BARBARALONE NUCLEUS VIA PHOTOCYCLIZATION OF AN ALKYNYL TROPONE†

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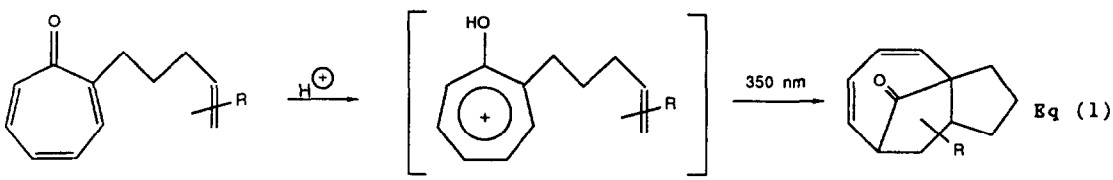
Summary: Cyclopentannulated barbaralones 5/6a-c are formed in fair to good yield upon irradiation of 2-alkynyl tropones 3a-c.

Recently, we reported that intramolecular photochemical cyclizations of various alkenyl tropones 1 afford the bridged [6π+2π] adducts 2, Eq (1).[1] The tricyclo[5.3.1.0]dodecane structures of the photoadducts are of interest to us as potential intermediates in studies directed toward the synthesis of related bicyclo[6.3.0]undecane-containing natural products.[2] As part of our investigation of the scope and utility of this novel cyclization reaction, we now have examined the photochemistry of the alkynyl tropones 3a-c,[3] Eq. (2).



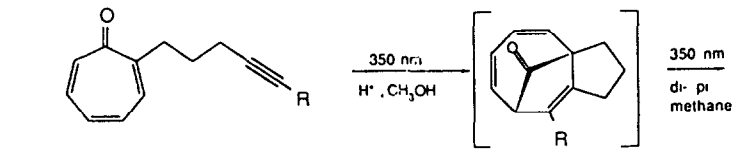

Eq (1)

1 2

To our surprise, irradiation of these tropone derivatives in aqueous acidic methanol at 350 nm did not produce the expected trienones 4a-c but rather furnished the interesting fluxional barbaralone derivatives 5/6a-c in moderate yield after chromatography.[4] We postulate that trienones 4a-c are intermediates in this process and that these trienones are rapidly converted via di-π-methane rearrangement to the barbaralone nucleus in a second photochemical step. Precedent for this latter process can be found in the conversion of the trienone

†Dedicated to Professor L. M. Jackman on the occasion of his 60th birthday.

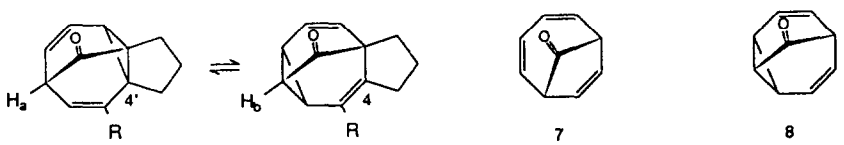
7 to the parent barbaralone 8 upon triplet-sensitized irradiation.[5] In general, the synthesis of barbaralone derivatives has utilized intramolecular carbene addition to cycloheptatrienes or functional group manipulation on the bicyclo[3.2.2]- or [3.3.1]nonane framework to deliver the desired tricycle.[6] The simplicity of our preparation of the barbaralone skeleton compares favorably with these multi-step approaches.




3 a R = $CH_3$
b R = TMS
c R = H

4 a R = $CH_3$
b R = TMS
c R = H

Eq (2)




5 a R = $CH_3$
b R = TMS
c R = H

6 a R = $CH_3$ 63 %
b R = TMS 16 %
c R = H 26 %

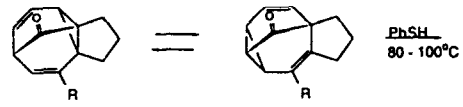
7

8

Cope rearrangement of barbaralone 5a is slow below -70°C on the 360 MHz NMR time scale. Analysis of the $^1H$ NMR spectrum at -90°C indicated that 5a and 6a exist in a 1:3 ratio. This ratio of tautomers is similar to the value reported by Schleyer for 2-methylbarbaralone, suggesting that a preference for alkyl substitution on the olefin (C-4) rather than the cyclopropyl ring (C-4') controls the position of equilibrium.[7] $^1H$ spin saturation transfer experiments at -78°C (i.e. irradiate Hb, observe Ha) allowed calculation of the activation energy of the non-degenerate Cope rearrangement of barbaralone 5a/6a.[8] The experimentally determined value of $\Delta G$ (-78°C) for the conversion of 5a into 6a is 10.7±0.1 kcal $mol^{-1}$.[9] The activation energy for the rearrangement of this cyclopentannulated barbaralone 5a is approximately 1.2 kcal $mol^{-1}$ higher than that of the parent barbaralone 8.[10] Thus, the geometrical constraints imposed by the cyclopentane ring appear to have little effect on the activation barrier for rearrangement.

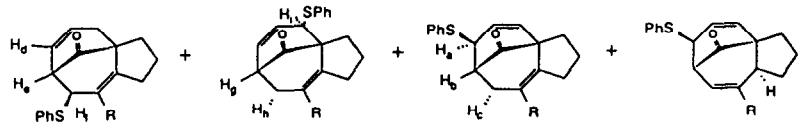
Cleavage of the cyclopropane bond joining the two alkene moieties in the barbaralones 5/6 would afford a bicyclo[6.3.0]undecane-containing carbocycle, as was initially sought in connection with our efforts in natural products synthesis. Toward this end, treatment of the fluxional barbaralones 5a/6a and 5b/6b with thiophenol at 100°C provided a static mixture of 1:1 adducts in the ratios indicated (Eq. (3)).[11] It should be noted that adducts 9a,b and 11a,b derive from regioisomeric thiophenol additions to the convex face of barbaralone tautomers 5a,b, while 10a and 10b arise from thiophenol addition to the convex face of the

isomeric barbaralones 6a,b. The adducts 9-12 are not formed through equilibration, as resubmission to the reaction conditions did not lead to interconversion of the sulfides. Free radical addition of thiophenol to the divinylcyclopropane moieties in the equilibrating mixtures 5a/6a and 5b/6b could each, in principle, lead to 20 different thiophenol adducts. However, good selectivity is observed, as only three thiophenyl ethers are produced from the methyl barbaralone 5a/6a, while four adducts are formed from the silyl barbaralone 5b/6b.




5a R = $CH_3$
b R = TMS

6a R = $CH_3$
b R = TMS



Eq (3)

| | 9 | 10 | 11 | 12 |
|---|---|---|---|---|
| a R = $CH_3$ (68 %) | 70 | 40 | 1.0 | ..... |
| b R = TMS (44 %) | 62 | 25 | 1.6 | 10 |

The regio- and stereochemistry of the thiophenol addition products were established by a combination of $^1H$ decoupling and difference NOE techniques. For example, in adduct 11a, decoupling experiments allowed assignment of Ha and Hc ($J_{ab}=J_{bc}=1$ Hz, in accord with the 90° dihedral angles), and the syn disposition of these diagnostic protons was confirmed when irradiation of Ha produced a 16% NOE in Hc. In a similar manner, irradiation of $H_f$ ($J_{ef}=1.4$ Hz) led to enhancements of 6% in $H_d$ and 3% in the vinyl methyl signal in 9a, while for 10a irradiation of $H_h$ ($J_{gh}=1$ Hz) produced an enhancement of 9% in $H_i$. Furthermore, the structural assignment of adduct 9b was confirmed by a single crystal X-ray diffraction analysis.[12]

In summary, irradiation of alkynyl tropones 3a-c produced the novel fluxional barbaralone derivatives 5/6a-c, presumably via the [6π+2π] cycloadducts 4a-c. Thiophenol addition to the barbaralone cleaves the cyclopropane ring to produce regioisomeric cyclooctadiene thioethers. These thiophenol adducts contain the bicyclo[6.3.0]undecane skeleton which is found in several cyclooctanoid natural products, and hence this two-step sequence may provide an efficent entry into this class of terpenes.

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3.) Alkynyl tropones 3a-c were prepared by the method of Funk: Funk, R. L.; Bolton, G. L. J. Am. Chem. Soc. 1986, 108, 4655.

4.) $^1$H NMR (360 MHz, $CD_2Cl_2$, -90°C) 5a: $\delta$ 5.90 (t, J=6.8 Hz, 1H), 5.70 (dd, J=6.8, 5.6 Hz, 1H), 5.52 (d, J=5 Hz, 1H), 2.96 (t, J=6.5 Hz, Ha), 1.78 (s, 3H). 6a: $\delta$ 5.64 (dd, J=8.5, 5.6 Hz, 1H), 5.56 (dd, J=8.5, 2.0 Hz, 1H), 2.20 (t, J=7.3 Hz, Hb), 1.71 (s, 3H). $^{13}$C NMR (90 MHz, $CD_2Cl_2$, -90°C) 5a: $\delta$ 211.2, 131.7, 130.6, 121.4, 120.6, 55.7, 49.4, 40.2, 38.2, 28.7, 23.4, 19.4, 19.1. 6a: $\delta$ 213.4, 142.5, 131.7, 119.2, 117.3, 57.4, 34.6, 31.2, 29.7, 27.7, 25.5, 22.8, 18.7; IR ($CCl_4$) 1705 cm$^{-1}$; mass spectrum, m/e 186 ($M^+$, 100%), 171 ($M^+-CH_3$, 82%), 158, 143, 130.

5.) Paquette, L. A.; Meisinger, R. H.; Wingard, Jr., R. E. J. Am. Chem. Soc. 1972, 94, 2155.

6.) For a survey of approaches to the synthesis of substituted barbaralones, see: Quast, H.; Schneider, E.; Mayer, A.; Jackman, L. M.; Colson, K. L. Tetrahedron 1986, in press.

7.) Barborak, J. C.; Chari, S.; Schleyer, P. v. R. J. Am. Chem. Soc. 1971, 93, 5275.

8.) Fallen, J. W., in "Determination of Organic Structures by Physical Methods" Vol. 5, eds. F. C. Nachod and J. J. Zuckerman, Academic Press, New York, 1973, p. 75.

9.) The rate constant for conversion of 5a into 6a was determined to be 3.84 s$^{-1}$. $\Delta G^{\ddagger}$ was calculated using the Eyring equation. The spectrometer probe temperature was calibrated using a standard methanol sample.

10.) Lambert, J. B. Tetrahedron Lett. 1963, 1901.

11.) The thiophenol adducts 9-12 all exhibited satisfactory $^1$H NMR, IR, and mass spectral data.

12.) Crystal data for 9b. $C_{21}H_{26}OSSi$; M 354.6; orthorhombic; space group Pbca; a=12.965(3), b=11.565(2), c=26.316(3) A; V=3945.8 A$^3$; Z=8; $D_{calc}$=1.19 gcm$^{-3}$, Enraf Nonius CAD4 diffractometer, MoK$\alpha$ ($\lambda$=0.71073 A) radiation, $\mu$=2.2 cm$^{-1}$; 2189 observed data [I>3$\sigma$(I)] refined to a conventional R=0.040 ($R\omega=[\Sigma w\Delta^2/\Sigma F_o^2]^{\frac{1}{2}}=0.052$).


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