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Organic & biomolecular chemistry, 2004, 2, 2421-2425 - Reproduced by permission of The Royal Society of Chemistry (RSC)
Kinetic stabilization of the o-quinoidal 3,4-benzotroponene system

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Received 2nd June 2004, Accepted 24th June 2004
First published as an Advance Article on the web 2nd August 2004

Kinetic stabilization of the o-quinoidal 3,4-benzotroponene system was investigated. The parent 3,4-benzotroponene 1 undergoes rapid [π8 + π10] dimerization in fluid solution even at −78 °C while triptycene-fused derivative 5 having a tert-butyl group at the C(6) position of the tropone moiety was found to be stable indefinitely under similar conditions. The relative importance of the triptycene moiety and the tert-butyl group in 5 for the kinetic stabilization was evaluated.

Introduction

3,4-Benzotropones, in which the benzo component is fused to the tropone ring in a manner to form an o-quinoidal structure, have long been a subject of theoretical1 and experimental2–3 interest. We have previously reported4 the generation of the parent 3,4-benzotroponene 1 using the electrocyclic ring-opening reaction of the corresponding benzo cyclobutene isomer 2. UV-vis and IR spectroscopic studies have revealed that 1 is electronically significantly polarized in the ground state, consistent with a substantial contribution of polarized resonance structure 1b. Despite the unique electronic structure, however, the thermal instability of 1 has thwarted the exploration of its physical and chemical properties; 1 is persistent only under matrix isolation conditions at low temperature and is rapidly consumed in fluid solution even at −78 °C. We were interested in investigating the kinetic stabilization5 of 1 to gain a more detailed understanding of this system. The lability of o-quinoidal 1 arises from its high propensity to undergo dimerization to form dimers 3 and 4. This tendency suggests that the system may be kinetically stabilized, to some extent at least, by introducing sterically demanding substituents that specifically shield the reaction sites, and we designed derivatives 5–8. Herein we report the results of synthetic investigation of 5–8 aimed at generating the kinetically stabilized derivatives of 1.

Results and discussion

A major path of the thermal decomposition of 1 is a kinetically controlled [π8 + π10] dimerization at the 2,5- and 2,7-positions to form 3 and 4.4 To prevent such dimerization, triptycene-fused derivative 5 having a tert-butyl group at the C(6) position was designed as an initial target molecule. Related compounds 6 and 7 were also investigated to evaluate the relative importance of the tert-butyl group and the fused triptycene moiety for the kinetic stabilization of this system.

On the basis of our previous successful generation of 1 from the corresponding benzo cyclobutene valence isomer 2, we envisaged 13 as a promising precursor for 5, and 13 was prepared as outlined in Scheme 1. Thus, addition of benzyle to 9 afforded triptycene derivative 10 in 73% yield. Bromination of 10 followed by dehydrobromination and deprotection afforded enone 12 in 47% yield. 1,2-Addition of tert-butyllithium to 12 followed by PCC oxidation produced 13 in 61% yield. On the other hand, 1,2-addition of tert-butyllithium to 21 followed by PCC oxidation produced 14 in 58% yield (Scheme 2).

The photochemical generation of 5 from 13 was examined under matrix isolation conditions at low temperature and the reaction was monitored by UV-vis spectroscopy. When a degassed EPA (a 5:5:2 mixture of ether, isopentane, and ethanol) solution of 13 in a Pyrex tube was frozen at liquid nitrogen temperature (−196 °C) and irradiated with a high-pressure mercury lamp, a new absorption extending to long-wavelength region with λmax around 450 nm was observed (Fig. 1). This newly developed absorption is almost superimposed on that reported4 for 1 with λmax at 353, 372, 392, 458, 482 (sh), 506 (sh) and 518 (sh) nm. Similarly, irradiation of 12 or 14 in an EPA glass at −196 °C led to the development of a new absorption characteristic of the 3,4-benzotroponene system (see experimental section). Thus, we concluded that 3,4-benzotroponene derivatives 5, 6 and 7 were generated photochemically from 13, 12 and 14, respectively. The generated orange species 5–7 were stable in the frozen EPA glass, but were consumed smoothly in the fluid EPA solution at 0 °C. The decay of the absorption followed second-order kinetics (Fig. 2), so that dimer formation should be still a dominant pathway for their thermal decomposition. The rate constants (Table 1) for the dimerization of 5, 6 and 7 in EPA at 0 °C were determined to be 30 ± 6 M−1 s−1, 166 ± 33 M−1 s−1 and 60 ± 12 M−1 s−1, respectively. These observations demonstrate that
of 18 with 1-(ethynylsulfonyl)-4-methylbenzene followed by dehydrogenation gave 19 in 83% yield. Bromination of 19 followed by dehydrobromination and deprotection afforded 21 in 52% yield.

1,2-Addition of tert-butyllithium to 21 followed by PCC oxidation produced 22 in 32% yield.

The photochemical generation of 8 from 22 was examined as described for 5–7. However, unexpectedly, when a degassed EPA solution of 22 in a Pyrex tube was irradiated with a high-pressure mercury lamp at −196 °C, development of no absorption extending to long-wavelength region characteristic of the 3,4-benzotropones system was observed, even after prolonged irradiation. Molecular modeling suggests that 8 would be distorted from its ideal planar structure due to the steric repulsion between the tert-butyl group at the C(2) position and the hydrogen atom at the peri-position (Scheme 4). To relieve the steric repulsion, 8 may undergo, if it is generated, rapid pericyclic ring-closing photochemical reaction to form norcaradiene derivative 23. A similar photochemical transformation has been reported for related compounds.\(^\text{25c}\)
Scheme 3 (a) (E)-1,4-dichloro-2-butene, hv, 12 °C, 10 h, 82%; (b) ethylene glycol, TsOH, refluxing benzene, 2 h, 91%; (c) r-BuOK, 18-crown-6, THF, room temperature, 3 h, 95%; (d) 1-ethylthio-2-phenylcyclopentene, refluxing benzene, 5 h, 83%; (e) PyBBr₃, dichloromethane, room temperature, 40 h, then r-BuOK, 18-crown-6, refluxing THF, 5 d, 61%; (f) aqueous HCl, THF, 50 °C, 15 h, 86%; (g) r-BuLi, THF, −78 °C, 1 h, then PCC, dichloromethane, room temperature, 46 h, 32%.

Scheme 4 A possible explanation for the non-observation of 8.

Conclusions
The lability of α-styrenoid 3,4-benzotropolone 1 arises from its high propensity for undergoing dimerization and this tendency suggests that the system may be kinetically stabilized by introducing sterically demanding substituents that specifically shield the reaction sites. In fact, the skeleton of 1 is kinetically stabilized in derivatives 5–7. The related stabilities of 5–7 in EPA at 0 °C indicate that the tert-butyl group at the C(6) position is more effective than the fused-tetrahydrofuran moiety for kinetic stabilization of the 3,4-benzotropolone system. Preparation of 8 having two tert-butyl groups at the C(2) and C(6) positions of the tropone moiety was also examined using the corresponding benzocyclobutene derivative 22 as a precursor. However, photochemical generation of 8 from 22 could not be confirmed even under matrix isolation conditions at low temperature, possibly because of the photochemical lability of 8 for intramolecular rearrangement.

Experimental
General
1H and 13C NMR spectra were recorded at 300 and 75 MHz, respectively, on a JEOL EX-300 spectrometer using tetramethylsilane as an internal reference. IR spectra were taken on a Hitachi 139.36, 140.51, 145.04, 145.10, 145.42, 145.48, 145.87 and 147.05; δC 31.92, 45.30, 51.64, 54.55, 54.65, 63.97, 65.10, 115.63, 117.97, 139.36, 140.51, 143.38, 144.79, 145.25, 145.27, 145.32, 145.55 and 145.58; m/z (FD) 376 (M⁺, 100%).

Scheme 4 -1,4-bicyclo[3.2.0]hept-6-en-2-one ethylene acetal (10). To a solution of 10 (1.33 g, 3.51 mmol) in dichloromethane (80 mL) was added pyridinium tribromide (1.13 g, 3.51 mmol) in portions, and the mixture was stirred at room temperature for 5 h and then poured into 10% aqueous Na₂SO₄ (100 mL). The organic layer was separated, washed with brine (100 mL), dried with Na₂SO₄, and concentrated. The residue was dissolved in 100 mL of dry THF and used for the next reaction without further purification. To the THF solution was added potassium tert-butoxide (3.39 g, 30 mmol) and the mixture was refluxed for 20 h, cooled to room temperature, and evaporated. Water (80 mL) was added to the residue and the mixture was extracted with ethyl acetate (2 × 100 mL). The extracts were combined, washed with brine (100 mL), dried with Na₂SO₄, and concentrated. The residue was chromatographed on silica gel eluted with ethyl acetate/hexane (1 : 9) to give 11 (0.68 g, 52%); mp 237–239 °C (ether); (Found 376.1463); δC 1364, 1142, 990 and 740; δC 300 MHz (CDCl₃), 3.74 (d, J = 3.8 Hz, 1 H), 3.96–4.15 (m, 4 H), 4.24 (dd, J = 3.8 and 2.5 Hz, 1 H), 5.34 (s, 1 H), 5.37 (s, 1 H), 5.50 (d, J = 5.5 Hz, 1 H), 6.30 (d, J = 5.5 and 2.5 Hz, 1 H), 6.92–6.97 (m, 4 H), 7.11 (s, 1 H), 7.24 (s, 1 H) and 7.31–7.35 (m, 4 H); δC 75 MHz (CDCl₃) 51.74, 52.64, 54.89, 54.91, 64.69, 65.79, 115.61, 118.03, 121.47, 123.76, 123.79, 123.82, 124.21, 125.42, 125.43, 125.46, 130.85, 138.87, 139.34, 139.36, 140.51, 145.04, 145.10, 145.42, 145.48, 145.87 and 147.05; m/z (FD) 376 (M⁺, 100%).

6.7-[2',3'-9',10'-Dihydro-9',10'-benzenoanthro]bicyclo[3.2.0]hepta-3,6-dien-2-one ethylene acetal (11). To a solution of 11 (0.60 g, 1.6 mmol) in THF (50 mL) was added 10% aqueous HCl (5 mL) and the mixture was heated at 50 °C for 3 h. The mixture was cooled to room temperature, diluted with chloroform (100 mL), washed successively with 10% aqueous NaHCO₃ (50 mL) and...
brine (50 mL), dried with Na2SO4, and concentrated. The residue was chromatographed on silica gel eluted with ethyl acetate/hexane (1:9) to give 12 (0.50 g, 90%). mp 256–257 °C (ether); (Found 332.1196, C20H16O2 requires 332.1191; ) (KBr/ cm−1 1696; δH (300 MHz, CDCl3) 3.97 (d, J = 3.0 Hz, 1 H), 4.45 (dd, J = 3.0 and 2.6 Hz, 1 H), 5.38 (s, 1 H), 5.95 (d, J = 5.5 Hz, 1 H), 6.95–7.00 (m, 4 H), 7.21 (s, 1 H), 7.26 (s, 1 H), 7.32–7.40 (m, 4 H) and 7.70 (dd, J = 5.5 and 2.6 Hz, 1 H); δC (75 MHz, CDCl3) 49.87, 51.83, 54.17, 54.25, 118.39, 119.54, 123.22, 123.25, 123.37, 123.41, 124.96, 123.98, 125.02, 125.07, 133.44, 137.95, 137.97, 143.22, 144.65, 144.71, 144.73, 144.79, 145.20, 161.53 and 205.06; m/z (FD) 332 (M+ 100%).

4-tert-Butyl-6,7-[2′,3′-9′,10′-dihydro-9′,10′-benzenoanthro]bicyclo[3.2.0]hepta-3,6-dien-2-one (13). To a solution of 12 (64 mg, 0.19 mmol) in dry THF (5 mL) was added 1.6 M tert-butylithium in pentane (0.24 mL, 0.38 mmol) over 1 min at −78 °C. The mixture was stirred at the same temperature for 1 h, allowed to warm to room temperature, diluted with ethyl acetate (50 mL), washed with brine (30 mL), dried with Na2SO4, and concentrated to give the crude alcohol as a brown oil (58 mg), which was diluted in 5 mL of dry dichloromethane and added to a suspension of PCC (50 mg, 0.23 mmol) in dichloromethane (2 mL). After 40 h at room temperature, ether (50 mL) was added and the mixture was filtered through a short pad of Florisil. The filtrate was washed with water (30 mL), dried with Na2SO4, and concentrated. The residue was subjected to chromatography on silica gel eluted with ethyl acetate/hexane (1:9) followed by preparative GPC (chloroform) to give 13 (45 mg, 61%); mp 280–281 °C (ether); (Found 388.1825, C20H16O2 requires 388.1823; ) (KBr/cm−1 1692, 1592 and 1460; δH (300 MHz, CDCl3) 1.26 (s, 9 H), 3.09 (d, J = 3.0 Hz, 1 H), 4.44 (d, J = 3.0 Hz, 1 H), 5.37 (s, 1 H), 5.40 (s, 1 H), 5.77 (s, 1 H), 6.96–7.00 (m, 4 H), 7.27 (s, 1 H), 7.26 (s, 1 H) and 7.33–7.39 (m, 4 H); δC (75 MHz, CDCl3) 29.08, 25.36, 49.37, 53.89, 54.33, 54.50, 119.31, 119.59, 123.39, 123.52, 123.58, 123.64, 123.75, 122.29, 121.75, 138.82, 143.87, 144.90, 144.93, 145.00, 145.05, 145.07, 145.09, 145.32, 187.28 and 204.81; m/z (FD) 338 (M+ 100%).

4-tert-Butyl-6,7-benzobicyclo[3.2.0]hepta-3,6-dien-2-one (14). To a solution of 2′ (50 mg, 0.19 mmol) in dry THF (5 mL) was added 1.6 M tert-butylithium in pentane (0.24 mL, 0.38 mmol) over 1 min at −78 °C. The mixture was stirred at the same temperature for 1 h, allowed to warm to room temperature, diluted with ethyl acetate (50 mL), washed with brine (30 mL), dried with Na2SO4, and concentrated to give the crude alcohol as a brown oil (58 mg), which was diluted in 5 mL of dry dichloromethane and added to a suspension of PCC (50 mg, 0.23 mmol) and molecular sieves 4A (50 mg) in dichloromethane (2 mL). After 40 h at room temperature, ether (50 mL) was added and the mixture was filtered through a short pad of Florisil. The filtrate was washed with water (30 mL), dried with Na2SO4, and concentrated. The residue was subjected to chromatography on silica gel eluted with ethyl acetate/hexane (1:4) by preparative GPC (chloroform) to give 14 (40 mg, 58%) as a viscous oil; (Found 388.1825, C20H16O2 requires 388.1823; ) (KBr/cm−1 1692, 1592 and 1460; δH (300 MHz, CDCl3) 1.26 (s, 9 H), 3.09 (d, J = 3.0 Hz, 1 H), 4.44 (d, J = 3.0 Hz, 1 H), 5.37 (s, 1 H), 5.40 (s, 1 H), 5.77 (s, 1 H), 6.96–7.00 (m, 4 H), 7.27 (s, 1 H), 7.26 (s, 1 H) and 7.33–7.39 (m, 4 H); δC (75 MHz, CDCl3) 29.08, 25.36, 49.37, 53.89, 54.33, 54.50, 119.31, 119.59, 123.39, 123.52, 123.58, 123.64, 123.75, 122.29, 121.75, 138.82, 143.87, 144.90, 144.93, 145.00, 145.05, 145.07, 145.09, 145.32, 187.28 and 204.81; m/z (FD) 338 (M+ 100%).

4-tert-Butyl-6,7-benzobicyclo[3.2.0]hepta-3,6-dien-2-one (14). To a solution of 2′ (50 mg, 0.19 mmol) in dry THF (5 mL) was added 1.6 M tert-butylithium in pentane (0.24 mL, 0.38 mmol) over 1 min at −78 °C. The mixture was stirred at the same temperature for 1 h, allowed to warm to room temperature, diluted with ethyl acetate (50 mL), washed with brine (30 mL), dried with Na2SO4, and concentrated to give the crude alcohol as a brown oil (58 mg), which was diluted in 5 mL of dry dichloromethane and added to a suspension of PCC (50 mg, 0.23 mmol) and molecular sieves 4A (50 mg) in dichloromethane (2 mL). After 63 h at room temperature, ether (50 mL) was added, diluted with ethyl acetate (50 mL) and Na2SO4 and concentrated. The residue was subjected to chromatography on silica gel eluted with ether/hexane (1:4) followed by preparative GPC (chloroform) to give 14 (40 mg, 58%) as a viscous oil; (Found 388.1825, C20H16O2 requires 388.1823; ) (KBr/cm−1 1692, 1592 and 1460; δH (300 MHz, CDCl3) 1.26 (s, 9 H), 3.09 (d, J = 3.0 Hz, 1 H), 4.44 (d, J = 3.0 Hz, 1 H), 5.36 (s, 1 H), 5.77 (s, 1 H), 6.96–7.00 (m, 4 H), 7.27 (s, 1 H), 7.26 (s, 1 H) and 7.33–7.39 (m, 4 H); δC (75 MHz, CDCl3) 29.08, 25.36, 49.37, 53.89, 54.33, 54.50, 119.31, 119.59, 123.39, 123.52, 123.58, 123.64, 123.75, 122.29, 121.75, 138.82, 143.87, 144.90, 144.93, 145.00, 145.05, 145.07, 145.09, 145.32, 187.28 and 204.81; m/z (FD) 338 (M+ 100%).
unchanged for more than 10 h at −78 °C, but disappeared rapidly at 510 (sh) nm. For development of a new absorption assigned to solution of precursor was observed, after irradiation for 150 min. TLC analysis of the photolysate showed complete consumption of 22 together with the formation of two products. However, preparative scale photolysis of 22 (16 mg, 0.06 mmol) in EPA (50 mL) at 12 °C resulted in the formation of a complex mixture. Similar medium dependent photochemical behavior has been reported\(^{45}\) for parent 2.

Acknowledgements

This work was partially supported by Grant-in-Aids for Scientific Research (12640508 and 15350080) from the Ministry of Education, Culture, Sports, Science, and Technology, Japan. M.O. gratefully acknowledges financial support from Shorai Foundation for Science and Technology.

References


Measurement of the electronic absorption spectra of 5–7. A solution of precursor 12, 13 or 14 in EPA was placed in a Pyrex tube and degassed by freeze-thaw cycles. The sealed tube was immersed in liquid nitrogen in a Dewar having two parallel windows facing each other and the sample was irradiated through the window with a high pressure Hg lamp. When a solution of the precursor (3.2 × 10⁻² M) in EPA was irradiated at −196 °C for 10 min, development of a new absorption assigned to 5–7 was observed. For 5: δmax 331 (sh), 353 (sh), 373, 394, 452, 473 (sh), 498 (sh) and 510 (sh) nm. For 6: δmax 331 (sh), 352 (sh), 371, 392, 445, 472 (sh), 496 (sh) and 507 (sh) nm. For 7: δmax 351, 369, 389, 453, 482 (sh), 503 (sh) and 517 (sh) nm. The absorption assigned to 5 remained unchanged for more than 10 h at −78 °C, but disappeared rapidly at 0 °C. The decay of the absorption followed second-order kinetics and the rate constant determined by monitoring the decay at 458 nm was 30 ± 6 M⁻¹ s⁻¹ in EPA at 0 °C. The molar absorptivity of 5–7 at 458 nm in EPA was estimated to be 2500 ± 500. Similarly, the rate constants for the dimerization of 6 and 7 in EPA at 0 °C were determined to be 166 ± 33 M⁻¹ s⁻¹ and 60 ± 12 M⁻¹ s⁻¹, respectively.