A Novel Synthesis of Nezukone *via* the Rearrangement of a Bicyclic Isomer: Evidence for the Intermediacy of Heptafulvenes

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The bicyclic methylenecyclopropane (2) is converted into nezukone (1) in 61% yield; evidence is presented which suggests heptafulvenes are involved in this conversion.

Tropones and heptafulvenes are of considerable synthetic and theoretical interest[1-3] and new routes to such systems continue to be developed.[1-3] The structural similarities between these two types of compound have been exploited synthetically to the extent that heptafulvenes have been prepared by the olefination of tropones.[1] However, the reverse process, *i.e.* the conversion of heptafulvenes into tropones, has received no attention as a possible route to the latter compounds. Herein, we report a novel and efficient synthesis of the naturally occurring tropone nezukone (1)[3] *via* rearrangement of the unusual bicyclic isomer (2) and provide evidence for the intermediacy of heptafulvenes of the type (3) in this conversion.

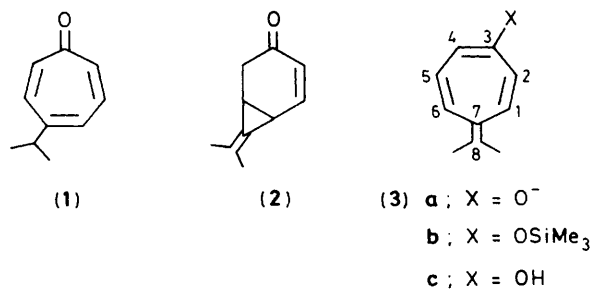The synthesis of the enone (2) began with the readily available[4] Δ³-norcarene (4) and was achieved as shown in Scheme 1.† In a reaction related to the conversion (6) → (9) (m.p. 101—102.5 °C) of this synthesis, attempted epoxidation of compound (6) afforded the hydroxyether (7) (m.p. 85—87 °C), the structure of which has been established by an X-ray determination‡ on the derived benzoate (8) (m.p. 93.5—94.5 °C).

The isomerisation of the methylenecyclopropane (2) to the tropone (1) was effected in the following manner: a solution of compound (2) (1 equiv.) in tetrahydrofuran (THF) was added to a 0.5 M solution of lithium *N*-isopropylcyclohexylamide (LiIPCA)[8] (1 equiv.) in THF containing hexamethylphosphoric triamide (HMPT) (3 equiv.) and maintained at −78 °C. The resulting solution was treated with Bu^{n}Li (1 equiv.) then chlorotrimethylsilane (3 equiv.) and allowed to warm to *ca.* 0 °C. The mixture thus obtained was quenched with tetra-n-

butylammonium fluoride trihydrate (2—3 equiv.) and the deep-red colour observed to this point was slowly discharged. Aqueous work-up followed by chromatography afforded nezukone (1) (61%). The spectral data for this compound were compared with spectra kindly provided by Professor Noyori.[3a]
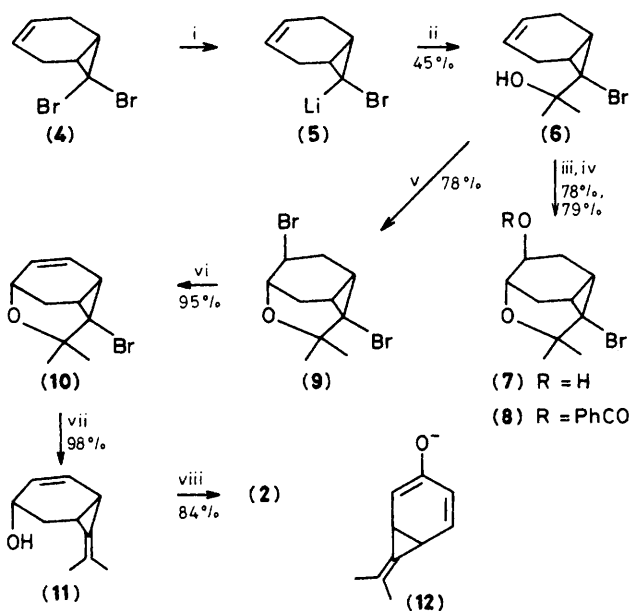
A plausible mechanism for the conversion (2) → (1) involves initial formation of the enolate ion (12) of the enone (2). The electrocyclic ring opening of ion (12) to heptafulvene (3a) is expected to occur readily[2] and presumably it is this latter species which is trapped by the added Me₃SiCl to give the silyl ether (3b). Hydrolysis of the enol ether moiety of heptafulvene (3b) followed by double-bond migration would give nezukone (1).

A number of observations support these mechanistic proposals. In particular, if the solution obtained by reaction of enone (2) with LiIPCA at −78 °C was warmed to *ca.* 0 °C, then treated with aqueous ammonium chloride prior to work-up, a very unstable deep-red oil was obtained which contained neither enone (2) nor tropone (1). The spectral data obtained

Scheme 1. *Reagents and conditions:* i, Bu^{n}Li (1 equiv.), THF, −100 °C, 1 h (ref. 5); ii, Me₂CO (1.2 equiv.), HMPT–THF (1:10), −100 °C, 3 h, then 2 M H₂SO₄ in THF (1.2 equiv.); iii, *m*-ClC₆H₄CO₃H (1.3 equiv.), NaHCO₃ (1.3 equiv.), CH₂Cl₂, 18 °C, 16 h; iv, PhCOCl (1.5 equiv.), 4-dimethylaminopyridine–pyridine (1:10), 20 °C, 16 h; v, *N*-bromosuccinimide (1.05 equiv.), CCl₄, 20 °C, 4—5 h (ref. 6); vi, 1,5-diazabicyclo[4.3.0]non-5-ene (DBN) (5.5 equiv.), PhMe, reflux, 2 h; vii, Bu^{t}Li (2.2 equiv.), THF–pentane (1:1), −100 to −35 °C over 2 h, then H₃O⁺; viii, pyridinium dichromate (3.4 equiv.), CH₂Cl₂, 20 °C, 6 h (ref. 7).

for this material are consistent with the presence of the heptafulvene (3c),§ the enol tautomer of nezukone.

Related attempts to isolate the heptafulvene (3b) were not successful. Subjection of compound (3c) to the conditions employed in the original isomerization reaction afforded nezukone in 20% overall yield from the enone (2). The low yield of compound (1) obtained by the two-step sequence (2) → (3c) → (1) can be attributed to the extensive polymerization of heptafulvene (3c) during isolation and characterization. Heptafulvenes which lack electron-withdrawing substituents at C-8 are known[1] to polymerize rapidly.

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§ Compound (3c) could not be obtained in pure form owing to its rapid polymerization, and the following data represent only those signals in the respective spectra which are attributed to the heptafulvene: δ (^{1}H; 60 MHz; CCl_4) 2.00 (s, 3H), 2.07 (s, 3H), and 5.00—7.13 (complex m, 5H) (the signal due to the hydroxy proton was not discernable); m/z (70 eV) 147 ($M - H$)$^+$, 146, 145, 121 ($M - C_2H_2$)$^{\cdot+}$, 118, 117, and 91 (C_7H_7)$^+$; $\lambda_{max.}$ (THF) 219 (log $\varepsilon \sim$3.9), 295 ($\sim$3.8), 395 (sh, $\sim$3.2), 481 (sh, $\sim$2.8), and 560 (sh, $\sim$2.5) nm.

References

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