Cyclopropanes *via* an Efficient 3-*Exo Trig* Radical Cyclisation Reaction[1]

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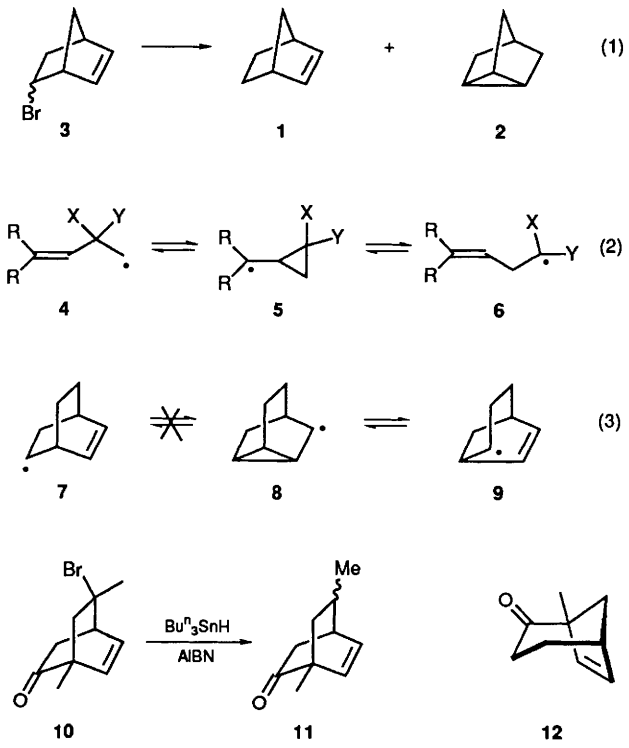
The first examples of an exclusive formation of a cyclopropane *via* the 3-*exo trig* radical cyclisation of homoallyl bromides **13** and **14** are reported.

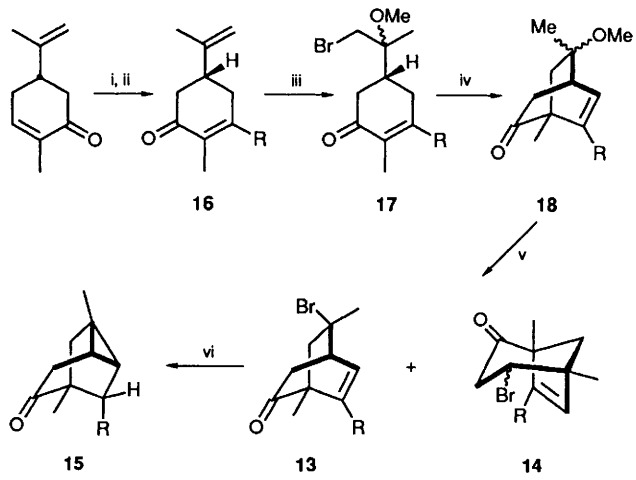
The formation of a 1:1 mixture of norbornene **1** and nortricyclene **2** from norbornenyl bromide **3** (eqn. 1) is, perhaps, the only example of a homoallyl–cyclopropylmethyl radical rearrangement (*via* 3-*exo trig* cyclisation, eqn. 2),[2,3] where a stable cyclopropane system was isolated in reasonable yields under standard radical cyclisation conditions.[4] One reason extended for the isolation of **2** in this reaction is the large strain in norbornene itself.† However, the higher homologue, the bicyclo[2.2.2]octenyl system **7**, did not undergo cyclisation (eqn. 3).[4b]† The presence of stabilising groups, such as phenyl (eqn. 2, R = Ph) induced the cyclopropane formation, albeit in low yield (≤10%).[3] Indeed, radicals were conveniently used to cleave cyclopropanes to homoallyl systems.[5] We now report the first examples of the ready formation of a cyclopropane, in the tricyclo-[3.2.1.$0^{2,7}$]octane system **8**, starting from either a bicyclo-[2.2.2]oct-5-en-2-yl radical **7** or a bicyclo[3.2.1]oct-6-en-2-yl radical **9** *via* 3-*exo trig* radical cyclisation.

In line with the earlier observation (eqn. 3)[4b] radical reaction of the bromide **10**, obtained from (*S*)-carvone as depicted in Scheme 1, under standard radical cyclisation conditions [Bu^n_3SnH, AIBN (AIBN = azoisobutyronitrile), 0.02 mol dm^{-3} in benzene] resulted in only the reduced product **11** as a mixture of diastereoisomers. The absence of any detectable amount of **12** indicates the nonexistence of any equilibrium between the initial radical formed with a cyclised radical (*e.g.*, eqn. 3). However, the presence of a stabilising group (*e.g.*, aryl) on the alkene changed the situation.

† According to molecular mechanics calculations, the strain energy (ΔSE) increase going from norbornene to nortricyclene is 21.43 kcal mol^{-1} as against an increase of 26.93 kcal mol^{-1} for the simple but-1-ene to cyclopropylmethane (1 cal = 4.184 J). The strain energy increase from bicyclo[2.2.2]octene (ΔSE 23.49 kcal mol^{-1}) and from bicyclo[3.2.1]octene (ΔSE 23.38 kcal mol^{-1}) to tricyclo[3.2.1.$0^{2,7}$] octane is intermediate between these values.



Refluxing a 0.02 mol dm^{-3} benzene solution of a 3 : 1 mixture of bromides **13a** and **14a** with Bu$^n_3$SnH (1.1 equiv.) in the presence of a catalytic amount of AIBN furnished exclusively the cyclopropane product **15a**, in 85% yield, in a stereospecific manner (Scheme 1).‡ The structure of **15a** was clearly delineated from its spectral data§ in particular the absence of alkenic protons and carbons (except the aromatic signals) in the ^{1}H and ^{13}C NMR spectra, and further confirmed by comparison of the ^{1}H and ^{13}C NMR data with those of unsubstituted compound.[6] The cyclisation takes place so readily that even the presence of 20 equivalents of a radicophile, *e.g.*, methyl acrylate, in the medium was not able to trap the initial radical and stop the cyclopropane formation. The generality of this cyclisation was established by the preparation of **15a–e** and the results are summarized in Table 1. Interestingly not only aryl groups, but even an acetylene group (entry e) stabilise the radical enough to produce only **15e**.



a; R = Ph
b; R = *p*-MeC$_6$H$_4$
c; R = *p*-MeOC$_6$H$_4$
d; R = *o*-MeOC$_6$H$_4$
e; R = PhC≡C

Scheme 1 *Reagents and conditions*: i, RMgBr, Et_2O, 0 °C to room temp., 6 h, or RLi, THF, −78 °C to room temp., 6 h; ii, PCC, silica gel, CH_2Cl_2, room temp., 8 h; iii, *N*-bromosuccinimide, CH_2Cl_2–MeOH (3 : 2), 0 °C to room temp., 16 h; iv, K$^+$ $^-$OBu^t, 1 : 1 Bu^{t}OH–THF (0.5 mol dm^{-3}), 0 °C to room temp., 16 h; v, BBr_3, CH_2Cl_2, −60 °C, 1 h; vi, Bu$^n_3$SnH, AIBN, C_6H_6 (0.02 mol dm^{-3}), reflux, 2.5 h

Table 1 Yields of various compounds (%)[a]

Entry	R	16[b]	17[c]	18[c]	13 and 14¶	15
a	Ph	75	60	76	78	85
b	*p*-tolyl	70	68	90	50	93
c	*p*-anisyl	55	87	70	45	85
d	*o*-anisyl	60[d]	70	60	55	60
e	–C≡C–Ph	50	70	68	55	82

[a] Yields refer to isolated and chromatographically pure compounds. All the compounds exhibited satisfactory analytical and spectral data. [b] Overall yield from (*S*)-carvone. [c] 1 : 1 mixture of diastereoisomers. [d] The corresponding RLi was prepared *via* orthometallation of anisole in THF (tetrahydrofuran) and TMEDA (tetramethylethylene diamine).

The radical precursors **13** and **14** were obtained from (*S*)-carvone as depicted in Scheme 1. Alkylative 1,3-enone transposition[7] of (*S*)-carvone, *i.e.*, 1,2 addition of RLi (or RMgBr) followed by oxidation [pyridinium chlorochromate (PCC)–silica gel] of the resulting allylic tertiary alcohol, furnished β-substituted carvones **16**. Transformation of **16** to the bicyclic compound **18** was achieved according to the recently developed[8] procedure, *via* regiospecific bromomethoxylation (to **17**) followed by an intramolecular alkylation (K$^+$ $^-$OBu^t–Bu^{t}OH–THF) reaction of the thermodynamic enolate. Treatment of **18** with BBr_3 generated an inseparable mixture¶ of bromides **13** and **14**. The composition of this mixture varied with the nature of R. Structures of **13** and **14** were derived from their ^{1}H and ^{13}C NMR spectroscopic

‡ The ^{1}H NMR spectrum of the crude reaction mixture (no alkenic signals) ruled out the presence of any trace amounts of uncyclised products. The ^{13}C NMR spectrum of the compound **15a** clearly established the presence of only one stereoisomer and we assigned, tentatively, the phenyl group as *endo*, since the *endo*-isomer is slightly more stable than the *exo*-isomer.

§ *Selected spectroscopic data*: 1,5-Dimethyl-6-phenyltricyclo-[3.2.1.0^{2,7}]octan-4-one **15a**. The stereochemistry of the phenyl group is tentative. Low melting (below room temperature) solid, b.p. 180 °C (bath temperature), at 0.2 torr; $[\alpha]_D$ −140° ($CHCl_3$, *c* 1.1); IR (neat) ν/cm^{-1} 3060, 1720, 760 and 710; ^{1}H NMR (270 MHz, $CDCl_3$): δ 7.25 (5H, br s, ArH), 3.45 (1H, d, *J* 2.5 Hz, 6-H), 2.68 (1H, dd, *J* 20.5, 2.2 Hz, 3a-H), 2.53 (1H, dd, *J* 20.5, 2.7 Hz, 3b-H), 1.93 and 1.99 (2H, ABq, *J* 12.9 Hz, 8-H), 1.48 (1H, dd, *J* 7.3, 2.9 Hz, 7-H), 1.35 (3H, s, 1-Me), 1.19 (1H, m, 2-H) and 1.11 (3H, s, 5-Me); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ 210.9 (s, C-4), 139.1, (s), 128.1 (2C, d), 127.5 (2C, d) and 126.8 (d) (aromatic), 55.9 (s, C-5), 53.7 (d, C-6), 43.2 (t, C-3), 34.8 (t, C-8), 26.7 (d, C-7), 20.2 (s, C-1), 19.5 (q, Me), 18.2 (d, C-2) and 17.3 (q, Me); Mass *m/z* 226 (100, M$^+$), 198 (18), 184 (25), 183 (31), 169 (35), 157 (47), 129 (32), 115 (33), 107 (25), 96 (89), 91 (61) and 77 (27); M, 226.1362.

¶ The composition of the bromides **13** and **14** varied from batch to batch. However, typical observations are as follows: when R = H, only **10** was formed; when R = Ph, a 3 : 1 mixture of **13a** and **14a**; when R = *p*-tolyl, *p*-anisyl or *o*-anisyl a 1 : 6 mixture of **13** and **14** (**14** as a mixture of diastereoisomers); and when R = –C≡C–Ph only **13e** were obtained.

data. Radical cyclisation of the bromide mixtures under standard conditions (except when R = H) furnished, exclusively, the cyclised products **15** irrespective of the composition of **13** and **14**. The yields of various intermediates along with the final radical cyclisations are listed in Table 1.

In conclusion, we have described the first examples of the formation of a cyclopropane product *via* an efficient homoallyl–cyclopropyl methyl radical cyclisation, potentially of synthetic value, which we are investigating.

Received, 7th August 1990; Com. 0/03649H

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