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Alkene-allenecyclopropane radical cyclisations promoted by tris-(trimethylsilyl)silane

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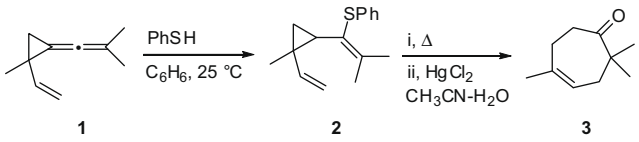
ABSTRACT

Treatment of the butenyl-substituted allenecyclopropanes **5** and **12** with tris-(trimethylsilyl)silane (TTMSS)–AIBN results in facile radical cyclisations into the cyclopropane-carbon centres of the allene moieties, followed by cyclopropane ring-opening and allene isomerisation, leading to the bicyclic 1,3-dienes **10** and **13**, respectively. By contrast, treatment of the pentenyl-substituted allenecyclopropane **15a** and the iodoethane **18** with TTMSS–AIBN, led to the alkylsilane **16**, and the enyne **21**, respectively. Desilylation of **10** and **13** gave the corresponding bicyclic hydrocarbons.

Allenes and methylenecyclopropanes are widely used in a range of useful synthetic processes, including electrophilic and nucleophilic additions, metallation reactions, cycloaddition and cyclometallation reactions, and free radical additions.[1,2] By contrast, synthetic applications of allenecyclopropanes, which incorporate both allene and methylenecyclopropane functionalities, are relatively sparse.[3] Early studies by Crandall et al.,[4] and later by others,[5] have shown that favoured cyclisation reactions involving carbon-centred radicals and allenes take place preferentially at the sp-carbon centre of the allene. In similar, related studies with methylenecyclopropanes, Kilburn et al.[6] established that the favoured radical cyclisations take place by initial addition of the carbon radical into the cyclopropane carbon centre of the methylenecyclopropane. In earlier work,[7] we showed that the C_{10}-allenecyclopropane **1**, derived from isoprene, reacted with thiophenol,[3,8] in a free-radical chain-addition process, to give exclusively the thioether **2**. The thioether **2** was then transformed into the natural product karahanaenone **3** by Cope rearrangement followed by hydrolysis of the resulting vinyl sulfide (Scheme 1). To our knowledge, no investigations of cyclisation reactions involving carbon-centred radicals and allenecyclopropanes have been reported. In this Letter we describe the formation of functionalised carbocycles resulting from intramolecular radical-mediated cyclisations involving allenecyclopropanes and alkenes promoted by tris-(trimethylsilyl)silane in the presence of AIBN.

In order to explore the scope for cyclisations involving carbon-centred radicals and allenecyclopropanes, we first decided to synthesise the substituted allenecyclopropane **5**, containing a terminal alkene group, from which the radical centre would be generated by hydrosilylation using tris-(trimethylsilyl)silane (TTMSS)–AIBN.[9] Thus, under phase–transfer conditions,[10] a solution of the known diene **4**[11] in benzene, was treated with 3-chloro-3-methylbut-1-yne[12] in the presence of aqueous KOH and debenzo-18-crown-6 at room temperature. Work-up followed by chromatography then gave the allenecyclopropane **5** in 46% yield.[13] When a solution of the allenecyclopropane **5** in dry toluene containing AIBN at 90 °C was treated with TTMSS for 2 h, the bicyclic allene **9** was produced as a 3:2 mixture of diastereoisomers in 73% yield. Interestingly, when the reaction mixture was left for longer periods of time at 90 °C, the isomeric 1,3-diene **10** was isolated instead, in similar yield (Scheme 2).



Scheme 1. Synthesis of karahanaenone **3** from the allenecyclopropane **1**.

The bicyclic allene **9** is produced from **5** by anti-Markovnikov addition of $(Me_3Si)_3Si^{\cdot}$ to the terminal alkene bond in **5**, leading to the secondary radical centre **6**, which then undergoes an intramolecular cyclisation into the allenecyclopropane group leading to the strained tricyclic vinyl radical species **7**. Fragmentation of the radical species **7**, accompanied by cleavage of the cyclopropane ring, regenerates the allene unit and leads to the tertiary radical centre **8**. The radical centre **8** is then quenched by $H^{\cdot}$ from its

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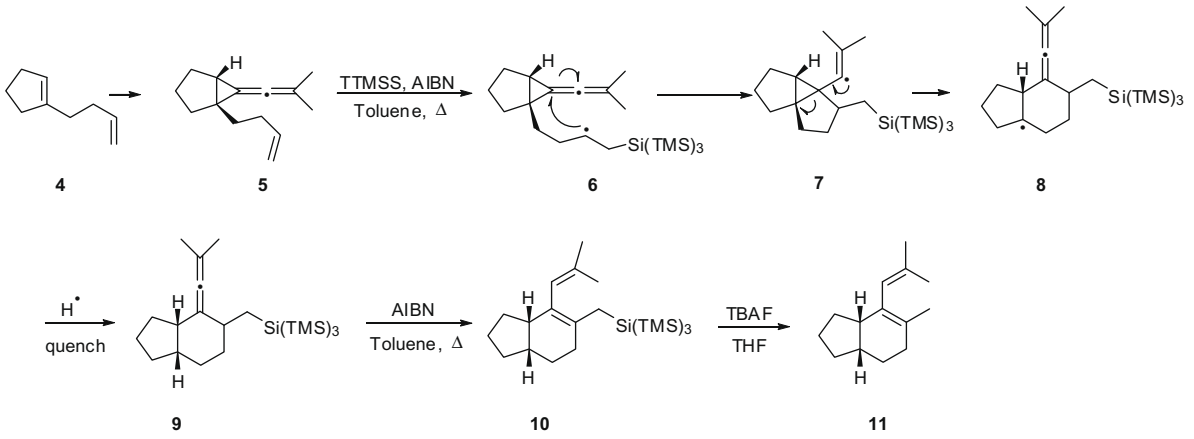
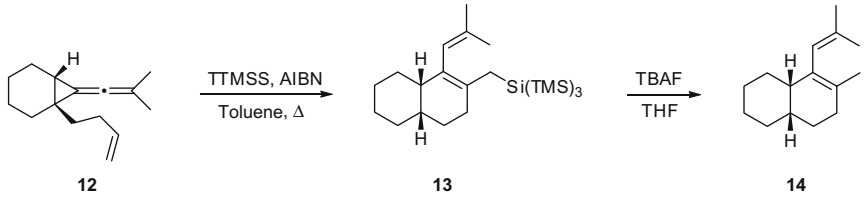


Scheme 2. Synthesis, and mechanism of formation, of the bicyclic 1,3-diene **10**.

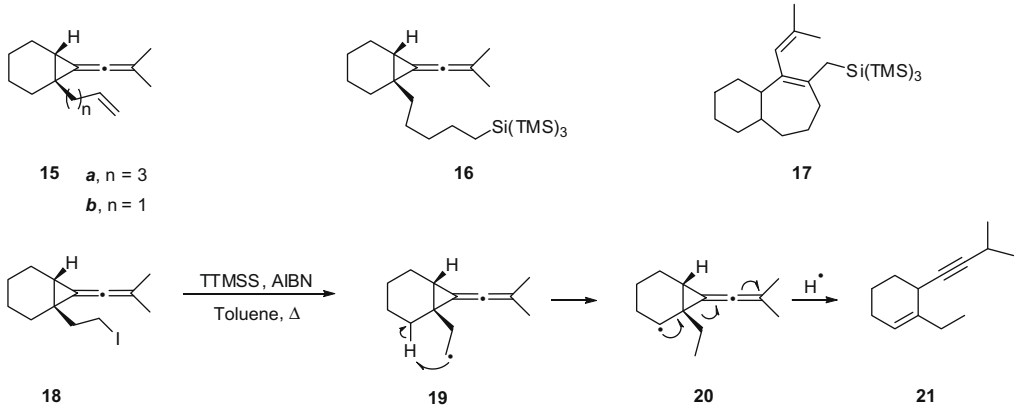
concave face producing the cis ring-fused system **9**. The major diastereoisomer of **9** could be cleanly separated by chromatography.[14] When either a mixture of the diastereoisomers of the allene **9**, or the separated diastereoisomer, was heated in toluene in the presence of a catalytic amount of AIBN, the same 1,3-diene **10** was produced,[13] interestingly as a 1:1 mixture of rotamers, in 80% yield. The 1,3-diene **10** was not obtained when the allene **9** was heated alone in toluene. Presumably, the conversion is initiated by H·-abstraction by AIBN from an allylic centre in **9**, propagated by an intermediate vinylic radical, and completed by a thermal 1,5-H shift process. Molecular models show that the rotation about the isobutenyl group in **10** is severely restricted by the proximate, sterically demanding, $-Si(SiMe_3)_3$ group, which accounts for the formation of the two rotamers of the substituted 1,3-diene. As expected, when the mixture of rotamers of **10** was desilylated, using TBAF at 9 °C, a single isomer of the corresponding hydrocarbon **11** was obtained, in 71% yield.

We next synthesised the analogous allenecyclopropane **12**, associated with a cyclohexane rather than with a cyclopentane ring, using the same synthetic steps that had been used to prepare **5**. Subsequent treatment of **12** with TTMSS–AIBN in toluene at 90 °C for 24 h, led to a 3:2 mixture of rotamers of the anticipated bicyclic 1,3-diene **13** in 62% yield.[14] Desilylation of **13**, using TBAF then gave the corresponding hydrocarbon **14** in 60% yield (Scheme 3).

To explore the scope of the interesting radical cyclisations **5**→**10** and **12**→**14**, we next synthesised the allenecyclopropane homologues **15** of **12** containing one more, that is, **15a** and one less, that is, **15b**, methylene groups in their terminal alkene side chains. To our surprise when the allenecyclopropane **15a** was treated with TTMSS–AIBN under the usual conditions the only product isolated, in 80% yield, was the alkylsilane **16** resulting from hydrosilylation of the terminal alkene unit in **15a**. None of the 1,3-diene product **17** resulting from the anticipated 7-*exo* radical cyclisation was produced, even as a minor product. Equally surprising was the observation that when the homologue **15b**, containing one carbon less than **12** in its side chain, was treated with TTMSS–AIBN, not even the product of hydrosilylation was obtained. Instead, only



Scheme 3. Conversion of the allenecyclopropane **12** into the 1,3-diene **14** via **13**.



Scheme 4. Conversion of the allenecyclopropane **15a** into the alkylsilane **16** and the iodide **18** into enyne **21**. Reaction of **15b** led to recovery of starting material.

starting material was recovered, even after prolonged reaction times. Realistically, we were not expecting to see any product resulting from a 4-*exo* radical cyclisation in **15b**, but we were hoping to observe other products resulting from competitive ring closure reactions within the allenecyclopropane ring in the starting material. We felt that one of the reasons for the failure of **15b** to react with TTMSS–AIBN could be associated with the steric demands of the bulky $Si(SiMe_3)_3$ group in the silane. In order to interrogate this system further, we decided to generate a carbon-centred radical from the corresponding iodide **18** and study its chemistry. The iodide **18** was easily available from iodination of the corresponding alcohol produced from 2-(1-cyclohexenyl)ethanol and 3-chloro-3-methyl-butyne, as described earlier. Interestingly, treatment of the iodide **18** with TTMSS–AIBN in toluene at 90 °C for 2 h resulted in the formation of the enyne **21** in 43% yield.[13] We suggest that the enyne **21** is produced from **18** by way of a rarely encountered 1,4-hydrogen abstraction process[15] from the radical intermediate **19**, leading to the cyclopropylmethyl radical centre **20** which then undergoes fragmentation to **21** (Scheme 4).

In summary, a new and interesting carbon radical cyclisation into an allenecyclopropane unit has been investigated which provides access to 5,6- and 6,6-ring-fused 1,3-dienes, for example, **11** and **14**. Efforts to extend the scope of the method to the synthesis of smaller and larger ring systems instead led to products, for example, **21** and **16**, resulting from alternative reaction pathways.

Acknowledgements

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13. All new compounds showed satisfactory spectroscopic and mass spectrometric data. Selected data: For the allenecyclopropane **5**: IR (film/cm^{-1}) ν_{max} 2999, 2905, 2850, 2010, 1641; ^1H NMR ($CDCl_3$, 250 MHz) δ (ppm): 5.90 (1H, ddt, J = 17.1, 10.3, 5.2 Hz, $CH_2{=}CHCH_2$), 5.00 (1H, dd, J = 17.1, 2.0 Hz, $CH_2{=}CHCH_2$), 4.95 (1H, dd, J = 10.3, 2.0 Hz, $CH_2{=}CHCH_2$), 2.05–2.27 (2H, m, $CH_2{=}CHCH_2$), 1.75 (6H, s, $C(CH_3)_2$), 1.27–2.02 (9H, m, $4CH_2$ + cyclopropyl CH); ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ (ppm): 187.3 (s), 138.8 (d), 114.0 (t), 96.3 (s), 86.1 (s), 36.5 (s), 33.5 (t), 33.2 (t), 31.9 (t), 30.4 (d), 29.3 (t), 22.1 (t), 21.4 (q), 21.2 (q); HRMS m/z 188.1582 [M^+], $C_{14}H_{20}$ requires 188.1565. Allene **9**: IR (film/cm^{-1}) ν_{max} 2950, 2854, 2050, 1970; ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ (ppm): (major diastereoisomer) 196.8 (s), 110.5 (s), 98.9 (s), 44.0 (d), 41.5 (d), 41.4 (d), 32.5 (t), 30.5 (t), 27.3 (t), 27.1 (t), 22.4 (t), 21.5 (q), 21.3 (q), 12.7 (t), 2.1 (q); (minor diastereoisomer) 197.5 (s), 109.0 (s), 95.8 (s), 44.7 (d), 40.3 (d), 35.8 (d), 35.1 (t), 31.6 (t), 29.7 (t), 28.6 (t), 23.0 (t), 22.0 (q), 21.8 (q), 12.1 (t), 1.9 (q); HRMS m/z 363.2352 [M^+, $C_{23}H_{48}Si_4$– $SiMe_3$], requires 363.2360. Bicyclic 1,3-diene **10**: IR ($CHCl_3/cm^{-1}$) ν_{max} 2949, 2850; ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ (ppm) (rotamer mixture): 139.7 (s), 133.9 (s), 132.7 (s), 131.7 (s), 131.6 (s), 128.7 (s), 126.8 (d), 125.4 (d), 44.5 (d), 41.6 (d), 39.0 (d), 37.0 (d), 34.0 (t), 33.4 (t), 32.0 (t), 31.3 (t), 30.0 (t), 29.6 (t), 27.3 (t), 25.2 (q), 25.1 (q), 23.9 (t), 23.7 (t), 19.8 (q), 19.6 (q), 14.5 (t), 1.4 (q), 1.2 (q); HRMS m/z 436.2816 [M^+], $C_{23}H_{48}Si_4$ requires 436.2833. Bicyclic hydrocarbon **11**: IR ($CHCl_3/cm^{-1}$) ν_{max} 2917, 2854; ^1H NMR ($CDCl_3$, 250 MHz) δ (ppm): 5.46 (1H, br s, $CH{=}C(CH_3)_2$), 2.04 (2H, m, allylic CH_2), 1.85–1.14 (10H, m, $4CH_2$ and 2CH), 1.76 (3H, d, J = 1.2 Hz, ${=}CCH_3$), 1.53 (3H, s, $={=}CCH_3$), 1.51 (3H, s, $={=}CCH_3$); ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ (ppm): 133.0 (s), 132.0 (s), 129.0 (s), 125.9 (d), 44.2 (d), 37.1 (d), 31.7 (t), 31.4 (t), 30.9 (t), 26.9 (t), 25.2 (q), 23.8 (t), 20.6 (q), 19.5 (q); HRMS m/z 190.1711 [M^+], $C_{14}H_{22}$ requires 190.1722. Alkylsilane **16**: IR (film/cm^{-1}) ν_{max} 2927, 2852, 2005; ^1H NMR ($CDCl_3$, 250 MHz) δ (ppm): 1.78 (3H, s, CH_3), 1.76 (3H, s, CH_3), 1.90–1.20 (17H, m, $8CH_2$ and cyclopropyl CH), 0.74 (2H, m, $CH_2Si(TMS)_3$), 0.16 (27H, s, $3Si(CH_3)_3$); ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ (ppm): 185.1 (s), 96.9 (s), 89.6 (s), 39.9 (t), 34.4 (t), 29.3 (t), 28.3 (t), 28.0 (s), 26.0 (t), 24.9 (d), 23.7 (t), 21.8 (t), 21.6 (t), 21.4 (q), 7.5 (t), 1.2 (q); HRMS m/z 464.3177 [M^+], $C_{25}H_{52}Si_4$ requires 464.3146. Iodide **18**: IR ($CHCl_3/cm^{-1}$) ν_{max} 2932, 2853, 2008, 1602; ^1H NMR ($CDCl_3$, 250 MHz) δ (ppm): 3.15 (2H, m, CH_2CH_2I), 1.77 (6H, s, $2CH_3$), 2.20–1.10 (11H, m, $5CH_2$ and cyclopropyl CH); ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ (ppm): 186.0 (s), 99.0 (s), 88.0 (s), 44.4 (t), 28.9 (s), 27.5 (t), 24.8 (d), 23.4 (t), 21.4 (t), 21.3 (2 × C, q), 21.2 (t), 2.2 (t); HRMS m/z 302.0474 [M^+], $C_{13}H_{19}I$ requires 302.0532. Enyne **21**: IR ($CHCl_3/cm^{-1}$) ν_{max} 2932, 2862; ^1H NMR ($CDCl_3$, 250 MHz) δ (ppm): 5.43 (1H, m, $C{=}CH$), 2.95 (1H, br s, $C{\equiv}CCH$), 2.55 (1H, m, $CH(CH_3)_2$), 2.15 (2H, m, $C{=}CCH_2$), 2.00 (2H, m, $C{=}CCHCH_2$), 1.76 (2H, m, CH_2CH_3), 1.55 (2H, m, $CH_2CH_2CH_2$), 1.15 (6H, d, J = 6.8 Hz, $CH(CH_3)_2$), 1.03 (3H, t, J = 7.4 Hz, CH_2CH_3); ^{13}C NMR ($CDCl_3$, 67.8 MHz) δ (ppm): 139.1 (s), 120.4 (d), 86.0 (s), 81.9 (s), 30.4 (t), 30.1 (d), 28.6 (t), 25.1 (t), 23.4 (2 × C, q), 20.6 (d), 20.0 (t), 12.3 (q); HRMS m/z 176.1552 [M^+], $C_{13}H_{20}$ requires 176.1565.
14. The ^1H NMR spectra recorded for compounds **9**, **10** and **13** could not be analysed in detail due to the complicated, overlapping, resonances over the region δ 0.74–1.74 ppm.
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