Intramolecular Competitive Addition of Vinyl Radicals to Keto and Alkenyl Groups in Wieland–Miescher Ketones—Synthesis of Carbocycles and Propellanes

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Wieland–Miescher ketone analogues are prepared by monoalkylation of cyclohexane-1,3-dione with bromomethylcycloalkenyl bromides followed by annulation with methyl vinyl ketone; they undergo 5-*exo-trig* competitive intramolecular radical addition to the keto and enone olefins to give angularly fused carbocycles and propellanes, respectively.

As part of our continuing programme to explore the potential of intramolecular vinyl radical cyclisation towards the stereocontrolled construction of carbocycles, we have recently reported[1] transformation of the bicyclo[2.2.2]octenone derivatives to tricyclic carbocyclic frameworks *via* radical C–C bond formation. Our interest in free-radical mediated reactions prompted us to investigate the possibility of extending this strategy to the synthesis of propellanes **1**[2] by an intramolecular Michael addition[3] of the vinyl radicals generated from the Wieland–Miescher ketones **2**.

In this communication, we report our findings on intramolecular vinyl radical cyclisation in the presence of keto (C=O) and enone (C=C) as 5-*exo-trig* carbon centres.

The substrates **2** required for our study were prepared by monoalkylation of cyclohexane-1,3-dione with bromomethylcycloalkenyl bromides[4] followed by Michael addition with methyl vinyl ketone and annulation (Scheme 1).

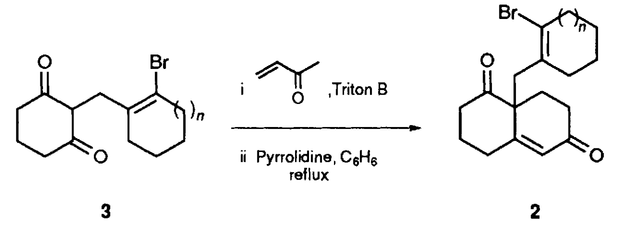
When the vinyl bromide **2a** was treated with $Bu^{n}{}_{3}SnH$ in benzene in the presence of azobisisobutyronitrile (AIBN) as the radical initiator, the reaction was found to proceed to completion in 5–6 h, leading to the formation of the expected product, *viz.* the propellane **1a**,† along with a more polar product **4a** (Scheme 2). Surprisingly, it was found that the product arising from vinyl radical addition on the carbonyl carbon was the major one (**1a**:**4a** = 35:65). This radical cyclisation is found to be general and in all the cases studied, the product due to addition to the keto C=O, *viz.* **4**, was found to be the major product (see Table 1).

Although the alkyl carbon radicals derived from selenides and iodides are reported to add to aldehydic[5] and keto[6] carbonyl groups, the substrates used in these studies could not undergo competitive C=C additions. However, intramolecular vinyl radical addition to cyclohexanone was reportedly unsatisfactory,[7] leading to a very poor yield of the required product. Interestingly, the aryl[8] radicals and a few vinyl[9] radicals generated from the acetylenic precursors by addition of trialkyl stannyl radical were found to undergo intramolecular addition to the keto carbonyl more efficiently.

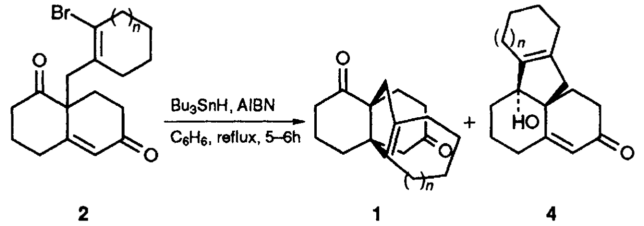
Recently, Fraser-Reid *et al.*[10] reported a competitive intramolecular addition of carbon radicals to CHO *vs.* $CH{=}CH_2$ and it was observed that carbonyl addition was preferred over addition to the olefinic system in the case of the formation of cyclohexanols *vs.* methylcycloalkanes, but the cyclopentanol and methylcyclopentane processes can be competitive. It is interesting to note that in our case the competition is between vinyl radical addition to an activated enone C=C and keto C=O groups, both of which are 5-*exo-trig* processes. In all the cases studied, we observed that addition to the keto group overwhelms the Michael addition, and the ratio remains almost constant. It is also important to mention that in our previous studies,[1] though we had a keto and an olefinic moiety in the molecule, we found that there was an exclusive preference for the addition of the vinyl radicals to the C=C (6-*exo-trig*) and addition to the carbonyl (5-*exo-trig*) did not occur. A similar observation was also made by Stork *et al.* in the synthesis of seychellene.[11]

Interestingly, using aryl radicals instead of vinyl radicals, resulted only in Michael type addition, leading to the formation of propellane **1d** only,‡ albeit in moderate yields (Scheme 3).

In conclusion, the intramolecular vinyl radical cyclisation in Wieland–Miescher ketones was found to be competitive, furnishing the angularly fused carbocycles and propellanes by addition of radicals to keto and olefinic groups, respectively. A greater preference for the keto carbonyl addition over the olefinic addition was observed in all the examples studied. The intermediate alkoxy radicals were assumed to take up hydrogen atoms in a very fast step to form the allyl alcohols, as



Scheme 1

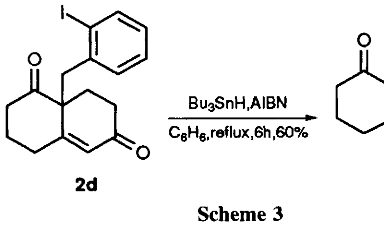


Scheme 2

Table 1

	Wieland–Miescher ketone	Propellane	Angularly fused carbocycle	Yield (%)
$n = 1$	**2a**	**1a** (35)[a]	**4a** (65)	85
$n = 2$	**2b**	**1b** (32)	**4b** (68)	76
$n = 3$	**2c**	**1c** (36)	**4c** (64)	79

[a] The numbers in parentheses represent the product ratio of 1 and 4.



Scheme 3

products due to alkoxy radical rearrangements were not observed.

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Footnotes

† All the new compounds reported in this communication have been thoroughly characterised by analytical and spectral data. **1a**: ^{1}H NMR (CDCl$_3$, 400 MHz) δ 2.72 (d, *J* 16.6 Hz, 1 H), 2.95–1.26 (m, 21 H); ^{13}C NMR (CDCl$_3$, 100 MHz) δ 214.10(s), 211.60(s), 137.61(s), 134.89(s), 57.04(s), 55.23(s), 47.72(t), 46.92(t), 37.46(t), 35.41(t), 32.74(s), 29.29(t), 25.54(t), 22.80(t), 22.67(t), 21.08(t), 18.56(t).

4a: ^{1}H NMR (CDCl$_3$, 400 MHz) δ 5.81 (s, 1 H), 2.5–1.5 (m, 21 H); ^{13}C NMR (CDCl$_3$, 100 MHz) δ 199.88(s), 169.61(s), 138.84(s), 134.53(s), 126.03(d), 86.99(s), 49.74(s), 42.30(t), 34.93(t), 33.53(t), 31.63(t), 28.54(t), 25.80(t), 22.68(t), 22.60(t), 21.13(t), 19.31(t).

‡ **1d**: ^{1}H NMR (CDCl$_3$, 400 MHz) δ 7.3–7.00 (m, 4 H), 3.55 (d, *J* 16 Hz, 1 H), 2.91 (d, *J* 16 Hz, 1 H), 2.6–1.65 (m, 12 H); ^{13}C NMR (CDCl$_3$, 100 MHz) δ 212.92(s), 210.41(s), 147.71(s), 140.27(s), 127.64(d), 127.46(d), 125.29(d), 121.90(d), 58.67(s), 56.82(s), 48.92(t), 40.53(t), 37.51(t), 37.13(t), 35.11(t), 29.58(t), 20.84(t).

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