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SUBSTITUENT INDUCED FINE-TUNING OF NOVEL CATIONIC REARRANGEMENTS IN [3.3.3] PROPELLANIC SYSTEMS

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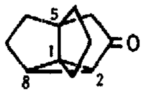
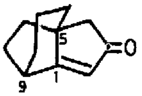
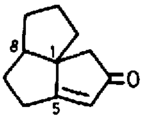
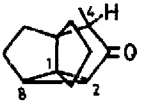
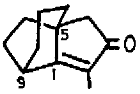
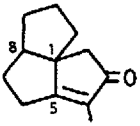
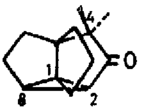
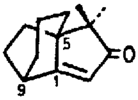
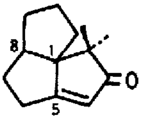
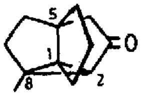
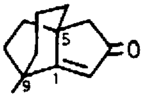
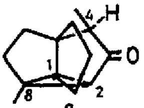
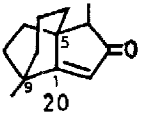
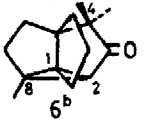
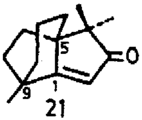
Summary : Profound effect of alkyl substituents on the course of cationic rearrangements of [3.3.3] propellan-3-ones has been observed.

Propellanes, because of their molecular shape, variation in size and presence of quaternary centres, are prone to a variety of interesting rearrangements.[1] In particular, acid catalysed rearrangements of [m.n.2] propellane ($m \geq 3$, $n \geq 3$) derivatives have been extensively studied and found applications in natural product synthesis.[2] On the other hand, the corresponding [3.3.3] propellanes have been known to be remarkably passive to cationic rearrangements and have been generally regarded as thermodynamic dead-ends.[3] However, we have recently shown[4] that the strategic placement of a carbonyl functionality on a [3.3.3] propellane framework induces its facile rearrangement to the tricyclo [$4.3.2.0^{1,5}$] undecane (quadrane) and the tricyclo [$6.3.0.0^{1,5}$] undecane (angular triquinane) ring systems (entry 1, Table 1) present in several natural products.[4,5] In view of the potential of $\underline{1} \rightarrow \underline{7} + \underline{8}$ rearrangement in synthesis, it was deemed expedient to investigate the generality and mechanistic aspects of this novel rearrangement. In the present communication, we wish to report the dramatic influence of alkyl substitution at strategic positions on the course of the acid catalysed rearrangement of [3.3.3] propellanes.

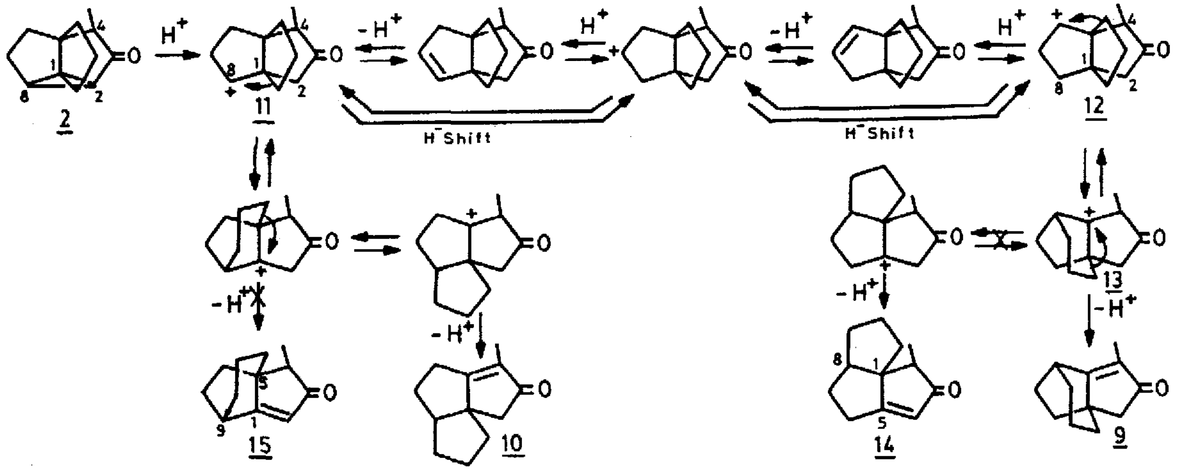
In addition to 1, five methyl substituted [3.3.3] propellane derivatives (2-6, Table 1) were synthesised and their rearrangement in 95% H_2SO_4 medium was investigated. Rearrangement of monomethylated propellanone 2 furnished two tricyclic enones 9 and 10 in ~1:1 ratio and the mechanism of their formation is presented in Scheme 1. While the formation of 10 could be considered as arising through sequential 1,2-shifts and proton elimination, the genesis of the tricyclic enone 9 must involve a 'merry-go-round' equilibrium process in which the cation 11 rearranges to 12 through a series of protonation-deprotonation or 1,2-hydride shift steps. 1,2-Bond migration in 12 to 13 and proton elimination leads to the observed product 9. It is interesting to note that neither of the enones 14 & 15 are encountered in this rearrangement and enones 9 and 10 do not interconvert, under the reaction conditions. Further support for the process ($\underline{11} \rightarrow \underline{12} \rightarrow \underline{13}$) came from the rearrangement of 1 in D_2SO_4, Scheme 2. The incorporation of as many as 8 deuterium atoms[6] in the products

Table 1 :

Entry	Substrates	Products[d]	Yield[c]
1.	 1[4]	 7 + (1:1)  8	85%
2.	 2[a]	 9 + (1:1)  10	75%
3.	 3[b]	 16 + (1:1)  17	70%
4.	 4[7]	 19	75%
5.	 5[a]	 20	75%
6.	 6[b]	 21	85%

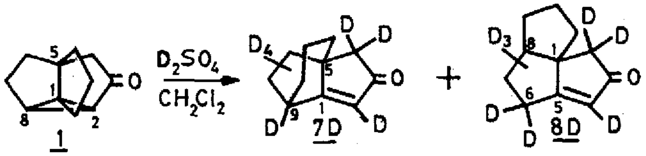
a. Prepared via kinetic methylation (LHMDS, -78°C, THF, MeI) of 1[4] & 4[7]; b. Prepared via thermodynamic methylation ($K^+Bu^tO^-$, THF, MeI, r.t.) of 1[4] & 4[7]; c. The yields indicated represent the isolated yields of the pure products obtained; d. All the reactions were carried out in the presence of 95% H_2SO_4 (0.1 mL) in dichloromethane medium at r.t. for 1-2 h. The products obtained were completely characterised on the basis of IR, ^1H & ^{13}C NMR and elemental analysis. Spectral data for selected compounds are given here: Compound 9: UV:238 nm; IR: 1700, 1640 cm^{-1}; δ_H: 3.1-2.9 (m, 1H), 2.23 (s, 2H), 2.0-1.2 (m, 10H), 1.70 (s, 3H); 10: UV: 238 nm; IR: 1700, 1640 cm^{-1}; δ_H: 2.6-2.4 (t, J = 8 Hz, 2H), 2.38 (s, 2H), 2.2-1.30 (m, 9H), 1.70 (s, 3H); 16: mp: 61-62°C; UV: 231 nm; IR: 1700, 1640 cm^{-1}; δ_H: 5.64 (s, 1H), 3.1-2.9 (m, 1H), 2.0-1.5 (m, 10H), 1.03 (s, 3H), 1.00 (s, 3H); M^+: Calcd.: 190.1353; Found: 190.1352; 17: mp: 82-83°C; UV: 232 nm; IR: 1700, 1640 cm^{-1}; δ_H: 5.66 (s, 1H), 2.7-2.3 (m, 2H), 3.0 - 1.2 (m, 9H), 1.10 (s, 3H), 0.95 (s, 3H); 20: UV: 229 nm; IR: 1700, 1640 cm^{-1}; δ_H: 5.55 (s, 1H), 2.23-1.30 (m, 11H), 1.20 (s, 3H), 1.0 (d, J = 7Hz, 3H).

Scheme 1



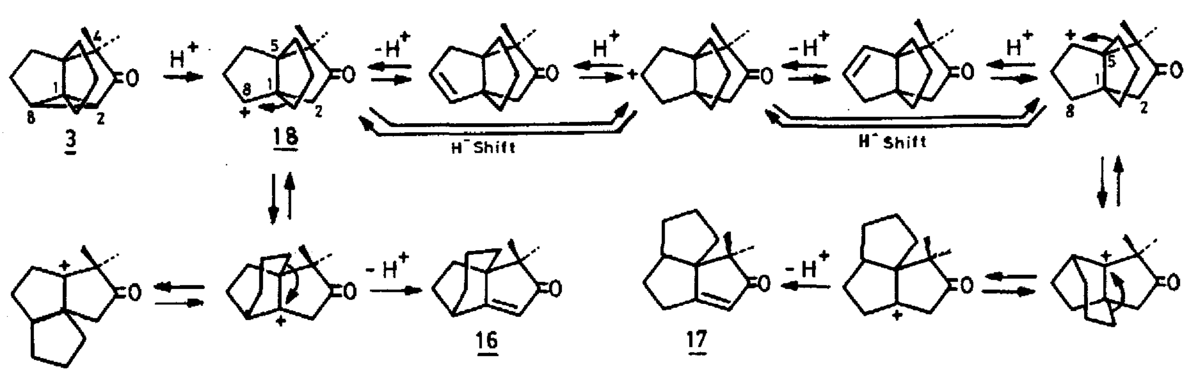
7D & 8D and in particular, location of deuterium at C(9) in 7D and C(6) in 8D provided definitive indication of extensive protonation-deprotonation and translocation of the cation 11 to 12 during the rearrangement process.

Scheme 2



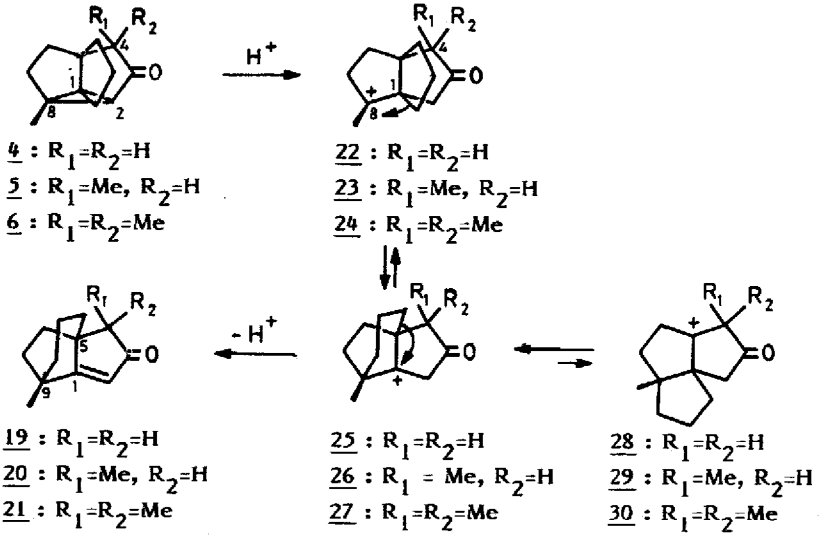
Rearrangement of 3 also afforded two rearranged enones 16 & 17 (1:1). Formation of these enones was quite unexpected as it was anticipated that the presence of *gem*-dimethyl group at C(4) in 3 would block the formation of angular triquinane enone 17. However, a 'merry-go-round' equilibrium process is again operative with several cationic species present in equilibrium, Scheme 3.

Scheme 3



Next, we investigated the rearrangement of propellanes 4, 5 & 6 having C(8)-methyl group. In contrast to 1-3, the tetracyclic ketones 4-6 afforded single enone products 19-21, respectively, after rearrangement. These observations can be reconciled through regioselective protonation to 22-24, 1,2-bond migration to 25-27 and proton elimination, respectively, Scheme 4. The absence of angular triquinane products in the rearrangements of 4, 5 & 6 is a notable feature. Apparently, the presence of C(8)-methyl group blocks further rearrangement of the cations 25-27 as they become highly stabilised neopentyl-type carbonium ions and render the equilibrium 25-27 $\rightleftharpoons$ 28-30, respectively, unfavourable towards the latter. These stabilised cations 25-27 rapidly escape through proton elimination to furnish the enones 19-21, respectively. Thus, the subtle effect of the C(8)-methyl group on the rearrangement can be exploited for gaining exclusive access to the tricyclo $[4.3.2.0.^{1,5}]$ undecane ring systems.

Scheme 4



The present investigation has demonstrated that the cationic rearrangements of [3.3.3] propellan-3-ones are fairly general and thermodynamically controlled. The methyl substitution at C(4) and C(8) profoundly influences the course and product distribution of the rearrangement, which can be gainfully exploited.

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5. Subsequently, other groups have also observed cationic rearrangement of the [3.3.3]-propellanes, see, K. Kakaiuchi, et.al., J. Org. Chem., 51, 281 (1986); L. Fitzer, A. Kanschika, M. Majewski, Tetrahedron Lett., 26, 5277 (1985); idem., 1263 (1988); idem., 5525 (1988).
6. Position and extent of deuterium incorporation was revealed through ^{1}H NMR and mass spectral (D_0 = 9.3%, D_1 = 9.4%, D_2 = 18.7%, D_3 = 23.3%, D_4 = 19.6%, D_5 = 9.4%, D_6 = 5.6%, D_7 = 2.8%, D_8 = 2.0%) analysis.
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