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DEAMINATION OF EPIMERIC 2-AMINOMETHYLNORBORNAN-2-OLS AND THE STEREOCHEMISTRY OF RING ENLARGMENT OF NORBORNAN-2-ONE BY DIAZOMETHANE

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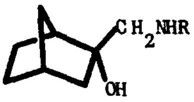
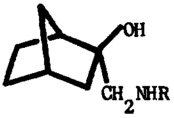
Evidence for the preferred direction of attack by a large variety of reagents on compounds with the bicyclo[2.2.1] skeleton is available. This contrasts with the homologation of ketones with diazoalkanes where, in the absence of specific evidence, it has been tentatively assumed that ring expansion is initiated by preferential attack by the diazoalkane from the exo direction.[1] However, lack of experimental data for an adequate model compound of a reagent like diazomethane (clearly a Grignard compound, being largely associated, may be a very unsuitable model) leaves much doubt about the extent of the preference for the exo direction so that rationalization of such homologation reactions is highly speculative.[1]

We report a study of model reactions for the homologation of norbornan-2-one by diazomethane. This concerns the nitrous acid deamination of 1a and 2a which have been obtained from the reaction of norbornan-2-one with HCN followed by acetylation, $LiAlH_4$ reduction, and anhydrous treatment with p-nitrocarbobenzoxy chloride and pyridine to give a mixture of 1b and 2b which have been separated by fract. crystallisation into pure 1b (mp 123-125°) and 2b containing 18% of 1b (mp 152-154°). Reduction of 1b and 2b with H_2 over Pd-C and subsequent precipitation with HCl in Et_2O gave 1a and 2a, the free bases of which are unstable and are characterised by AB quartets centered at, respectively, δ_{TMS} 2.66 and 2.76 ppm in $CDCl_3$. Configurations were established by a stereospecific synthesis of 1a (by the reaction of norbornan-2-one with ethylbromoacetate and zinc followed by degradation into 1a; it is quite safe to assume that the Reformatsky reagent behaves as a Grignard reagent,[2] attacking stereospecifically from the exo side).



1 a R= H_2Cl
b R= $COOCH_2C_6H_4(p\text{-}NO_2)$



2 a R= H_2Cl
b R= $COOCH_2C_6H_4(p\text{-}NO_2)$

Nitrous acid deamination of 1a in $AcOH\text{-}H_2O$ led to an identical product mixture (ketones 3 and 4 in the ratio 0.4) obtained from the reaction of norbornan-2-one with diazomethane in MeOH-

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Et_2O (Table). This sharply contrasts with the deamination of 2a where the 3:4 ratio is lower by a power of ten. When the products arising from 1a present as impurity are accounted for on the basis of the above results for 1a, it turns out that 2a gives only 4. Epoxides were not observed in any case.

TABLE

Product Distribution from Ring Expansion Reactions

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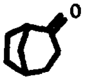
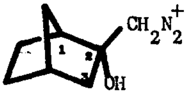


4

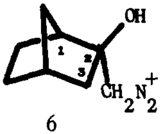
	3 yield %	4	ratio (3):(4)
Norbornan-2-one + CH_2N_2 (0.06eq.)			0.4*
1a + HNO_2	20.0	51.4	0.4
2a + HNO_2	2.9	57.3	0.05

*Corrected for a very small amount of the next higher homologous ketones.[1]

These results suggest that diazomethane attacks exclusively from the exo side. Contrary to the reactions of cyclopropanones with diazoalkanes,[3] the observed migratory aptitudes cannot be explained according to ground state conformation populations of 5 and 6. Assuming in our case a late transition state from 5 or 6 to the products, it may be envisaged that migration of C(3) is favoured in the case of 6 because a cyclohexane chair-like transition state is involved. However, according to this hypothesis, in the case of 5 preferential, if not exclusive, migration of C(1), also involving a cyclohexane chair-like transition state, would have been expected, contrary to what has been actually observed. With reservations about such use of conformational criteria with transition states, where bond lengths may markedly differ from ground states, possibly migration of C(3) in the case 5 is favoured by the release of repulsions between eclipsed bonds. Clearly, that this factor may be operative does not contrast with our findings for 6.



5



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2) R.R. Sauers, J.Amer.Chem.Soc., 81, 4873, 1959.
3) N.J. Turro and R.G. Gagosian, ibid., 92, 2036, 1970.