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UNUSUALLY FACILE BASE-CATALYZED EPIMERIZATION OF AN ALCOHOL A CASE FOR NEIGHBORING PARTICIPATION BY A GEMINAL DINITRO GROUP

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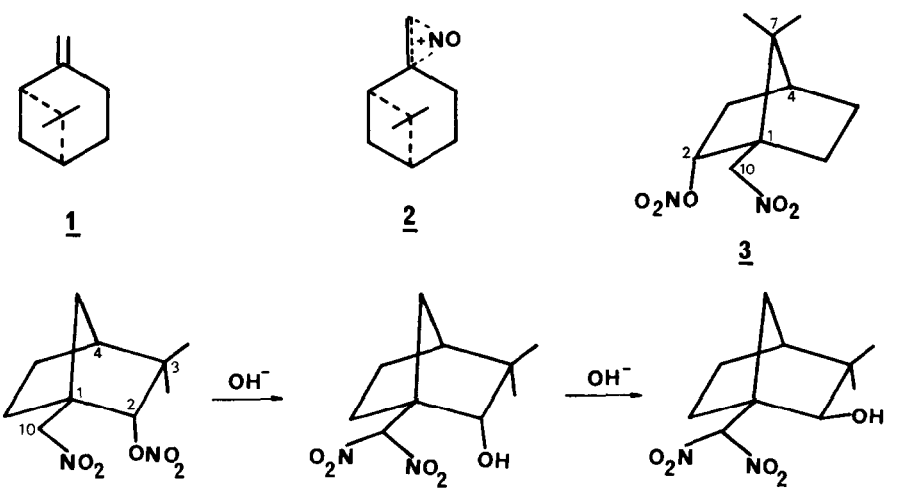
Abstract Mild basic treatment of (1R,4S)-2-endo-hydroxy-10,10-dinitrofenchane (5) led to (1R,4S)-2-exo-hydroxy-10,10-dinitrofenchane (6) The participation of the 10,10-dinitro group is essential for the epimerization to take place

During the course of our chemical studies on the reaction of nitrous acid with olefins, as a method for nitroimine synthesis,[1] we have investigated the action of this acid on (-)-β-pinene (1) Among other nitro-compounds[2] we have isolated (1S,4S)-2-*endo*-nitrato-10-nitrobornane[3] (3) and (1R,4S)-2-*endo*-nitrato-10-nitrofenchane[3] (4) produced by Wagner-Meerwein rearrangement of the *nitrosonium* ion (2) and subsequent oxidation in the reaction conditions

We have submitted compounds (3) and (4) to base, in order to achieve chemical support for these structures and also to study the interesting intramolecular transfer of the nitro group from the C-2 nitrate to carbon-10, reported by Stevens[4] during the alkaline treatment of (±)-

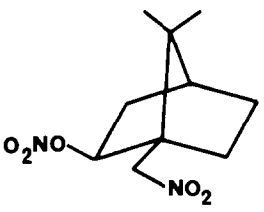


1 2 3 4 5 6

2-*exo*-nitrato-10-nitrobornane[5] (7, only one enantiomer shown)

Thus, reaction of (4) with 2% methanolic potassium hydroxide at 25°C for 30 min gave, after acidulation, the *endo* alcohol[6] (5) in 90% yield Treatment of (5) in stronger basic conditions (4% KOH/MeOH, 60°C, 5 h) produced, after acidification, the epimeric *exo*-alcohol[7] (6) in 80% yield The oxidation of compounds (5) and (6) by pyridinium chlorochromate to the same ketone[8] (8) demonstrated that they differ only in the stereochemistry of the C-2 hydroxyl groups This very unusual mild base-catalyzed epimerization of the C-2 hydroxyl group can only be explained if we consider a neighboring group participation of the nitro groups at C-10

As expected, *endo*-fenchyl alcohol (10) was recovered unchanged after 22 h treatment with 4% KOH/MeOH at 60°C Indeed, attempts to epimerize the mononitroalcohol[9] (11) were unsuccessful, giving a complex mixture in which the epimeric *exo*-alcohol was not detected Hence, we conclude that the presence of the geminal dinitro group is essential to produce the epimerization



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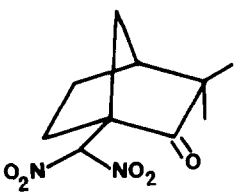

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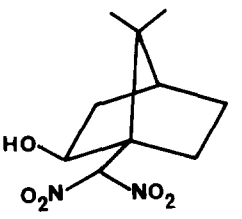

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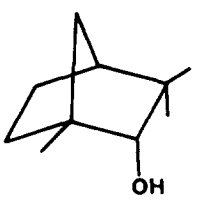

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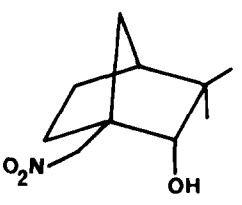

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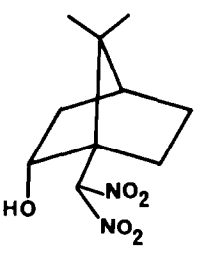

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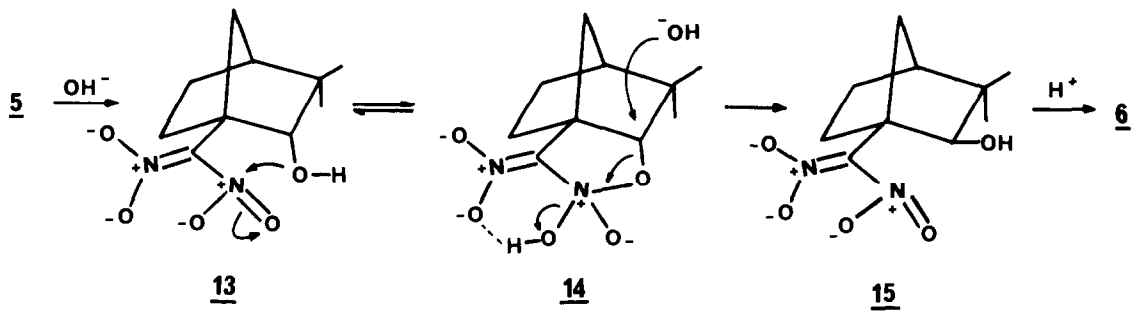
A reasonable mechanism accounting for these observations is shown in the Scheme This involves the formation of the cyclic intermediate (14) produced by intramolecular nucleophilic attack of the 2-hydroxyl function to the nitro of the nitro-nitronate group (13)

To study further this unexpected reaction we have prepared, by basic treatment (3% KOH/MeOH, 60°C, 3 h) of (3), the (1S,4S)-2-*endo*-hydroxy-10,10-dinitrobornane[10] (12) It should be noted that the intramolecular migration of the nitro group takes place with retention of configuration at C-2, as happens in the migration from the 2-*exo*-nitrate[5] (7) Prolonged basic treatment of (12)(4% KOH/MeOH, 60°C, 22 h) did not give the epimeric alcohol (9), the starting material being quantitatively recovered The *exo*-alcohol[5] (9) was also recovered unchanged when submitted to these conditions

The non-epimerization of the 2-*endo*- and the 2-*exo*-alcohols in the bornane series [compounds (12) and (9)] could be a consequence of the larger steric hindrance[11] to the hydroxyl anion approach by either of the two faces in bornane intermediates like (14)

As far as we know, this reaction is the first case of neighboring dinitro group participation

Scheme



in alcohol epimerization We are currently investigating other examples of this reaction

Acknowledgements

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Notes and References

1 C G Francisco, D Melián, J A Salazar, and E Suárez, J Chem Soc , Perkin Trans 1, 923 (1982), A G González, R Freire, M G Garcia-Estrada, J A Salazar, and E Suárez, Anales de Quim , 68, 1145 (1962)

2 Details of the study of the reaction of nitrous acid on β-pinene will be reported elsewhere

3 Compound (3) m p 94-95°C (n-hexane), $[\alpha]_D$ -64° (c, 0 24, $CHCl_3$), IR ($CHCl_3$) 1640,1550, 1380, 1280, 855 cm^{-1}, ^1H NMR ($CDCl_3$) δ 5 56 (1H, m, W 18 Hz, 2-*exo*-H), 4 49 (2H, s, 10-H_2), 1 03 (6H, s, 7-Me_2), MS m/z 245 (M^++1, chemical ionization), 198 1136 (M^+-NO_2, calcd for $C_{10}H_{16}NO_3$ 198 1130)
Compound (4) b p 80°C (0 05 mm), $[\alpha]_D$ +34° (c, 0 23, $CHCl_3$), IR ($CHCl_3$) 1635, 1550, 1380, 1280, 855 cm^{-1}, ^1H NMR ($CDCl_3$) δ 4 83 (1H, br s, W 5 Hz, 2-*exo*-H), 4 58, 4 48 (total 2H, AB, J 12 Hz, 10-H_2), 1 18, 0 93 (total 6H, each s, 3-Me_2), MS m/z 245 (M^++1, chemical ionization)
The stereochemistry of compounds (3) and (4) is that expected for a Wagner-Meerwein rearrangement, the patterns of the ^1H NMR signals of the 2-H allowed us to distinguish unequivocally between 2-*exo* and 2-*endo* bornane derivatives the 2-H is observed as a triplet for *exo* isomers and as two well defined multiplets for the *endo* ones See, *inter alia*, J I Musher, Mol Phys , 6, 93 (1963), H Schmidt, M Muhlstadt, and P Son, Chem Ber , 99, 2736 (1966), S Masson and A Thuillier, Bull Soc Chim Fr , 4368

(1969), P H Boyle, W Cocker, D H Grayson, and P V R Shannon, J Chem Soc (C), 2136 (1971), B Olejniczak, K Osowska, and A Zwierzak, Tetrahedron, 34, 2051 (1978)

4 T E Stevens, J Org Chem , 24, 865 (1959)

5 Racemic compound (7), prepared according to ref 4, has m p 99-100°C (n-pentane), IR ($CHCl_3$) 1635, 1550, 1375, 1280, 850 cm^{-1}, ^1H NMR ($CDCl_3$) δ 5 17 (1H, t, J 7 Hz, 2-*endo*-H), 4 73, 4 28 (total 2H, AB, J 12 Hz, 10-H_2), 1 03, 0 94 (total 6H, each s, 7-Me_2), MS m/z 198 (M^+-NO_2, chemical ionization) Although not specifically determined at the time, the *exo* stereochemistry of the 2-nitrate group could be easily inferred from the above ^1H NMR data

Compound (9), prepared by treatment of (7) with 2% KOH/MeOH for 30 min at 25°C has m p 130-159°C (n-pentane), IR (KBr) 3580, 1565, 1330 cm^{-1}, ^1H NiiR ($CDCl_3$) δ 6 64 (1H, s, 10-H), 4 28 (1H, t, J 7 Hz, 2-*endo*-H), 1 28, 0 83 (total 6H, each s, 7-Me_2), MS m/z 243 (M^+-1, chemical ionization)

6 Compound (5) m p 68-69°C (n-pentane), $[\alpha]_D$ +67° (c, 0 2, $CHCl_3$), IR ($CHCl_3$) 3610, 1570, 1330 cm^{-1}, ^1H NMR ($CDCl_3$) δ 6 71 (1H, s, 10-H), 3 60 (1H, br s, $W_{1/2}$ 6 Hz, 2-*exo*-H), 1 05, 1 02 (total 6H, each s, 3-Me_2), MS m/z 243 (M^+-1, chemical ionization)

7. Compound (6) m p 70-71°C (n-pentane), $[\alpha]_D$ +50° (c, 0 22, $CHCl_3$), IR (KBr) 3545, 1570, 1330 cm^{-1}, ^1H NMR ($CDCl_3$) δ 6 41 (1H, s, 10-H), 3 81 (1H, br s, $W_{1/2}$ 6 Hz, 2-*endo*-H), 1 04, 0 91 (total 6H, each s, 3-Me_2), MS m/z 243 (M^+-1, chemical ionization)

8 Compound (8) m p 48-49°C (n-pentane), $[\alpha]_D$ -83° (c, 0 2, $CHCl_3$), IR ($CHCl_3$) 1740, 1575, 1330 cm^{-1}, ^1H NMR ($CDCl_3$) δ 6 56 (1H, s, 10-H), 1 18, 1 11 (total 6H, each s, 3-Me_2), MS m/z 243 (M^++1, chemical ionization)

9 Compound (11) was obtained (86% yield) by catalytic hydrogenation of (5) (PtO_2, EtOAc, r t , 1 atm), m p 72-73°C (n-pentane), $[\alpha]_D$ -15° (c, 0 13, $CHCl_3$), IR ($CHCl_3$) 3610, 1545, 1380 cm^{-1}, ^1H NMR ($CDCl_3$) δ 4 86, 4 39 (total 2H, AB, J 12 Hz, 10-H_2), 3 33 (1H, br s, $W_{1/2}$ 6 Hz, 2-*exo*-H), 1 00 (6H, s, 3-Me_2), MS m/z 198 (M^+-1, chemical ionization)

10 Compound (12) m p 110-130°C (n-pentane), $[\alpha]_D$ -60° (c, 0 16, $CHCl_3$), IR ($CHCl_3$) 3600, 1575, 1320 cm^{-1}, ^1H NMR ($CDCl_3$) δ 6 38 (1H, s, 10-H), 4 89 (1H, m, $W_{1/2}$ 18 Hz, 2-*exo*-H), 1 03, 0 96 (total 6H, each s, 7-Me_2), MS m/z 243 (M^+-1, chemical ionization), 227 1049 (M^+-OH, calcd for $C_{10}H_{15}N_2O_4$ 227 1032)

11 H C Brown, "The Nonclassical Ion Problem", Plenum Press, New York, 1977, p 123, J A Berson, "Molecular Rearrangements", vol 1, P de Mayo, Ed , Interscience, New York, 1963, p 121

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