J. Org. Chem. 1993, 58, 4639–4641

Oxygenation of Bicyclo[2.2.1]heptane and Bicyclo[2.2.2]octane with Nitronium Tetrafluoroborate[1]

G. A. Olah* and Pichika Ramaiah

Donald P. and Katherine B. Loker Hydrocarbon Research Institute and Department of Chemistry, University of Southern California, Los Angeles, California 90089-1661

Received April 5, 1993

Reaction of bicyclo[2.2.1]heptane (1) with nitronium tetrafluoroborate in nitroethane gives bicyclo[2.2.1]heptan-2-one (2). Bicyclo[2.2.1]heptan-2-yl nitrite (3) was observed as the intermediate of the reaction. The reaction of *exo*-bicyclo[2.2.1]heptan-2-ol (4) with nitrosonium tetrafluoroborate also gave 2. The reaction of 2-norbornyl cation with silver nitrite gave 2. When *exo*-2-bromobicyclo[2.2.1]heptane (10) reacted with silver nitrite in ether, 2 and 2-nitrobicyclo[2.2.1]heptan (8) were obtained in 1.3:1 ratio. Reaction of bicyclo[2.2.2]octane (5) with nitronium tetrafluoroborate yields upon aqueous workup bicyclo[2.2.2]octan-1-ol (6). No nitro products were observed in either of the reactions. The mechanism of the observed reactions is discussed.

Introduction

Electrophilic reactions at saturated, sp^3 carbon atoms involving σ bond substitution (cleavage) are by now well established.[2] Primary, secondary, and tertiary hydrogens of alkanes can undergo hydrogen exchange by treatment with superacids.[3] Nitration with nitronium salts,[4] Lewis acid-catalyzed halogenation by halogen,[5] Gif-type substitutions, chromic acid oxidation,[6] oxidations with cobalt, manganese, and lead trifluoroacetates,[7] lead tetraacetate,[8] and silver peroxide,[9] and electrochemical methods[10] are representative reactions of saturated hydrocarbons involving σ bond substitution.

The electrophilic oxygenation of alkanes and cycloalkanes was studied *via* superacid-catalyzed reactions with ozone[11] and hydrogen peroxide,[12] respectively.

We have previously studied[1] the nitration of adamantane with nitronium tetrafluoroborate. We have extended our studies to other bicyclic saturated hydrocarbons, such as bicyclo[2.2.1]heptane (1) and bicyclo[2.2.2]octane (5). Unexpectedly, the reaction of 1 with $NO_2^+BF_4^-$ gave only bicyclo[2.2.1]heptan-2-one (2), and no nitrobicyclo[2.2.1]heptanes were obtained. This is in contrast to the reaction of admantane with nitronium tetrafluoroborate in pure nitromethane or nitroethane where 1-nitroadamantane was obtained in 60–70% yield.

Bach et al. reported[13] that reaction of 1 with nitronium tetrafluoroborate in acetonitrile gave *N*-*exo*-bicyclo[2.2.1]heptan-2-ylacetamide *via* Ritter reaction of the intermediate 2-norbornyl cation. Haas et al.[14] have carried out nitration of 1 under free radical conditions. Vapor phase nitration of 1 at 400 °C by concd nitric acid was reported to give 1-nitrobicyclo[2.2.1]heptane (7) in 50% yield. Smith[15] reported liquid phase nitration of 1 with nitrogen dioxide to 2-nitrobicyclo[2.2.1]heptane (8) in 30% yield. Studying the reaction of 1 and 5 with $NO_2^+BF_4^-$ in pure nitroethane, we now observed only electrophilic oxygenation indicative of the ambient reactivity of NO_2^+. Herein we report our results.

Results and Discussions

Dried, freshly distilled nitrile-free nitroethane was used as a solvent. 1 (13 mmol) was added to the stirred suspension of nitronium tetrafluoroborate (15 mmol) in nitroethane. The reaction mixture was stirred at ambient temperature under nitrogen atmosphere for up to 1 week. Analysis of the reaction mixture after 2 h by GC/MS [m/e 95 (M – 46)] showed the presence of bicyclo[2.2.1]heptan-2-yl nitrite (3) as the intermediate of the reaction. We compared the GC/MS results with those of an authentic sample of 8, eliminating the presence of the latter. The reaction mixture was subjected to GC/MS for every 18 h. Little 2 is formed during the initial period of the reaction. As the reaction proceeds, the amount of 2 is increased with decreasing 3. After stirring for 4 d and analysis of the reaction mixture, the products 2 and 3 were determined to be formed in 5.4:1 ratio. After 1 week 2 was found to be only the product. Aqueous workup gave 2 with no bicyclo[2.2.1]heptanols or nitrobicyclo[2.2.1]heptanes detected.

---

[1] Electrophilic Reactions at Single Bonds. 26. For part 25 see: Olah, G. A.; Ramaiah, P.; Rao, C. B.; Sandford, G.; Trivedi, N. J.; Olah, J. A. *J. Am. Chem. Soc.*, in press.

[2] Olah, G. A. *Carbocations and Electrophilic Reactions*; Wiley: New York, 1974.

[3] (a) Olah, G. A. *Angew. Chem. Int. Ed. Engl.* **1973**, *12*, 173. (b) Olah, G. A.; Schleyer, P. v. R. *Carbonium Ions*; Wiley Interscience: New York, 1970; Vol. 11, p 463. (c) Olah, G. A.; Halpern, Y.; Shen, J.; Mo, Y. K. *J. Am. Chem. Soc.* **1973**, *95*, 4960. (d) Olah, G. A.; Halpern, Y.; Shen, J.; Mo, Y. K. *J. Am. Chem. Soc.* **1971**, *93*, 1251. (e) Olah, G. A.; Klopman, G.; Schlosberg, R. H. *J. Am. Chem. Soc.* **1969**, *91*, 3261.

[4] Olah, G. A.; Lin, H. C. *J. Am. Chem. Soc.* **1971**, *93*, 1259.

[5] Olah, G. A.; Renner, R.; Schilling, P.; Mo, Y. K. *J. Am. Chem. Soc.* **1973**, *95*, 7686.

[6] (a) Bingham, R. C.; Schleyer, P. v. R. *J. Org. Chem.* **1971**, *36*, 1198. (b) Wiberg, K. B.; Foster, G. *J. Am. Chem. Soc.* **1961**, *83*, 423.

[7] Jones, S.; Mellor, J. M. *J. Chem. Soc. Perkin Trans. 1* **1977**, 511.

[8] Jones, S.; Mellor, J. M. *J. Chem. Soc. Perkin Trans. 1* **1976**, 2576.

[9] Crivello, J. V. *Synth. Commun.* **1976**, *6*, 543.

[10] Fleischmann, J.; Pletcher, D. *Tetrahedron Lett.* **1971**, 349.

[11] (a) Cohen, Z.; Keinan, E.; Mazur, Y.; Varkony, T. H. *J. Org. Chem.* **1975**, *40*, 2141. (b) Olah, G. A.; Yoneda, N.; Parker, D. G. *J. Am. Chem. Soc.* **1976**, *98*, 5261.

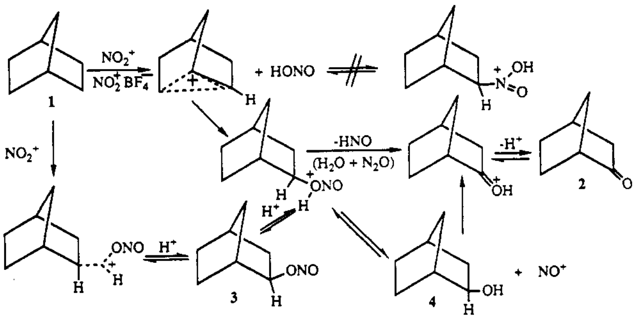
[12] Olah, G. A.; Yoneda, N.; Parker, D. G. *J. Am. Chem. Soc.* **1977**, *99*, 483.

[13] Bach, R. D.; Holubka, J. W.; Badger, R. C.; Rajan, S. J. *J. Am. Chem. Soc.* **1979**, *101*, 4416.

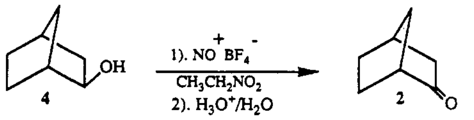
[14] Blickenstaff, R. T.; Hass, H. B. *J. Am. Chem. Soc.* **1946**, *68*, 1431.

[15] Smith, G. *J. Am. Chem. Soc.* **1959**, *81*, 6319.

0022-3263/93/1958-4639$04.00/0

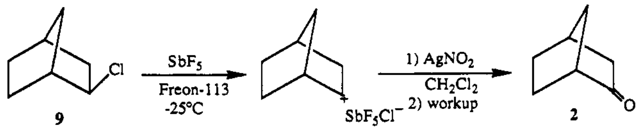


We also found that the reaction of *exo*-bicyclo[2.2.1]heptan-2-ol (4) with nitrosonium tetrafluoroborate under similar conditions gave also 2.



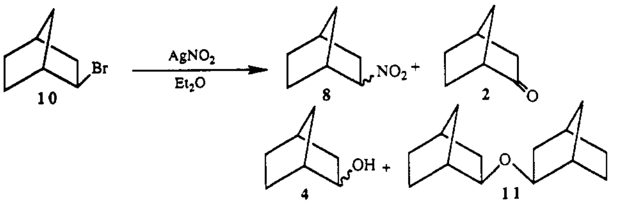
Neither 2 or 4 were formed when 1 was reacted with nitrosonium tetrafluoroborate. No 8 was found during the course of any of the reactions. To account for the results it is suggested that initial hydride abstraction with NO_2^+ takes place to give 2-norbornyl cation with HNO_2 as the byproduct. No 1-norbornyl cation is formed due to the high energy of the bridgehead carbocation. HNO_2 subsequently reacts with the 2-norbornyl cation to give 3. 3 is readily cleaved by the byproduct acid HBF_4 to give 4, which is then further oxidized[16] to 2. 2 was obtained in 70% isolated yield based on 1 converted. In comparison, oxyfunctionalization of 1 with ozone[17] and methyl(trifluoromethyl)dioxirane[18] affords 2 and 4, respectively.

The reaction of 2-norbornyl cation (formed from 1[19] or *exo*-2-chlorobicyclo[2.2.1]heptane (9) with SbF_5[20]) with silver nitrite in dichloromethane gave upon aqueous workup 2 as the only identified product. The reaction of the highly stabilized 2-norbornyl ion leads only to nitrite formation and no nitro product is observed.



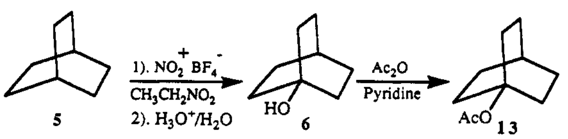
For comparison we also carried out the conventional Victor–Mayer reaction of *exo*-2-bromobicyclo[2.2.1]heptane (10) with nitrite ion. 10 did not react with $NaNO_2$ in DMSO at room temperature. However the reaction with dried $AgNO_2$ in anhydrous diethyl ether at room temperature gave a mixture of 2, 8, 4, and bis(2-bicyclo[2.2.1]heptanyl) ether 11. 2 and 8 were formed in 1.3:1 ratio.

The formation of 8 and 3 is due to the ambient nature of the nitrite ion. There are several factors involved in N vs O attack of the ambident anion. The yield of nitro compounds decreases from primary to secondary and tertiary halides on treatment with silver nitrite. On the contrary, the yield of nitrite esters rises in going from primary to secondary to tertiary halides, as the ease of carbocation formation is increased. Silver polarizes the carbon–halogen bond, thus carbon undergoes electron deficiency in the transition state. So the yield of nitrite ester rises more than the nitro compound. There is also a greater steric requirement for C–NO_2 bond formation by backside attack. On the basis of electrostatic consideration, the nitrite ion has a nitrogen that is a neutral while the oxygen atoms share the negative charge between them. Hence the oxygen of the nitrite ion attacks the carbon more rapidly than does the nitrogen. The ratio of C-nitro to C-nitrite can also be explained in terms of "hard" and "soft" acids and bases theory. In the reaction of alkyl halide, replacement of a "hard" leaving group will occur more readily with a "hard" rather than a "soft" nucleophile. Since the O-terminus of the ambient nitrite ion is "harder" than its N-terminus, a low C–NO_2/C–ONO ratio will be favored by alkyl halides. The yield of nitrite esters increases with increasing polarity of the solvent. In other words, carbocation character increases with the polarity of solvent in the transition state.



In order to study the stability of 8 in this reaction system, we treated an authentic sample of 8 with $NO_2^+BF_4^-$. The 8 was recovered unchanged. This indicates that 2 is not formed *via* 8 by subsequent cleavage of the nitro group. The reaction of 1 with nitronium tetrafluoroborate to give 2 therefore proceeds in all probability *via* intermediate formation of 3 through initial formation of the 2-norbonyl cation. Ambident direct attack by NO_2^+ yielding 3 can also be considered to take place, although there is no direct evidence for this path.

In addition to the reaction of 1 with $NO_2^+BF_4^-$, the reaction of bicyclo[2.2.2]octane (5) was also investigated. 5 reacts with nitronium tetrafluoroborate in nitrile-free nitroethane to give upon workup bicyclo[2.2.2]octan-1-ol (6) rather than bicyclo[2.2.2]octan-2-one (12). Again no nitro products were obtained.



In contrast, oxyfunctionalization of 5 with methyl(trifluoromethyl)dioxirane[18] afforded 6 and 12 in 1.3:1 ratio. In 5, oxidation of the tertiary C–H bond thus predominates over that of CH_2. The tertiary alcohol, which is the initial oxidation product, is not further oxidized. The bicyclic system prevents dehydration of the alcohol (Bredt's rule). Tertiary bridgehead hydroxyl of course cannot be converted to a ketone. Therefore, oxygenation at a bridgehead position stops at the alcohol. In contrast, the reaction of 5 with nitronium tetrafluoroborate in acetonitrile by Bach et al. gave a 3:1:0.5 mixture of the 1- and 2-acetamides as well as rearranged 2-bicyclo[2.3.1]octylacetamide.[13]

---

(16) Olah, G. A.; Ho, T. L. *Synthesis* **1976**, 609.

(17) Giamalva, D.; Church, D. F.; Pyror, W. P. *J. Org. Chem.* **1988**, *53*, 3429.

(18) Mello, R.; Fiorentino, M.; Fusco, C.; Curci, R. *J. Am. Chem. Soc.* **1989**, *111*, 6749.

(19) Lukas, J.; Krammer, P. A.; Kouwenhoven, A. P. *Recl. Trav. Chim-Pays*-Bas. **1973**, *92*, 44.

(20) Olah, G. A.; White, A. M.; De Member, J. R.; Commegras; Lui, C. Y. *J. Am. Chem. Soc.* **1970**, *92*, 4627.

Experimental Section

Nitroethane was a gift from the W. R. Grace Co. and distilled under nitrogen over CaH_2 prior to use. Nitronium tetrafluoroborate (85%), nitrosonium tetrafluoroborate, silver nitrite, **1**, **4**, **9**, and **10** were purchased from Aldrich Chemical Co. **5** was obtained from Chemical Samples Co. GC/MS analyses were obtained on a INCOS-50 mass spectrometer. NMR data was obtained from a Varian VXR-200 spectrometer.

Reaction of Bicyclo[2.2.1]heptane (1) with Nitronium Tetrafluoroborate. Nitronium tetrafluoroborate (2 g, 15 mmol) was placed in a flame-dried three-neck 25-mL round-bottom flask under nitrogen atmosphere followed by addition of nitrile-free nitroethane (20 mL) by hypodermic syringe. The suspension was kept at 0 °C, and **1** (1.30 g; 13 mmol) was added in one portion under nitrogen atmosphere. The ice bath was removed and the reaction mixture was subjected to GC/MS after 2 h. The GC/MS showed a mixture of **3** and starting material **1** in minor and major amounts. The reaction is slow and aliquots were taken for every 18 h to monitor the progress of the reaction. After the reaction was stirred a total of 4 d, the GC/MS showed a mixture of **2** and **3** in 5.4:1 ratio. The reaction mixture was stirred at ambient temperature for up to 1 week until no further increase in the yield of **2**. The reaction mixture was then treated with dichloromethane and extracted with cold aqueous $NaHCO_3$ (5%) (3 × 30 mL) solution. The aqueous layer was reextracted with dichloromethane (20 mL). The combined organic layer was washed with water and saturated brine solution. The organic phase was dried over anhydrous $MgSO_4$ and concentrated, and the products were analyzed by their GC/MS (in comparison to authetic samples). Isolated yield of **2** is 1 g (70%).

Reaction of 2-Norbornyl Cation[20] with Silver Nitrite. A solution of a freshly distilled SbF_5 (6.5 g, 30 mmol) in anhydrous 1,1,2-trichlorotrifluoroethane (30 mL) was taken in a three-neck round-bottom flask under nitrogen atmosphere and cooled to −30 °C in a dry ice–acetone bath. The solution was protected from moisture and kept stirring under dry N_2 at the same temperature. To this solution was added **9** (2 g, 15 mmol) dropwise with vigorous stirring in the same solvent (5 mL). After the addition was completed, the reaction mixture was stirred for 30 min at −30 °C. The solvent was removed under vacuum through the side frit. The light-yellow-colored salt was washed with cold (−25 °C) anhydrous 1,1,2-trichlorotrifluoroethane (2 × 25 mL) and dired in vacuo. The corresponding 2-norbornyl cation was then treated with anhydrous dichloromethane (20 mL) with vigorous stirring under dry N_2 at −25 °C followed by the addition of dried $AgNO_2$ (4.62 g, 30 mmol). The reaction mixture was stirred at −25 °C for 2 h and 0 °C for 3 h. The ice-bath was removed and the reaction mixture was brought into room temperature. The reaction mixture was quenched with cold water. The organic layer was extracted with dichloromethane (2 × 15 mL) and washed with $NaHCO_3$ (5%, 2 × 10 mL) and water. After being dried with $MgSO_4$, the solvent was removed in vacuum to give **2** (0.86 g, 52%). The NMR, GC/MS, and IR data are identical with that of an authentic sample.

Reaction of *exo*-2-Bromobicyclo[2.2.1]heptane (10) with Silver Nitrite. The bromo compound **10** (1.43 g, 8.1 mmol) in dry ether (5 mL) was added dropwise to a stirred suspension of dried $AgNO_2$ (2.13 g, 13.8 mmol) in dry ether (20 mL) at 0 °C for 10 min. The reaction mixture was stirred for 2 h in an ice-bath under dry N_2. The ice-bath was removed and stirring was continued at room temperature for 40 h. The silver salts were removed by filtration and washed with dry ether (2 × 10 mL). The combined ethereal solutions were concentrated in vacuo. The residue was subjected to GC/MS analysis. The residue was then loaded on a silica gel column (30 g) and eluted with hexane–$CHCl_3$. After removal of the solvents in vacuum, the major products were weighed to calculate the isolated yields for **2** (0.44 g, 50%) and **8** (0.43 g, 38%).

Oxidation of *exo*-Bicyclo[2.2.1]heptan-2-ol (4). A solution of the alcohol **4** (0.92 g, 8.2 mmol) in dry nitroethane (5 mL) was added to a stirred suspension of nitrosonium tetrafluoroborate (1.18 g, 10.1 mmol) in dry nitroethane (10 mL). Aliquots were taken and subjected to GC/MS for every 18 h. The GC/MS showed only one product **2**. The reaction mixture was stirred at ambient temperature for 4 d until no further increase in the yield for **2**. The reaction mixture was poured into water and extracted with dichloromethane (10 mL). The organic extract was washed with cold $NaHCO_3$ solution (2 × 10 mL) and water and dried. The solvent was removed under vacuum to furnish **2** (0.53 g, 55%).

Reaction of Bicyclo[2.2.2]octane (5) with Nitronium Tetrafluoroborate. **5** (1.0 g, 10 mmol) was reacted with nitronium tetrafluoroborate (2.3 g; 12 mmol) in nitrile-free nitroethane (20 mL) according to the procedure given for **1**. GC/MS indicated a single product **6**. After workup and removal of the solvent, the reaction mixture was treated with acetic anhydride and pyridine for 1 h under gentle reflux. It was then cooled and diluted with ice–water, and the solution was extracted with ether. The extracts were washed with 10% aqueous HCl, water, and saturated brine and dried. Bicyclo[2.2.2]oct-1-yl acetate (**13**) was obtained as a clear liquid after distillation. The yield is 1.2 g (72%). NMR and IR data are in identical with those reported in the literature.[18]

Acknowledgment. Support of our work by the National Science Foundation and the Office of Naval Research is gratefully acknowledged.