Bromination Reactions of 2-Substituted Derivatives of 7-Oxabicyclo[2.2.1]hept-5-ene†

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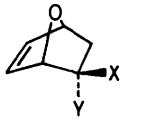
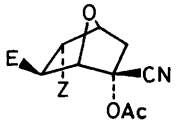
The bromination reactions of the endocyclic double bond of some 2-substituted derivatives of 7-oxabicyclo[2.2.1]hept-5-ene with bromine and *N*-bromosuccinimide in different conditions have been studied. The stereochemical outcome of the reaction and the nature of the products (derived from addition, rearrangement and/or fragmentation) is discussed as a function of the reaction conditions and of the nature of the substituent on C-2. In the case of 2-*exo*-methyl-7-oxabicyclo[2.2.1]hept-5-en-2-*endo*-ol, the reaction allows for a straightforward synthesis of 2-*exo*-bromo-5-*exo*-methyl-4,7-dioxatricyclo[3.2.1.$0^{3,6}$]octane.

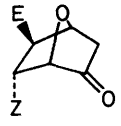
The chemistry of systems derived from 7-oxanorbornene has attracted a great deal of attention in the past few years,[1] largely due to its wide applicability to the synthesis of natural products and derivatives of biological interest.[2] Within this context, oxanorbornenic substrates (**1**) are particularly versatile



(**1**)



(**2**)



(**3**)

a: X = CN, Y = OAc

b: X, Y = O

c: X, Y = O–CH$_2$–CH$_2$–O

E = PhSe, PhS, $pNO_2C_6H_4S$, $(NO_2)_2C_6H_4S$

Z = Cl, Br

starting materials for the preparation of a variety of natural products.[3] Furthermore, these synthetic intermediates ('naked sugars')[3a] are now readily available,[4] even in optically pure form.[5]

A remarkable feature of these systems is that electrophilic additions of arylselenenyl and arylsulphenyl halides to 2-substituted 7-oxanorbornenes (**1**) take place with complete control of the regio- and stereo-selectivity to produce adducts (**2**) or (**3**) depending upon the nature of the substituent on C-2.[6] This completely regio- and stereo-selective process has been successfully applied in synthesis.[7]

In the course of our studies concerning new aspects of the reactivity of these systems[8] we have explored the electrophilic additions of bromine and *N*-bromosuccinimide to this class of compounds in a number of experimental conditions, and this study constitutes the objective of the present report.

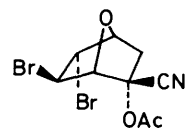
Results and Discussion

The reaction of compound (**1a**) with bromine yields products (**4**)–(**6**) in different relative ratios depending upon the reaction conditions employed (Table). It should be pointed out that the reaction in Bu^{t}OH–H_2O led to (**6**), structurally related to cyclopentenyl aldehyde (**7**), a fundamental synthon for the preparation of terpenes with the triquinane skeleton.[9]

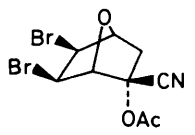
The addition of bromine in CCl_4 to (**1b**) led to a 3:1 mixture of adducts (**8**) and (**9**). The use of more polar reaction media with this substrate led to intractable reaction mixtures.

The formation of *trans* products [(**4**) and (**8**)] may be rationalized by admitting a reaction pathway *via* brominium ion (**10**)[10] (Scheme 1). The attack of the counter-ion is controlled by the characteristics of the substituent on C-2.[6] In the case of the bromination of (**1a**), nucleophilic attack takes place on C-5 (route a), while the ketone functionality behaves as an electron homodonating group, inducing attack of the counter-ion on C-6 (route b).

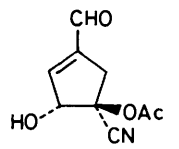
The formation of *cis* products [(**5**) and (**9**)], may be rationalized through a migration process on cation (**10**)[11] (Scheme 2)



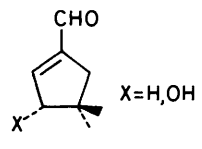
(**4**)



(**5**)



(**6**)



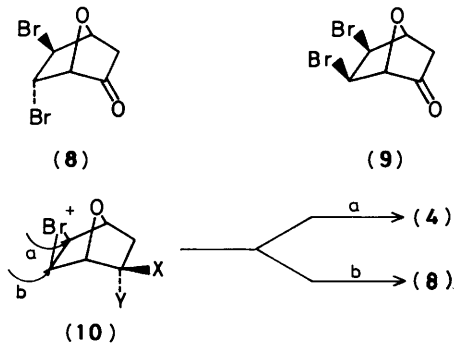
(**7**)

Table. Experimental conditions and relative ratio of products obtained in the addition of bromine to (**1a**).

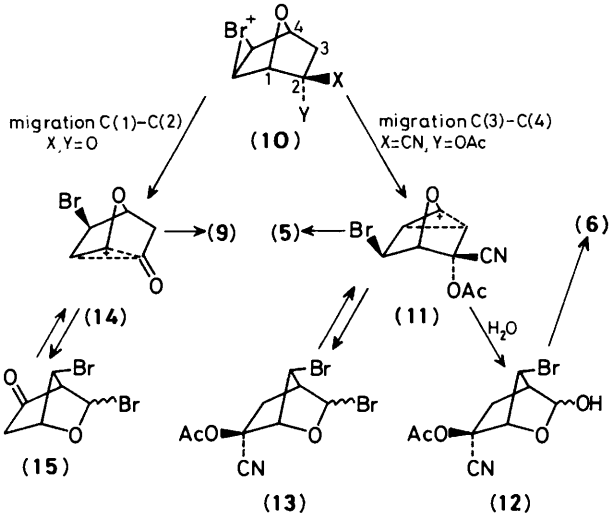
Reagent/solvent	(4)	(5)	(6)	Overall yield (%)
Br_2/CCl_4	2	3	—	90
$Br_2/CH_2Cl_2/AcOH/H_2O$[a]	1	1	—	80
Br_2/Bu^{t}OH/H_2O[b]	3	—	7	50

[a] CH_2Cl_2–AcOH–H_2O (20:20:1). [b] Bu^{t}OH–H_2O (2:1).

† Since submission of this paper, a report describing the reaction between 5,5-bis(benzyloxy)-7-oxabicyclo[2.2.1]hept-2-ene and bromine to produce 6-*endo*-benzyloxy-5-*exo*-bromo-7-oxabicyclo[2.2.1]heptan-2-one in high yield has been published: see J.-L. Reymond and P. Vogel, *Tetrahedron Lett.*, 1989, **30**, 705.



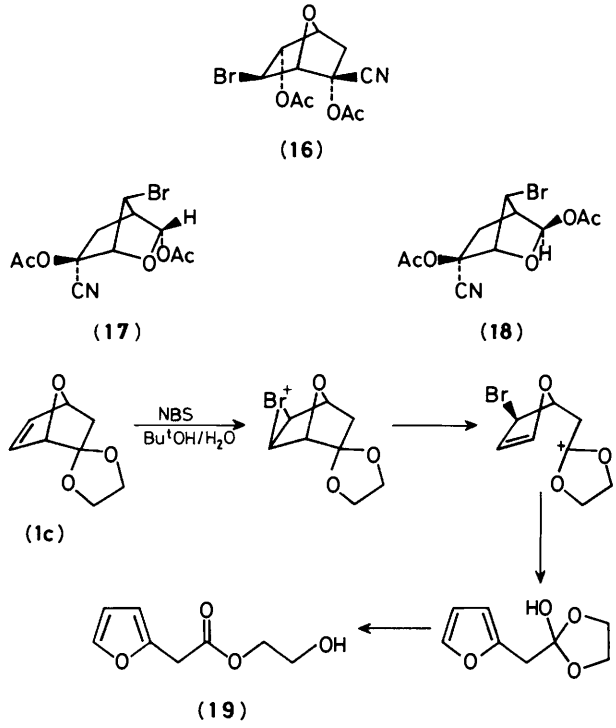
Scheme 1.



Scheme 2.

leading to (**11**) or (**14**), for which *exo* attack to (C-5 or C-6) or C-4 is favoured. In the last case, the process could revert (Br^- leaving group) from (**13**) or (**15**) to cations (**11**) or (**14**); this does not occur for (**12**), (**17**), and (**18**) (see below). Similar observations have been made in electrophilic additions to other oxanorbornenic systems.[12] The orientation of the migration would be determined by the nature of the substituents on C-2.[13] Finally, nucleophilic attack by water [only when the reaction was carried out in Bu^tOH–H_2O, (2:1) and not in CH_2Cl_2–AcOH–H_2O, (20:20:1)] on (**11**) yields hemiacetal (**12**), which undergoes ring opening followed by elimination of HBr to afford (**6**). The formation of systems related to (**6**) has been observed in solvolytic processes of other 7-oxanorbornenic systems substituted on position two,[14] as well as in the reaction between 7-oxanorbornenic tricyclic derivatives and electrophiles.[15]

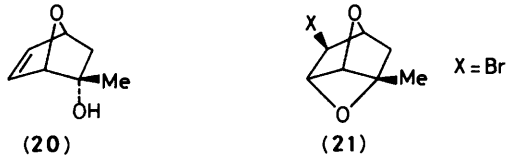
The addition of NBS in polar media (a source of Br^+)[16] to (**1a**) leads to different results depending upon the nature of the solvent employed. In CH_2Cl_2–AcOH–H_2O (20:20:1), a mixture (90%) of adducts (**16**), (**17**), and (**18**) in a 1:2:2 ratio was obtained. Alternatively, the use of a mixture of Bu^tOH–H_2O (2:1), led again to products (**4**) and (**6**) (50%) in a 3:7 ratio. These results may be interpreted using the rationale discussed before. The *trans* derivatives (**4**) and (**16**) would arise from the *anti* attack on brominium ion (**10**) by the nucleophiles present in the reaction medium. Partial decomposition of NBS[16] in the reaction conditions may be responsible for the formation of the bromide ion which would produce (**4**). The *endo* and *exo* acetoxy isomers (**17**) and (**18**) would be derived from nucleophilic attack of acetate on the onium cation (**11**) generated by migration of the C(3)–C(4) bond.



Scheme 3.

7-Oxanorbornenone (**1b**), under the experimental conditions shown above, led to a complex reaction mixture from which no pure products could be isolated. However, the reaction of ethylenedioxy derivative (**1c**) with NBS in Bu^tOH–H_2O afforded (70%) product (**19**), a monoester of 2-furylacetic acid and ethyleneglycol. A reasonable reaction pathway for the process (Scheme 3) involves the initial fragmentation of the C(1)–C(2) bond, a process previously observed for this type of substrate.[13a] The fragmentation proceeded with the expected orientation, considering the homodonating nature of the ethylenedioxy moiety in 7-oxanorbornenic systems.[6]

The peculiar behaviour of *endo*-oxanorbornenic alcohols, such as (**20**), which readily undergo intramolecular attack in electrophilic additions to yield tricyclic oxetanes (**21**),[17] prompted us to study the reaction between (**20**), Br_2, and NBS. Both electrophiles led to oxetane (**21**) (X = Br) under several reaction conditions examined: Br_2–CCl_4 (100%), Br_2–CH_2Cl_2–AcOH–H_2O (100%), and NBS–Bu^tOH–H_2O (40%).



The structural assignment of all new compounds was made from spectroscopic data (see the Experimental section). The coupling constants and splitting patterns of 1-H and 4-H were useful in assigning the *cis* or *trans* stereochemistry on positions 5 and 6 for compounds (**4**), (**5**), (**8**), (**9**), and (**16**). Rearrangement products (**17**) and (**18**) were assigned by correlation of their spectral data with the data of structurally related products previously reported.[13] Tricyclic oxetane (**21**) presents a strongly deshielded 1-H[19] (δ 5.07), consistent with a strained oxetane functionality. The stereochemistry at C-5 follows from the observed multiplicity for 4-H (d).[17]

Conclusions

The reaction between 7-oxanorbornenic substrates (**1**), Br_2, and NBS, takes place with remote control of the regioselectivity by the substituents on C-2, in a similar fashion to addition of phenylselenenyl or phenylsulphenyl halides. Nevertheless, rearrangements and/or fragmentations are encountered, in sharp contrast with the experimental findings for the Se and S electrophiles mentioned before.*

Experimental

Materials and Methods.—Analytical t.l.c. was carried out on Merck precoated silica gel plates (60 F-254) (0.20 mm), with detection by u.v. light, iodine or acidic vanillin solution. Column chromatography was performed using Merck 230–400 mesh or 70–230 mesh silica gel. Hexane, ethyl acetate, methylene dichloride, and carbon tetrachloride were distilled from phosphorus pentaoxide, and Bu^{t}OH from $KMnO_4$. I.r. spectra were recorded on a Perkin-Elmer 781 or 257 grating spectrophotometer. ^{1}H N.m.r. spectra were recorded on a Varian T-60A, Bruker AM-200 or Varian XL-300 instrument. ^{13}C N.m.r. spectra were measured on a Varian FT-80-A, and are completely decoupled. In both the ^{1}H n.m.r. and ^{13}C n.m.r. spectra, chemical shifts are reported in δ units downfield from tetramethylsilane. Starting materials were prepared by previously described methods: (**1a**) and (**1b**), ref. 5(*b*); (**20**), ref. 8(*b*). All new compounds described are racemic.

General Procedure for the Reaction between 7-Oxanorbornenic Substrates (**1a–c**), (**20**), *and* Br_2 *or NBS.*—To a solution of 3 mmol of the oxanorbornenic substrate in the corresponding solvent (10 cm^3 mmol^{-1}): CCl_4, CH_2Cl_2–AcOH–H_2O (20:20:1), or Bu^{t}OH–H_2O (2:1), was added a solution of the electrophile (Br_2 or NBS) in CCl_4, CH_2Cl_2, or Bu^{t}OH (5 cm^3 mmol^{-1}; 1.2 equiv.) respectively. The reaction mixture was stirred at 50 °C for 3 h or at room temperature for 48 h, after which time the mixture was diluted with CCl_4 (20 cm^3), EtOAc (100 cm^3), or EtOAc (50 cm^3) respectively, and the layers separated. The organic layer was washed with a saturated solution of sodium hydrogen sulphite (2 × 15 cm^3), water (2 × 15 cm^3), a saturated solution of sodium hydrogen carbonate (4 × 15 cm^3), and brine (2 × 15 cm^3), and dried ($MgSO_4$). After filtration the solution was concentrated under reduced pressure to afford a crude product which was purified by chromatography on silica gel or by recrystallization, utilizing the appropriate solvents for each case.

Reaction of (**1a**) *with* Br_2 *in* CCl_4.—A mixture of (**4**) and (**5**) [915 mg (90%); 2:3] was isolated from (**1a**) (537 mg, 3 mmol) and Br_2 (1.2 equiv.). These isomers were separated by chromatography (hexane–ethyl acetate, 2:1) to afford pure (**4**) (305 mg, 30%), and (**5**) (458 mg, 45%) as white solids.

2-endo-*Acetoxy*-5-endo,6-exo-*dibromo*-7-*oxabicyclo*[2.2.1]-*heptane*-2-exo-*carbonitrile* (**4**). M.p. 122–123 °C (from ether–hexane) (Found: C, 31.8; H, 2.65 N, 4.1; Br, 47.25. $C_9H_9NO_3Br_2$ requires C, 31.88; H, 2.67; N, 4.13; Br, 47.14%); ν_{max}(KBr) 1 750 cm^{-1} (C=O); δ_H($CDCl_3$) 5.14 (1 H, d, *J* 0.9 Hz, 1-H), 4.80 (1 H, m, 4-H), 4.40 (1 H, dd, *J* 3.5, 4.8 Hz, 5-H), 4.22 (1 H, d, *J* 3.5 Hz, 6-H), 2.74 (2 H, d, *J* 2.8 Hz, 3_{exo}-H, 3_{endo}-H), and 2.24 (3 H, s, CH_3); δ_C($CDCl_3$) 168.5, 116.8, 88.6, 80.8, 73.2, 52.8, 47.5, 37.9, and 20.12; R_F 0.42 (hexane–ethyl acetate, 2:1).

2-endo-*Acetoxy*-5-exo,6-exo-*dibromo*-7-*oxabicyclo*[2.2.1]-*heptane*-2-exo-*carbonitrile* (**5**). M.p. 152–153 °C (from ether) (Found: C, 31.75; H, 2.6; N, 4.15; Br, 47.1. $C_9H_9NO_3Br_2$ requires C, 31.88; H, 2.67; N, 4.13; Br, 47.14%); ν_{max}(KBr) 1 750 cm^{-1} (C=O); δ_H($CDCl_3$) 5.25 (1 H, s, 1-H), 4.86 (1 H, d, *J* 6.0 Hz, 4-H), 4.60 (1 H, d, *J* 7.0 Hz, 5-H or 6-H), 4.35 (1 H, d, *J* 7.0 Hz, 5-H or 6-H), 2.82 (1 H, dd, *J* 14.6, 6.0 Hz, 3_{exo}-H), 2.22 (3 H, s, CH_3), and 1.92 (1 H, d, *J* 14.6 Hz, 3_{endo}-H); δ_C([$^2H_6$]DMSO) 169.5, 117.9, 88.5, 85.3, 72.5, 54.3, 48.7, 41.1, and 20.4; R_F 0.27 (hexane–ethyl acetate, 2:1).

Reaction of (**1b**) *with* Br_2 *in* CCl_4.—A mixture of (**8**) and (**9**) [704 mg (87%); 3:1] was isolated from treatment of (**1b**) (330 mg, 3 mmol) with Br_2 (1.2 equiv.) at room temperature for 3 h. These isomers were separated by chromatography (hexane–ethyl acetate, 4:1) to afford pure (**8**) (324 mg, 40%), and (**9**) (121 mg, 15%) as white solids.

5-exo,6-endo-*Dibromo*-7-*oxabicyclo*[2.2.1]*heptan*-2-*one* (**8**). M.p. 125–126 °C (from ether–hexane) (Found: C, 26.55; H, 2.2; Br, 59.25. $C_6H_6O_2Br_2$ requires C, 26.69; H, 2.24; Br, 59.21%); ν_{max}(KBr) 1 760 cm^{-1} (C=O); δ_H($CDCl_3$) 4.96 (1 H, dm, *J* 6.3 Hz, 4-H), 4.49 (1 H, dm, *J* 5.8 Hz, 1-H), 4.37 (1 H, ddm, *J* 5.8, 2.4 Hz, 6-H), 4.24 (1 H, d, *J* 2.4 Hz, 5-H), 2.64 (1 H, ddm, *J* 18.1, 6.3 Hz, 3_{exo}-H), and 2.29 (1 H, d, *J* 18.1 Hz, 3_{endo}-H); δ_C($CDCl_3$) 202.6, 84.2, 82.3, 53.1, 46.1, and 41.3; R_F 0.47 (hexane–ethyl acetate, 3:1).

5-exo,6-exo-*Dibromo*-7-*oxabicyclo*[2.2.1]*heptan*-2-*one* (**9**). M.p. 159–160 °C (from ether) (Found: C, 26.75; H, 2.3; Br, 59.3. $C_6H_6O_2Br_2$ requires C, 26.69; H, 2.24; Br, 59.21%); ν_{max}(KBr) 1 765 cm^{-1} (C=O); δ_H($CDCl_3$) 5.10 (1 H, d, *J* 5.0 Hz, 4-H), 4.51 (1 H, s, 1-H), 4.41 (2 H, s, 5-H, 6-H), 2.60 (1 H, dd, *J* 18.0, 5.0 Hz, 3_{exo}-H), and 2.18 (1 H, d, *J* 18.0 Hz, 3_{endo}-H); δ_C([$^2H_6$]DMSO) 206.5, 87.3, 85.5, 54.0, 49.6, and 41.9; R_F 0.24 (hexane–ethyl acetate, 3:1). This product was also obtained from (**5**) with MeO^-–MeOH and formalin.

Reaction of (**1a**) *with* Br_2 *in* CH_2Cl_2–AcOH–H_2O (20:20:1).—A 1:1 mixture of (**4**) and (**5**) [814 mg (80%); 1:1] was isolated from (**1a**) (537 mg, 3 mmol) and Br_2 (1.2 equiv.). These isomers were separated by chromatography (hexane–ethyl acetate, 2:1) to afford pure (**4**) (407 mg, 40%), and pure (**5**) (398 mg, 39%) as white solids.

Reaction of (**1a**) *with* Br_2 *in* Bu^{t}OH–H_2O (2:1).—A mixture of (**4**) and (**6**) [360 mg (50%): 3:7] was isolated from (**1a**) (537 mg, 3 mmol) and Br_2 (1.2 equiv.). These products were separated by chromatography (hexane–ethyl acetate, 1:1) to afford pure (**4**) as a white solid (153 mg, 15%), and pure (**6**) as a light yellow oil (205.5 mg, 35%).

1β-*Acetoxy*-4-*formyl*-2α-*hydroxycyclopent*-3-*ene*-1α-*carbonitrile* (**6**) (Found: C, 55.4; H, 4.7; N, 7.2. $C_9H_9NO_4$ requires C, 55.38; H, 4.65; N, 7.18%); ν_{max}(neat) 3 400 (OH), 1 740 (C=O), and 1 680 cm^{-1} (conjugated aldehyde); δ_H($CDCl_3$) 9.74 (1 H, s, C*H*O), 6.66 (1 H, dt, *J* 3.6, 1.8 Hz, 3-H), 5.08 (1 H, dt, *J* 3.6, 1.5 Hz, 2-H), 3.47 (1 H, dt, *J* 17.7, 1.5 Hz, 5α-H or 5β-H), 2.97 (1 H, dt, *J* 17.7, 1.5 Hz, 5α-H or 5β-H), and 2.13 (3 H, s, CH_3); δ_C($CDCl_3$) 188.8, 170.3, 144.9, 142.3, 115.3, 81.8, 81.2, 39.8, and 20.5; R_F 0.15 (hexane–ethyl acetate, 1:1).

Reaction of (**1a**) *with NBS in* CH_2Cl_2–AcOH–H_2O (20:20:1).—A mixture of compounds (**16**), (**17**), and (**18**) [859 mg (90%); 1:2:2] was isolated from (**1a**) (537 mg, 3 mmol) and NBS (2 equiv.). This crude product was suspended in ether and a white solid crystallized (**18**), (334 mg, 35%); the mother liquors were treated with hexane–ethyl acetate at −10 °C, and a white solid crystallized (**17**), (315 mg, 33%); the residue was purified by chromatography (hexane–ethyl acetate, 2:1) to afford (**16**) as a white solid (153 mg, 16%).

* Ferrari and Vogel describe an exception to this, which, to the best of our knowledge, would be the first report of highly *trans* stereoselective bromination of a 7-oxanorbornenic substrate. This unique example appears not to involve competitive rearrangements and/or fragmentations. See: T. Ferrari and P. Vogel, *Tetrahedron Lett.*, 1986, **27**, 5507.

2-endo,5-endo-*Diacetoxy*-6-exo-*bromo*-7-*oxabicyclo*[2.2.1]-*heptane*-2-exo-*carbonitrile* (**16**). M.p. 98–99 °C (from hexane) (Found: C, 41.6; H, 3.7: N, 4.3; Br, 25.30. $C_{11}H_{12}NO_5Br$ requires C, 41.53; H, 3.80; N, 4.40; Br, 25.12%); ν_{max}(KBr) 1 765 (C=O), 1 745 cm^{-1} (C=O); $\delta_H(CDCl_3)$ 5.26 (1 H, m, 5-H), 5.13 (1 H, s, 1-H), 4.88 (1 H, dd, *J* 5.7, 5.2 Hz, 4-H), 4.04 (1 H, d, *J* 2.6 Hz, 6-H), 2.63 (1 H, ddd, *J* 14.4, 5.7, 1.3 Hz, 3_{exo}-H), 2.24 (1 H, d, *J* 14.4 Hz, 3_{endo}-H), 2.22 (3 H, s, CH_3), and 2.11 (3 H, s, CH_3); $\delta_C(CDCl_3)$ 169.2, 168.6, 117.1, 88.4, 81.3, 78.0, 73.4, 44.2, 35.7, and 20.1; R_F 0.22 (hexane–ethyl acetate, 2:1).

3-endo,6-exo-*Diacetoxy*-7-cisoid-*bromo*-2-*oxabicyclo*[2.2.1]-*heptane*-6-endo-*carbonitrile* (**17**). M.p. 115–116 °C (from hexane–ethyl acetate) (Found: C, 41.6; H, 3.75; N, 4.3; Br, 25.25. $C_{11}H_{12}NO_5Br$ requires C, 41.53; H, 3.80; N, 4.40; Br, 25.12%); ν_{max}(KBr) 1 750 cm^{-1} (C=O); $\delta_H(CDCl_3)$ 6.60 (1 H, d, *J* 2.4 Hz, 3-H), 4.52 (1 H, s, 1-H), 4.20 (1 H, d, *J* 1.5 Hz, 7-H), 3.11 (1 H, d, *J* 14.5 Hz, 5_{endo}-H), 2.83 (1 H, m, 4-H), 2.17 (3 H, s, CH_3), 2.15 (3 H, s, CH_3), and 2.03 (1 H, dd, *J* 14.7, 3.8 Hz, 5_{exo}-H); $\delta_C(CDCl_3)$ 169.1, 167.8, 115.5, 90.6, 82.9, 72.3, 48.2, 44.7, 36.0, 20.6, and 20.3; R_F 0.21 (hexane–ethyl acetate, 2:1).

3-exo,6-exo-*Diacetoxy*-7-cisoid-*bromo*-2-*oxabicyclo*[2.2.1]-*heptane*-6-endo-*carbonitrile* (**18**). M.p. 166–167 °C (from EtOH) (Found: C, 41.45; H, 3.75; N, 4.35; Br, 25.05. $C_{11}H_{12}NO_5Br$ requires C, 41.53; H, 3.80; N, 4.40; Br, 25.12%); ν_{max}(KBr) 1 750 (C=O), 1 740 cm^{-1} (C=O); $\delta_H(CDCl_3)$ 5.87 (1 H, s, 3-H), 4.65 (1 H, s, 1-H), 4.03 (1 H, d, *J* 1.5 Hz, 7-H), 2.87 (1 H, d, *J* 4.2 Hz, 4-H), 2.39 (1 H, d, *J* 14.9 Hz, 5_{endo}-H), 2.12 (1 H, dd, *J* 14.9, 4.2 Hz, 5_{exo}-H), 2.08 (3 H, s, CH_3), and 2.05 (3 H, s, CH_3); $\delta_C([^2H_6]DMSO)$ 169.2, 168.9, 116.8, 97.5, 83.2, 71.9, 45.0, 44.7, 37.5, 21.0, and 20.7; R_F 0.21 (hexane–ethyl acetate, 2:1).

Reaction of (**1a**) *with NBS in* Bu^{t}OH–H_2O (2:1).—A mixture of (**4**) (15%) and (**6**) (35%) was obtained, similarly to the results encountered in the reaction of (**1a**) with Br_2 in Bu^{t}OH–H_2O (2:1).

Reaction of (**1c**) *with NBS in* Bu^{t}OH–H_2O (2:1): *Synthesis of* 2-(2-*Furyl*)-2′-*hydroxyethyl Acetate* (**19**).—Treatment of (**1c**) (308 mg, 2 mmol) with NBS (1.2 equiv.) at room temperature for 30 min, followed by chromatography (hexane–ethyl acetate, 1:2, R_F 0.35) gave compound (**19**) [238 mg (70%)] as a light yellow oil (Found: C, 56.5; H, 6.0. $C_8H_{10}O_4$ requires C, 56.46; H, 5.92%); ν_{max}(neat) 3 400 (OH) and 1 740 cm^{-1} (C=O); $\delta_H(CDCl_3)$ 7.32 (1 H, dd, *J* 2.0, 1.0 Hz, 5-H), 6.25 (1 H, dd, *J* 3.2, 2.0 Hz, 4-H), 6.20 (1 H, *J* 3.2, 1.0 Hz, 3-H), 4.25 (2 H, m, CO_2CH_2), 3.80 (2 H, m, CH_2OH), 3.75 (2 H, s, CH_2CO), and 2.60 (1 H, br, O*H*); $\delta_C(CDCl_3)$ 169.6, 147.2, 141.9, 110.3, 107.9, 66.3, 60.4, and 33.6.

Reaction of (**20**) *with* Br_2 *in* CCl_4 *or* CH_2Cl_2–AcOH–H_2O, *or with* NBS *in* Bu^{t}OH–H_2O. *Synthesis of* 2-exo-*Bromo*-5-exo-*methyl*-4,7-*dioxatricyclo*[3.2.1.0^{3,6}]*octane* (**21**).* Compound (**21**) was isolated quantitatively (205 mg, 100%) as a light yellow oil from (**20**) (126 mg, 1 mmol) and Br_2 or NBS (1.2 equiv.), when CCl_4 or CH_2Cl_2–AcOH–H_2O (20:20:1) were used as solvent. With Bu^{t}OH/H_2O (2:1), (**21**) was isolated in 40% yield after chromatography (hexane:ethyl acetate, 1:1, R_F 0.41) (Found: C, 41.1; H, 4.5; Br, 39.1. $C_7H_9O_2Br$ requires C, 41.00; H, 4.42; Br, 38.97%); ν_{max}(neat) 1 050 cm^{-1} (C–O–C); $\delta_H(CDCl_3)$ 5.07 (1 H, d, *J* 3.5 Hz, 1-H), 4.95 (1 H, d, *J* 4.0 Hz, 4-H), 4.75 (1 H, dd, *J* 3.5, 1.5 Hz, 6-H), 4.20 (1 H, s, 5-H), 2.15 (1 H, d, *J* 13.0 Hz, 3_{endo}-H), and 1.70 (1 H, dd, *J* 13.0, 4.0 Hz, 3_{exo}-H); $\delta_C(CDCl_3)$ 91.7, 84.9, 82.7, 80.8, 50.3, 43.8, and 20.6.

* Product (**21**) is arbitrarily numbered as a bicyclic derivative to facilitate comparison of the spectral data.

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