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Ring Expansions of 2-Haloethynyl-2-norbornanols

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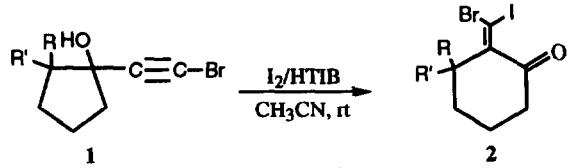
Abstract: 2-Haloethynyl-2-norbornanols react with iodine and Koser's reagent in acetonitrile to afford two ring-expanded products, 2-[(*Z*)-haloiodomethylidene]bicyclo[3.2.1]octan-3-one and 3-[(*Z*)-haloiodomethylidene]bicyclo[3.2.1]octan-2-one. These results contrast with the 2-haloethynyl-2-bornanols which lead to the corresponding 3-octanones.

We have been examining the reactions of α-alkynols with iodonium-producing reagents because they represent methods of forming α-iodoenones, β-iodoenones and mixed β,β-bromoiodoenones.[1-4] Since such compounds are formed usually in a stereospecific manner, they represent templates for more complex molecules via selective metal-catalyzed coupling reactions.[5]

Examples of these reactions are the ring expansion of α-bromoalkynylcyclopentanols with iodine and Koser's reagent[6] (HTIB, [hydroxy(tosyloxy)iodo]benzene).[7] The combination of I_2 and HTIB in stoichiometric quantities can sometimes be replaced with *N*-iodosuccinimide (NIS) and catalytic amounts of HTIB.

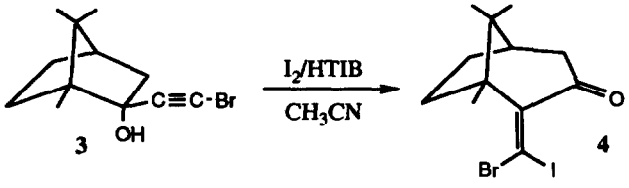


1 2

	R	R'
a	H	H
b	CH_3	CH_3
c	CH_3	H

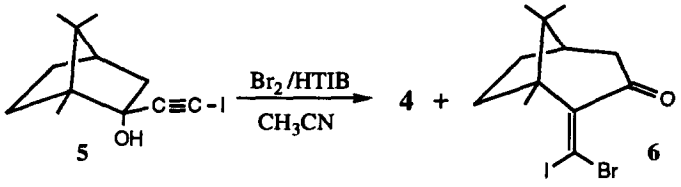
The yields of these ring expansions ranged from 75 to 82%. The preponderances of *Z*-isomers vary from greater than 12/1 for **2a**, through 7 / 1 for **2b**, to 3.3 / 1 for **2c**.

The extension of these reactions to bicyclic systems is the subject of this report. An initial step into this area was reported for a camphor derivative.[8]



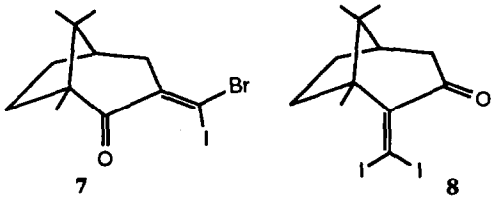
3 4

The ring-expanded product **4** was formed in 60% yield (isolated; 85% by GC). It was also one of the products (40%) when the iodo version of **3**, 2-*exo*-iodoethynyl-1,7,7-trimethylbicyclo[2.2.1]heptan-2-ol (**5**) was reacted with bromine with the express aim of obtaining the *E*-isomer **6**, which was formed in lesser amount than **4**. This is a reflection on the greater stability of an iodine-bridged vinyl cation versus a bromine-bridged vinyl cation observed in acyclic systems.[3,4]



5 6

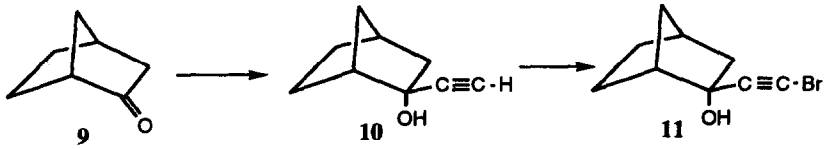
In the conversion of **5** to **4** and **6** there remained the possibility that **6** was not the *E* isomer of **4** but another isomer **7**, that could have arisen from a shift of C-3 of iodoalkynol **5**. To that end we have treated iodoalkynol **5** with stoichiometric amounts of iodine and HTIB in acetonitrile at room temperature and obtained one product in 67% conversion.



7 8

Its assignment as **8**, 2-[diiodomethylidene]-1,8,8-trimethylbicyclo[3.2.1]octan-3-one, is consistent with spectral data. These data parallel the values for **4**. Of importance are the ^{13}C chemical shifts at 58.5 and 13.8 ppm. The latter is due to the alkene carbon bearing the two iodine atoms. The other is characteristic of a methylene carbon *alpha* to a 3-keto group in a bicyclo[3.2.1] octane system.[9] This value would be inappropriate for structure **7** or its diiodo form since there are no α-keto methylene carbons and the methylene carbon in that bridge segment is an allylic one.

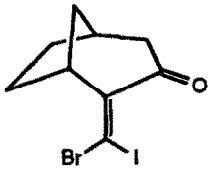
Extensions of these reactions to norcamphor derivatives are clearly in order. The next set of results pertain to the results of this direction. The bromoalkynol as well as the iodoalkynol relatives of **3** and **5** were examined. Norcamphor (**9**) was treated with lithium acetylide in THF to obtain 2-*exo*-ethynylbicyclo[2.2.1]heptan-2-ol (**10**). The product was a low melting solid that matched the properties reported in the literature.[10,11]



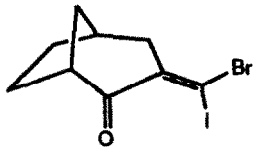
9 10 11

The alkynol **10** was treated with *N*-bromosuccinimide and catalytic amounts of $AgNO_3$ in acetone.[12] The spectral properties of **11** are in keeping with its assignment as 2-*exo*-bromoethynylbicyclo[2.2.1]heptan-2-ol.

When the alkynol **11** was subjected to the usual ring expanding conditions of iodine and HTIB in acetonitrile, a mixture of two products was formed in a ratio of about 60/40 according to GC. Separation by chromatography was not successful. The IR of the mixture indicated the disappearance of the OH bands and the appearance of a carbonyl band at 1675 cm^{-1}. The ^{13}C-NMR spectrum exhibited carbonyl lines at 193.4and 200.1 ppm as well as two alkene carbons at 143.5 and 150.0 ppm, and the MS of both provided a molecular ion at *m/z* 340 / 342. These data are consistent with a ring expansion to a tentative formula $C_9H_{10}BrIO$.

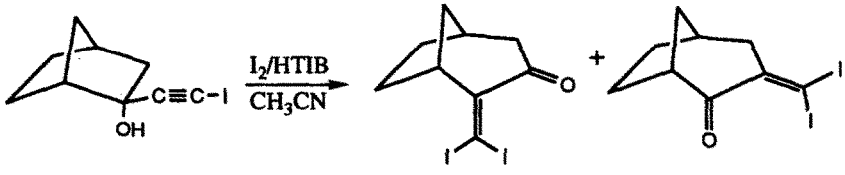


12



13

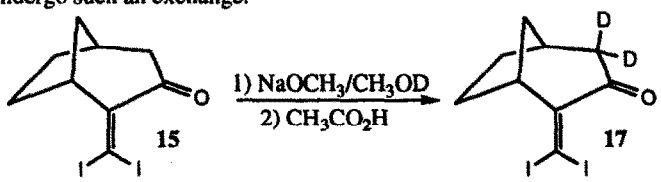
Were the two components the *E* and *Z* isomers of the expected **12**, the product of a tertiary carbon's migration, or were they the *Z*-forms of **12** and **13**, the product of a secondary carbon's migration ? To resolve the question we turned to the reaction of I_2 and HTIB with 2-iodoethynylbicyclo[2.2.1]-heptan-2-ol (**14**). If the previous mixture of the reaction were due to an *E/Z* mixture, there would be only one product in the reaction of **14**. If the mixture was the result of two modes of ring expansion, then there would be two products indicated as **15** and **16**.



14 **15** **16**

Alkynol **14** was prepared from **10** by the treatment with *N*-iodosuccinimide and catalytic amounts of $AgNO_3$ in acetone.[12] When alkynol **14** was reacted with I_2 and HTIB, the GC/MS data showed two isomeric products with parent peaks at 388. This finding demonstrated that the two products of alkynol **11** were not the *E* and *Z* isomers of **12**. In this case, however, one component was formed in much greater quantity. The mixture ratio was about 7 to 1. The IR of the mixture displayed a strong carbonyl absorption at 1675 cm^{-1}. One chromatography on silica and four recrystallizations (hot ethanol) were needed to isolate the major component **15**.

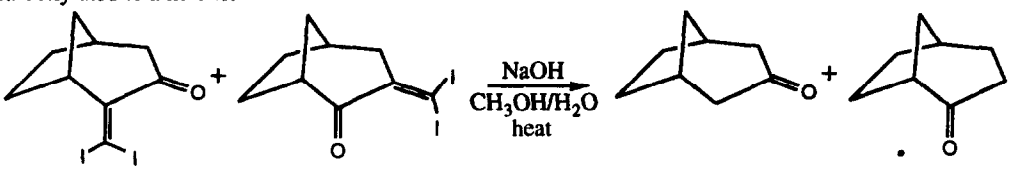
For further clarification that the major component was **15** and not **16**, a deuterium exchange experiment was undertaken. Structure **16** should not undergo any exchange since its α-hydrogen is at a bridgehead. Structure **15** should undergo such an exchange.



15 **17**

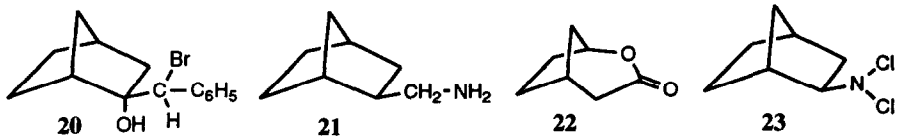
After treatment with $NaOCH_3$ in CH_3OD, the major component's ^{1}H-NMR indicated the absence of peaks centered at 2.34 and 2.48 ppm. In the ^{13}C-NMR spectrum the resonance at 51.4 ppm was not seen due to the increased relaxation time of the deuterated C-4 and the concomitant splitting by the deuterium atoms. The GC/MS was particularly instructive. The deuterated **17** had the following: *m/z* (rel. int.) 390(M^+,100), 362(10), 344(50), 263(40). About 5% of the other isomer **16** was present during the exchange process but its MS was unaffected. Both the deuterated **17** and the non-deuterated **15** had peaks at 344, which represent losses of 44 for **15** and 46 for **17**. These losses correspond to the enol of acetaldehyde, which could only have been formed from a juxtaposition of a carbonyl and a methylene as in **15** but not **16**. The minor isomer had no 344 peak. Thus the major component is assigned to structure **15**.

As a further confirmation of the structures of both **15** and **16**, their reaction mixture was treated with methanolic sodium hydroxide to convert them into a mixture of bicyclo[3.2.1]octan-3-one (**18**) and bicyclo[3.2.1]octan-2-one (**19**). Compounds **18** and **19** were identified by comparisons of GC/MS properties with authentic samples. This basic hydrolysis proceeded probably through a 1,4-addition of hydroxide to the diiodoenone system, followed by a hydrolysis of the resultant acyl iodide to a β-keto carboxylate which further decarboxylated to a ketone.



15 **16** **18** **19**

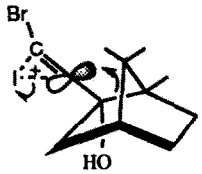
These haloalkynols from norcamphor lead to ring expansions that are different from those of the corresponding camphor-based haloalkynols. For the camphor system the shift represents a competition between a quaternary carbon versus a secondary carbon, and there is no evidence for any secondary shift.



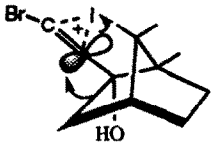
20 **21** **22** **23**

For the norcamphor system, the competition between a tertiary center and a secondary center does take place. Secondary shifts have been noted in other norbornyl compounds. An exclusive secondary shift in the ring enlargement of the magnesium salt of 2-*exo*-(α-bromobenzyl)-2-norborneol (**20**) led to bicyclo[3.2.1]-3-phenyloctan-2-one.[13] A competition was reported for a Demjanow rearrangement of 2-*exo*-norbornyl methyl amine (**21**) to bicyclo[3.2.1]octan-2-ol (40%, secondary migration) and bicyclo[3.2.1]octan-3-ol (28%, tertiary migration).[14] The *endo*- amine gave only the 2-octanol. Other norbornyl compounds have been examined for migrations to electron-deficient centers containing oxygen or nitrogen. For oxygen the Baeyer-Villiger reaction of norcamphor proceeds via a bridgehead move to the appropriate lactone (**22**) with peracids.[15] Mixed lactones are obtained with hydrogen peroxide and base.[16] For nitrogen, 2-*N,N*-dichloroaminonorbornanes (**23**) and aluminum chloride afford azabicyclo[3.2.1]octanes.[17] If the amine is *exo*, the chief product is derived from a movement of the bridgehead atom; if the amine is *endo*, the product is the result of a shift of the secondary atom. A common factor in this range of 1,2-shifts would be the need for an alignment of filled

orbitals of the shifting bonds to be parallel with the developing unfilled orbitals at the rear of the anti-periplanar leaving groups.



C-1/C-2 SHIFT



C-2/C-3 SHIFT

In the reactions at hand, the developing orbitals of the vinyl cations are formed anti-periplanar to the iodonium attack at the halogen-bearing carbons. The preferred direction of attack on the alkyne to form the vinyl cations should be from below an extended C-1/C-2/C-3 plane to avoid interactions with substituents on the bridging C-7 atom. The so-formed iodine-bridged vinyl cations can rotate about the C-2/C-1' (alkyne) bond to be parallel to one of the two migrating bonds. In the case of a shift of the tertiary C-1/C-2 bond, the vinyl cationic orbital must be generated by iodonium attack in an extended C-1/C-2/C-1' plane with the iodine atom *anti* to C-1. For the case of a shift of the secondary C-2/C-3 bond, the vinyl cationic orbital must be generated by iodonium attack in an extended C-2/C-3/C-1' plane *anti* to the C-3. In so doing the iodonium species in the first case would not be impeded by a methyl on C-1, but would be in the second case. This preference leads to the 3-keto isomers in the bornyl series. For the norbornyl cases the methyl intervention is replaced by the lesser interaction of the iodonium ion with a C-1 H . This qualitative analysis agrees with the findings that **8** is the major product from **5**, that **15** is formed in greater quantity than **16** in the ring expansion of **14**, and that **12** is formed in somewhat larger amounts than **13** in the reaction of **11**.

Although these findings diminish the value of norbornyl ring expansions to mixed dihaloenones suitable for synthetic templates, they are useful for the preparations of diiodoenones, which can serve as novel entries into a variety of functionalized ring systems derived from many terpenoid ketones.

EXPERIMENTAL SECTION

Melting points are uncorrected and were taken on a Hoover-Thomas melting point apparatus. IR spectra were obtained with a Polaris FTIR Mattson Instruments spectrophotometer. ^{1}H-NMR spectra were recorded on a Varian Gemini 200 operating in the Fourier Transform mode at 200 MHz. GC and MS analyses were carried out on a Hewlett Packard GC/MS HP5890 with a HP-5 column (95% methyl silicone, 0.25 mm x 30 m). Elemental analyses were performed by the E+R Microanalytical Laboratory, Corona, New York.

The ketones and lithium acetylide diamine complex were obtained from the Aldrich Chemical Co. Solvents such as carbon tetrachloride, acetonitrile and hexanes were received from the J.T. Baker Co. Methylene chloride and chloroform were obtained from Fisher Scientific.

Preparation of 2-*exo*-ethynyl-1,7,7-trimethylbicyclo[2.2.1]heptan-2-ol

Lithium acetylide ethylenediamine complex (2.43 g, 26.4 mmol) was suspended in 30 mL of freshly distilled THF cooled at 0 °C. (1*R*)-(+)-Camphor (1.56 g, 10.2 mmol) in 15 mL of THF was added dropwise to the stirring suspension. The mixture was allowed to stir at room temperature for a further 4 h. The reaction mixture was poured into ice water containing excess amounts of NH_4Cl. The aqueous layer was extracted with diethyl ether. The ether solution was subsequently washed 3 times with 50 mL of water, dried with $MgSO_4$ and evaporated to a red residue. The product was isolated by filtering the crude residue through a short pad of silica gel (40-140 mesh) with a 1:1 mixture of CH_2Cl_2 / hexanes. Evaporation of the filtrate under vacuum yielded a white solid (1.17 g, 64%): mp 57.5-59.5 °C (lit.[18] 61-62 °C); ^{1}H-NMR and ^{13}C-NMR spectra matched those of ref. 18; IR (Nujol) 3430 (s), 2300 (w), 1460 (s), 1370 (m), 1050 (m), 1030 (m), 1000 (m), 960 (m) cm^{-1}; GC/MS *m/z* (rel. int.) 163 (M-CH_3, 7), 162 (M-CH_3-H, 6), 145 (6), 122 (6), 110 (45), 95 (100), 68 (15), 65 (12), 56 (14), 53 (35), 41 (46).

Preparation of 2-*exo*-bromoethynyl-1,7,7-trimethylbicyclo[2.2.1]heptan-2-ol (3)

2-*exo*-Bromoethynyl-1,7,7-trimethylbicyclo[2.2.1]heptan-2-ol was prepared according to the procedure of Hofmeister.[12] 2-*exo*-Ethynyl-1,7,7-trimethylbicyclo[2.2.1]heptan-2-ol (207 mg, 1.16 mmol) was dissolved in 30 mL of acetone. NBS (241 mg, 1.35 mmol) and $AgNO_3$ (56 mg, 0.33 mmol) were added in one portion to the stirring solution. The reaction was protected from light and stirred at room temperature for 45 min. The product was filtered through a short pad of silica gel (40-140 mesh) in CH_2Cl_2 / hexanes (1:1) to give a light green solid: mp 60.5-62.5 °C: ^{1}H-NMR ($CDCl_3$) δ 0.86 (s, 3H), 0.94(s, 3H), 1.04(s, 3H). 1.40-1.90 (m, 6H), 2.15-2.28 (m, 1H); ^{13}C-NMR ($CDCl_3$) δ 10.8, 21.5, 21.9, 27.4, 30.3, 33.0, 43.7, 45.9, 48.5, 54.4, 79.7, 84.7; IR (Nujol) 3480 (s), 2200 (w), 1060 (s), 1000 (m), 975 (m), 920 (m), 760 (m), 740 (m) cm^{-1}; GC/MS *m/z* (rel. int.) 177 (M^+-Br, 6), 133 (18), 110 (40), 95 (100), 41 (33).

Synthesis of 2-[(*Z*)-bromoiodomethylidene]-1,8,8-trimethylbicyclo[3.2.1]octan-3-one (4)

2-*exo*-Bromoethynyl-1,7,7-trimethylbicyclo-[2.2.1]heptan-2-ol (923 mg, 3.59 mmol) was dissolved in 30 mL of acetonitrile cooled at ice bath temperature. A single portion of iodine (910 mg, 3.58 mmol) and HTIB (1.41 g, 3.60 mmol) was added to the acetonitrile solution. The solution was protected from light and stirred at room temperature for 4 h. The reaction mixture was then diluted with 100 mL of diethyl ether. The ether solution was subsequently washed with 50 mL of 5% $Na_2S_2O_3$ solution and 3 x 50 mL of water. It was dried with $MgSO_4$ and evaporated under vacuum to give a light green oily residue. The product was isolated by means of silica gel (40-140 mesh) column chromatography. The first fraction, iodobenzene, was eluted with hexanes. The product was obtained from the second fraction, which was eluted with 1:1 mixture of CH_2Cl_2 / hexanes to afford a light green solid after solvent evaporation under vacuum (779 mg, 60%). The product was characterized as follows: mp 59 -60 °C; ^{1}H-NMR ($CDCl_3$) δ 0.88 (s, 3H), 0.96 (s, 3H), 1.04 (s, 3H), 1.52 (m, 2H), 1.77 (m, 2H), 2.01 (m, 1H), 2.14 (m, 1H), 2.57 (m, 1H), 2.90 (m, 1H); ^{13}C-NMR ($CDCl_3$) δ 14.5, 20.2, 24.6, 28.6, 33.6, 41.4, 46.2, 47.3, 58.3, 59.0, 144.5, 203.1; IR (Nujol) 1700 (s), 1560 (m), 1220 (m), 1200 (m), 960 (m), 770 (s) cm^{-1}; MS *m/z* (rel. int.) 382/384 (M^+, 4), 354/356 ((M-CO)$^+$, 4), 227/229 ((M-CO-I)$^+$, 10), 148 ((M-CO-I-Br)$^+$, 24), 91 (34), 41 (100); Anal. Calcd for $C_{12}H_{16}BrIO$: C, 37.59; H, 4.22. Found: C, 37.79; H, 4.13.

Preparation of 2-*exo*-iodoethynyl-1,7,7-trimethylbicyclo[2.2.1]heptan-2-ol (5)

Compound **5** was prepared according to the procedure of Hofmeister from 2-*exo*-ethynyl-1,7,7-trimethylbicyclo[2.2.1]heptan-2-ol.[12] The product melted at 88-89.5 °C and had the following spectra: ^{1}H-NMR ($CDCl_3$) δ 0.88 (s, 3H), 0.95 (s, 3H), 1.04 (s, 3H), 1.40-1.90 (m, 6H), 2.2 (m, 1H); ^{13}C-NMR ($CDCl_3$) δ 0.2, 10.9, 21.5, 21.9, 27.4, 33.0, 45.9, 48.5, 48.6, 54.5, 80.3, 99.2; IR (Nujol) 3500 (s), 2100 (w), 1460 (s), 1380 (s), 1050 (m), 950 (m), 850 (w), 725 (m) cm^{-1}; MS *m/z* (rel. int.) 286 ($(M-H_2O)^+$, 1), 177 ($(M-I)^+$, 10), 152 ($M-C_2HI$, 2), 127 (I^+, 6), 108 (27), 95 (95), 91 (19), 79 (10), 77 (12), 69 (18), 41 (100). Anal. Calcd for $C_{12}H_{17}IO$: C, 47.39; H, 5.63. Found: C, 47.07; H, 5.71.

Preparation of 2-[diiodomethylidene]-1,8,8-trimethylbicyclo[3.2.1]octan-3-one (8)

Compound **5** (167 mg, 0.55 mmol) was dissolved in 10 mL of acetonitrile. To the resulting solution, iodine (154 mg, 0.61 mmol) and HTIB (230 mg, 0.59 mmol) were added in one portion at room temperature. The reaction mixture was protected from light and stirred at room temperature. After 18 h of stirring, the mixture was diluted with 50 mL of diethyl ether. The ether layer was then washed with saturated aqueous sodium thiosulfate, followed by water (2 x 50 mL) and subsequently dried with $MgSO_4$. A yellow semi-solid was obtained after solvent evaporation under vacuum. The product was purified by means of silica gel column chromatography (40-140 mesh). Iodobenzene was eluted in hexanes. The product was eluted next with a mixture of CH_2Cl_2/hexanes (1:1). A yellow solid (107 mg, 45%) was obtained after solvent evaporation and melted at 120-121 °C. It had the following spectral data: ^{1}H-NMR ($CDCl_3$) δ 0.87 (s, 3H), 0.95 (s, 3H), 1.03 (s, 3H), 1.25 (m, 1H), 1.52 (m, 1H), 1.77 (m, 1H), 2.00 (m, 1H), 2.12 (m, 1H), 2.53 (m, 1H), 2.70 (m, 1H); ^{13}C-NMR ($CDCl_3$) δ 14.4, 20.2, 24.5, 28.3, 33.2, 46.8, 47.1, 47.9, 59.0, 149.8, 202.9; GC/MS *m/z* (rel. int.) 430 (M^+, 100), 402 ($(M-CO)^+$, 30), 275 ($(M-CO-I)^+$, 15), 148 ($(M-CO-2I)^+$, 50), 91 (25); IR(Nujol) 1680 (s), 1530 (m), 1200 (m), 1140 (m), 1110 (m), 1050 (m), 1020 (m), 1000 (m), 970 (m), 750 (s) cm^{-1}. Anal. Calcd for $C_{12}H_{20}I_2O$: C, 33.50; H, 3.75. Found: C, 33.51; H, 3.92.

Preparation of 2-*exo*-ethynylbicyclo[2.2.1]heptan-2-ol (10)

Lithium acetylide ethylenediamine complex (11.23 g, 122 mmol) was suspended under N_2 in 80 mL of freshly distilled THF. A solution of (±)-norcamphor (3.51g, 31.86 mmol) in 20 mL of THF was added dropwise via an addition funnel to the reaction mixture, cooled with an ice-bath. The funnel was rinsed further with 20 mL of THF. The solution was stirred overnight at room temperature under a nitrogen atmosphere. The reaction mixture was quenched by pouring into a saturated solution of NH_4Cl. The product **10** was extracted from the aqueous layer with 50 mL of diethyl ether, which was then washed with saturated NH_4Cl (3 x 50 mL). This was followed by a water wash (50 mL) and a saturated NaCl wash. The ether layer was dried over $MgSO_4$. After the ether was evaporated, a clear brown oil was obtained (4.14 g, 96%). The product was purified by means of a silica gel column chromatography (40-140 mesh) with CH_2Cl_2 as the eluting solvent to afford a light green oil (3.97 g, 92 %), which upon refrigeration gave a yellow solid (mp 44-45 °C, lit[10] 44-45 °C). Its spectral properties were as follows: ^{1}H-NMR ($CDCl_3$) δ 1.27-1.44 (m, 4H), 1.48-1.59 (m, 1H), 1.77-1.82 (m, 1H), 1.91-2.26 (m, 3H), 2.38-2.45 (m, 1H), 2.51 (s, 1H); ^{13}C-NMR ($CDCl_3$) δ 21.5, 29.3, 37.5, 39.4, 48.3, 50.3, 71.4, 73.9, 90.3; GC/MS *m/z* (rel. int.) 136 (M^+, 15), 107 (30), 93 (25), 67 (100): IR (Nujol) 3400 (s), 3320 (s), 2150 (w), 1150 (s), 1100 (m) cm^{-1}.

Preparation of 2-*exo*-bromoethynylbicyclo[2.2.1]heptan-2-ol (11)

Compound **11** was prepared according to the procedure of Hofmeister[12] from 2-*exo*-ethynylbicyclo[2.2.1]heptan-2-ol (**10**). The spectral properties of **11** (mp 65.5-67 °C) are as follows: ^{1}H-NMR ($CDCl_3$) δ 1.32 - 1.39 (m, 3H), 1.55 (m, 1H), 1.77 (m, 1H), 1.95 (m, 1H), 2.12 (m, 2H), 2.22 (s, 1H), 2.40 (s, 1H), 2,49 (m, 1H); ^{13}C-NMR ($CDCl_3$) δ 21.0, 28.7, 36.9, 38.8, 43.4, 47.6, 49.6, 74.6, 85.5; GC/MS *m/z* (rel. int.) 214/216 (M^+, 1), 146/148 (30), 135 ($(M-Br)^+$, 25) 131/133 (20), 107 (20), 91 (85), 79 (85), 67 (100); IR (Nujol) 3400 (s), 2200 (m), 1175 (s), 1080 (m), 1050 (m), 1000 (s), 900 (s), 710 (s) cm^{-1}. Anal. Calcd for $C_9H_{11}BrO$: C, 50.26; H, 5.15. Found: C, 50.67; H, 5.35.

Preparation of 2-*exo*-iodoethynylbicyclo[2.2.1]heptan-2-ol (14)

Compound **14** was prepared by the procedure of Hofmeister[12] from 2-ethynylbicyclo[2.2.1]-heptan-2-ol (**10**). The product, a yellow solid, melted at 59-60 °C. and had these spectroscopic values: ^{1}H-NMR ($CDCl_3$) δ 1.31-1.46 (m, 3H), 1.50-1.60 (m, 1H), 1.77-1.82 (m, 1H), 1.89-1.96 (m, 1H), 2.02-2.05 (m, 2H), 2.11-2.21 (m, 1H), 2.40 (m, 1H); ^{13}C-NMR ($CDCl_3$) δ 0.1, 21.6, 29.3, 37.5, 39.9, 48.3, 50.3, 75.8, 100.6; GC/MS *m/z* (rel. int.) 234(5), 218 (20), 194 (70), 135 (20), 127 (10), 91 (70), 79 (100), 67 (80); IR (Nujol) 3250(s), 1160(m), 1060(s), 980(m), 770(m) cm^{-1}. Anal. Calcd for $C_9H_{11}IO$: C, 41.23; H, 4.23. Found: C, 41.28; H, 4.17.

Preparation of 2-[(*Z*)-bromoiodomethylidene]bicyclo[3.2.1]octan-3-one (12) and 3-[(*Z*)-bromoiodomethylidene]bicyclo[3.2.1]octan-2-one (13)

Compound **11** (240 mg, 1.04 mmol) was dissolved in 10 mL of acetonitrile. Iodine (279 mg, 1.10 mmol) and HTIB (418 mg, 1.07 mmol) were added together to the acetonitrile solution at room temperature. The reaction mixture was protected from light and stirred overnight at room temperature. After 18 h of stirring, the acetonitrile mixture was diluted with 75 mL of diethyl ether. The ether layer was washed with saturated aqueous $Na_2S_2O_3$ (2 x 60 mL) and then followed by 60 mL of water. The aqueous layer was then re-extracted with a further aliquot of ether (25 mL). The combined organic layer was washed with 60 mL of saturated NaCl solution and then dried with $MgSO_4$. A yellow oil (515 mg) was obtained after solvent evaporation under vacuum. The products were purified by means of an alumina column (basic). Iodobenzene was eluted first with carbon tetrachloride. The products were eluted next with a mixture of CCl_4 / CH_2Cl_2 (1:1). After evaporation of solvents, a yellow solid (182 mg, 51%) was obtained. An analysis by the GC/MS indicated that two products of identical masses were present in a ratio of 60:40. GC/MS *m/z* (rel. int.) larger peak: 340/342 (100), 312/314 (10), 296/298 (70), 281/283 (10), 169/171 (30), 155/157 (20), 105 (80), 91 (90), 51 (60); smaller peak: 340/342 (90), 312/314 (70), 281/283 (10), 155/157 (15), 105 (90), 79 (70), 67 (100). ^{13}C-NMR ($CDCl_3$) δ 200.1, 193.4, 150.0, 143.5, 59.6, 58.0, 54.2, 51.2, 50.9, 47.7, 44.5, 38.8, 38.2, 37.4, 36.9, 36.3, 35.6, 30.1, 29.7, 29.4, 28.3, 27.2. IR (Nujol) 1675 (s), 1600 (m), 1580 (m), 1450 (s), 1260 (s), 775 (s), 700 (s), 680 (s), 600 (s) cm^{-1}.

Preparation of 2-[diiodomethylidene]bicyclo[3.2.1]octan-3-one (15)

Iodine (95.0 mg, 0.37 mmol) and HTIB (128 mg, 0.28 mmol) were added in one portion to acetonitrile (10 mL) containing 2-iodoethynylbicyclo[2.2.1]-heptan-2-ol (**14**) (72.6 mg, 0.28 mmol). The reaction mixture was protected from light and stirred at room temperature for 18 h. The mixture was diluted with 50 mL of

diethyl ether and was then washed with saturated aqueous sodium thiosulfate. The organic layer was further washed with water (2 x 50 mL) and then dried with $MgSO_4$. A yellow semi-solid was obtained after the solvents were evaporated under vacuum. The product, **15**, was purified by means of silica gel column chromatography (40-140 mesh). Iodobenzene was eluted as the first fraction using hexanes as the eluant. The product was obtained as the next fraction using CH_2Cl_2 / hexanes (1:1) as the eluting solvents. After solvent removal, a yellow solid was obtained (67 mg, 62%). A GC/MS analysis of the product from the column showed that two products of identical masses were present in a ratio of 7:1. The GC/MS of the mixture : *m/z* (rel. int.) larger peak 388 (100), 360 (5), 344 (25), 261 (25), 217 (10), 179 (10), 134 (10), 106 (20), 91 (20), 51 (10); smaller peak 388 (100), 360 (40), 261 (10), 205 (5), 165 (15), 134 (10), 106 (20), 91 (15), 67 (20). IR (Nujol) of mixture: 1675 (s), 1550 (m), 1240 (s), 1200 (m), 1100 (s), 950 (m), 900 (m), 710 (s). Recrystallization from hot ethanol (4 times) afforded yellow crystals, which melted at 103-106 °C (50 mg, 47%). Analysis by GC/MS indicated that the yellow crystals had the cracking pattern of the larger peak and these other data: ^{1}H-NMR ($CDCl_3$) δ 1.54 -1.59 (m, 2H), 1.68 - 1.91 (m, 4H), 2.29 - 2.37 (m, 1H), 2.46 - 2.49 (m, 1H), 2.53 - 2.55 (m, 1H), 3.46 - 3.52 (m, 1H). ^{13}C-NMR ($CDCl_3$) δ 16.6, 28.9, 30.0, 36.9, 38.7, 51.4, 51.6, 156.7, 200.0. Anal. Calcd for $C_9H_{10}I_2O$: C, 27.86; H, 2.60. Found: C, 27.77; H, 2.50.

Preparation of 2-[diiodomethylidene]-4,4-dideuterobicyclo[3.2.1]octan-3-one (17)

CH_3OD (5 mL) was placed in a dry 2-necked round-bottomed flask under nitrogen. A small piece of sodium metal was added and allowed to stir for 5 min under nitrogen until it had dissolved. The ketone **15** (0.065 g, 0.17 mmol) was dissolved in 50% v/v CH_3OD / ether and added slowly into the Na / CH_3OD solution with a glass syringe. The solution was allowed to stir overnight under nitrogen. The solution was made slightly acidic upon addition of CH_3COOH before the solvent was evaporated almost to dryness. The solid product was dissolved in 40 mL ether and washed twice with 40 mL of $NaHCO_3$ solution followed by 40 mL water and then 40 mL brine. The ether layer was dried over $MgSO_4$. Solvent evaporation gave a yellow solid (0.061g) which was dried overnight *in vacuo*. GC/MS *m/z* (rel. int.) 390 (100), 362 (10), 344 (50), 263 (40), 217 (15), 179 (20), 136 (10), 107 (50), 91 (40), 79 (35), 51 (30). Minor peak 388 (100), 360 (30), 344 (20) 261 (10), 165 (40), 106 (50), 91 (50), 67 (50). ^{1}H-NMR ($CDCl_3$) δ 1.57 - 1.65 (m, 2H), 1.70 - 1.99 (m, 4H), 2.54 - 2.59 (m, 1H), 3.49 - 3.55 (m, 1H). ^{13}C-NMR ($CDCl_3$) δ 200.2, 156.7, 51.6, 38.7, 36.8, 29.9, 28.9, 16.3.

Preparation of bicyclo[3.2.1]octanones 18 and 19

A mixture of **15** (67 mg) and **16** (17 mg) isomers was dissolved in a solution of 24 mL CH_3OH and 8 mL H_2O and treated with 15 equivalents of NaOH. After a 4 h reflux, the mixture was extracted with ether. The ether was washed with water and dried over $MgSO_4$. After solvent removal the residue was analyzed by GC/MS *m/z* (rel. int.): **18** [24%] 124 (M^+,40), 109 (20), 95 (20), 80 (100), 67 (30), 55 (25); **19** [15%] 124 (M^+, 30), 95 (10), 80 (100), 67 (60), 55 (25); **15** [33%] 388 (M^+, 100), 360 (40), 261 (15), 205 (10), 165 (20), 127 (10), 106 (40), 91 (20), 67 (60); **16** [13%] 388 (M^+, 100), 360 (5), 344 (20), 261 (30), 165 (10), 127 (10), 106 (30), 91 (35), 67 (15).

When this procedure was repeated except that the refluxing period was 24 h, only the peaks corresponding to **18** (61%) and **19** (31%) were seen. Authentic samples of these compounds were obtained from the Aldrich Chemical Company.

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