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Reactions of the halonium ions of carenes and pinenes: An experimental and theoretical study

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ABSTRACT

The reactions of vinylcyclopropane (+)-2-carene (1) and vinylcyclobutanes (-)-β-pinene (7), (-)-α-pinene (11), and (-)-nopol (12) with electrophilic halogens in the presence of oxygen and nitrogen nucleophiles in various solvents have been investigated. The halonium ion intermediates that were presumably formed were very reactive and led to opening of the conjugated cyclopropane or cyclobutane. Reactions of chloramine-T trihydrate with compound 1 in acetonitrile gave amidine 13 and diazepine 14. Reactions of chloramine-T trihydrate with pinenes in methylene chloride gave allylic tosylamines 22, 16B and 24. Mechanisms to explain the observations are proposed and supported by *ab initio* and Density Functional Theory calculations on the carenes and pinenes in this report and their bromonium ion intermediates. For comparisons, the relative extent of conjugation with the bromonium ion moiety of these, as well as select cyclohexene and cyclohexadiene systems and their corresponding bromonium ions, were optimized at the B3LYP/cc-pVDZ level of theory, and then these geometries were analyzed using the absolute hardness index at the Hartree-Fock/aug-cc-pVDZ and B3LYP/aug-cc-pVDZ levels of theory. Additionally, Natural Population Analysis charges were calculated for these systems using Møller-Plessett Second-Order Perturbation Theory electron densities and the aug-cc-pVDZ basis set. Combining the results of these theoretical methods with analysis of structural details of their optimized geometries gives much electronic structure insight into the extent of conjugation of bromonium ions of the carenes and pinenes reported here, and places them in relative context of more traditional conjugated and non-conjugated bromonium ion systems. In particular, bromonium ions of compounds 1, 7, and 11 display structural distortions, charge delocalizations and hardness values comparable with those of traditional conjugated cyclohexadienes, with possible reasons for subtle differences presented.

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1. Introduction

(+)-2-Carene (**1**) is an important chiral terpene used as a starting material for asymmetric synthesis [1]. Chuiko and coworkers have reported a Prins reaction of compound **1** in which the cyclopropane ring was not opened, indicating that the tertiary carbocation was formed rather than the cyclopropyl carbinyl cation (Scheme 1) [2]. As Chuiko has pointed out [3], this suggests strongly that the vinyl cyclopropane in compound **1** is not conjugated. Chuiko [3,4] and Brown [5] have also presented further evidence of a lack of conjugation in compound **1**.

However, we have previously shown that (+)-2-carene epoxide (**2**), in which the epoxide is conjugated to the cyclopropane, displayed heightened reactivity compared to typical epoxides when treated with weak protic acids (Scheme 2) [6]. The non-conjugated epoxide (**4**) from (+)-3-carene (**3**) did not react in the same manner (Scheme 2) [6,7]. We have since found similar behaviour with the tosyl aziridines **5** and **6** (Scheme 3) [8-10]. We suggested that in the reactions of compound **2** or **5** with water, the positive charge on the protonated heteroatom was delocalized through the cyclopropane [8-13] and both rings were opened in a concerted fashion by the oxygen nucleophile (Scheme 2). This released the strain energy of both rings. The three-membered heterocycle and cyclopropane "together" (compounds **2** and **5**) were clearly much more reactive than either one by itself (compounds **4** and **6**).

We hypothesized that similarly, a positively charged bromonium or chloronium ion of compound **1** would also be delocalized through the cyclopropane, and that attack by a nucleophile, in general, would occur at the gem-dimethyl carbon of the cyclopropane ring to give, at least initially,

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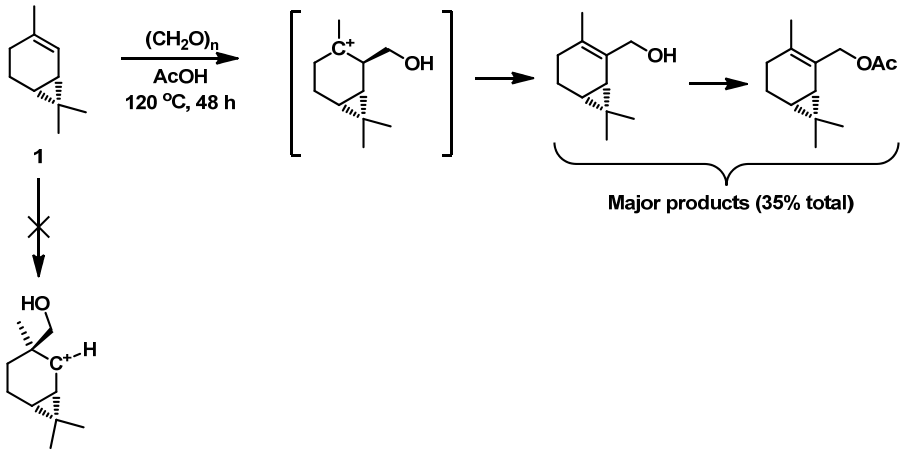
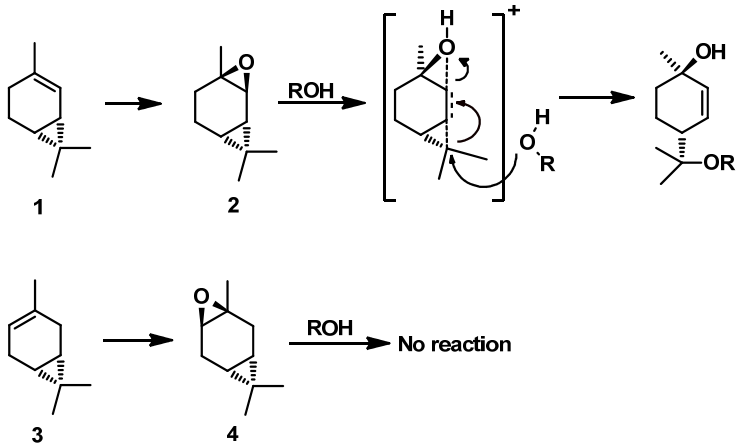
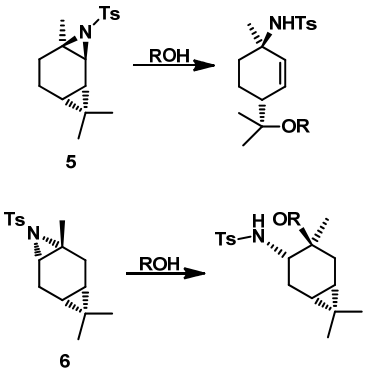


Scheme 1 [2]



Scheme 2 [6]

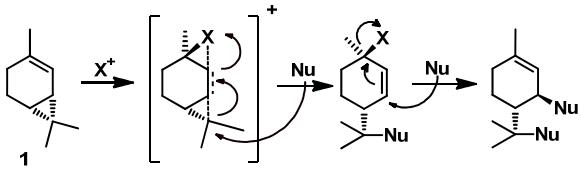


Scheme 3 [8-10]

similar products. We anticipated that the tertiary allylic halide might be displaced by another nucleophile (Scheme 4).

Also of interest to us was the formation of cyclobutyl halonium ions from pinenes. The likelihood of this succeeding was suggested by the work of Carman and coworkers, who in 1997 reported that reaction of β-pinene (**7**) with *N*-bromo-succinimide (NBS) and acetonitrile, followed by a water quench, produced amide **8** *via* a Ritter reaction in which the cyclobutane ring was opened (Scheme 5) [14]. The allylic bromide **8** was reported to be "surprisingly stable" [15]. In 2004, they also noted that trapping with hydride instead of water produced two other products, compounds **9** and **10** (Scheme 5) [15].

In this paper, we report our investigation of reactions of the halonium ions of compounds **1**, (-)-**7**, (-)-α-pinene **11**, and (-)-nopol **12**.

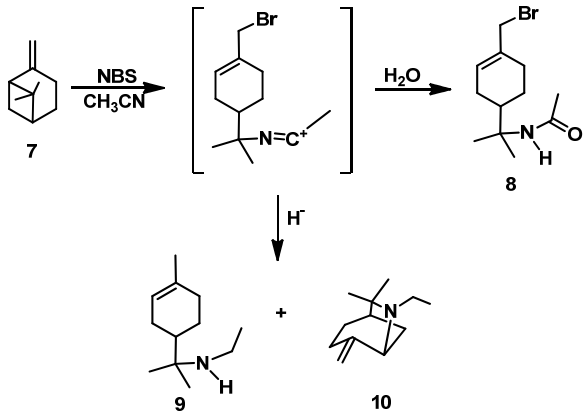


Scheme 4

2. Experimental

2.1. General

(+)-2-Carene (97%) used in the early experiments was purchased from TCI America (Portland, OR). (+)-2-carene (97%) used in the later experiments was purchased from Aldrich Chemical Company (Milwaukee, WI). No significant



Scheme 5 [14,15]

difference was observed in the results using the two different sources of (+)-2-carene. (-)-β-Pinene (99%), (-)-nopol (98%), phenyltrimethylammonium tribromide, chloramine-T trihydrate, *N*-chlorosuccinimide, *N*-bromo succinimide, calcium hypochlorite, anhydrous dichloromethane, and anhydrous acetonitrile were purchased from Aldrich. (-)-α-Pinene (98%) was obtained from TCI America. Dichloromethane was purchased from Mallinckrodt (Hazelwood, MO). TLC plates (Silica gel GF, 250 micron, 10 × 20 cm, catalog No. 21521) were purchased from Analtech (Newark, DE). TLC's were visualized under short wave UV, and then with I_2 and then by spraying with ceric ammonium nitrate/sulfuric acid and heating. Column chromatography was carried out using flash silica gel from Aldrich (cat. No. 60737). Infrared spectra were run on a Mattson Galaxy FTIR Series 3000 (Penn State Schuylkill) or a Perkin-Elmer Spectrum One using a diamond-ATR attachment for the direct powder analysis (Villanova University). Spectra were taken at a resolution 4 cm^{-1}, 16 scans averaged (Villanova University). NMR spectra were obtained on a Bruker 400 MHz Ultrashield NMR (Muhlenberg College), or Bruker CDPX-300 or DRX-400 instrument (Penn State University Park). Ultra-violet/Visible spectroscopy was performed on a Thermo Electron Corp. Genesys 10 UV. Optical rotation was measured using a Steeg and Reuter SR6 polarimeter (Muhlenberg College) or a Carl Zeiss Circle Polarimeter (Penn State Schuylkill). Elemental analysis was performed by Atlantic Microlab (Norcross, GA). X-ray Crystallography was performed using a Bruker-AXS SMART-APEX (Penn State University Park). An Applied Biosystems API 2000 Triple Quadrupole Mass Spectrometer was used to determine molecular masses by electrospray ionization (Villanova University). A 0.1% formic acid:methanol (*v*:*v*) mixture containing the compound at 100 ppm was infused at 20 μL/min into the electrospray source. Source and compound dependent parameters for the MS/MS product ion analysis were as follows: curtain gas (CUR) = 20; nebulizer gas (GAS1) = 15, heater gas (GAS2) = 15, electrospray voltage (IS) = 5500 V; source temperature (TEM) = 398 K; declustering potential (DP) = 40 V; focusing potential (FP) = 400 V; entrance potential (EP) = 10 V; collision energy (CE) = 25 V; cell exit potential (CXP) = 4 V. $[M+H]^+$ ions were selected as precursor ions in all MS/MS experiments. Melting points were determined on a Thomas Hoover Capillary Melting Point Apparatus (Arthur H. Thomas Co., Philadelphia, PA).

2.2. Synthesis

2.2.1. Synthesis of (4aR,8aS)-2,4,4,7-tetramethyl-1-[(4-methylphenyl)sulfonyl]-1,4,4a,5,6,8a-hexahydro quinazoline (13) [16,17]

A 50 mL two-necked round bottom flask was oven-dried, fitted with septa, and cooled under N_2. A stir bar, 0.58 mL (0.5 g, 3.67 mmol) of (+)-2-carene (**1**), 1.1357 g (4.04 mmol) of chloramine-T trihydrate, and 18.5 mL (0.2 M with respect to compound **1**) of anhydrous acetonitrile were added to the flask and stirred. Finally 0.1405 g (0.367 mmol) of phenyltrimethylammonium tribromide was added to the flask and left to stir at room temperature (22 °C). The solution was a heterogeneous white slurry. TLC (60% ethyl acetate:hexanes, *v*:*v*) after 30 minutes showed a complete reaction. The contents of the flask were gravity filtered to remove the undissolved solids and the liquid was concentrated *in vacuo* to a yellow solid. The crude product was chromatographed on flash silica gel with mixtures of ethyl acetate and hexanes. Fractions containing **13** were combined and concentrated to solid (0.6785 g). The solid was dissolved in a small amount of hot methyl *t*-butyl ether, hot-filtered, and allowed to stand at -10 °C overnight. Colorless crystals (0.2897 g, 22.8%) were isolated and washed twice with cold MTBE. A second crop was obtained from the mother liquor (0.0240 g, 1.9%). Crystals for X-ray crystallography were grown from toluene by slow evaporation.

(4aR, 8aS)-2, 4, 4, 7-Tetramethyl-1-[(4-methylphenyl)sulfonyl]-1,4,4a,5,6,8a-hexahydroquinazoline (**13**): R_f (60% ethyl acetate:hexanes): 0.37. M.p.: 163-173 °C (Dec.) (Lit. 163 °C [17]). ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 7.79 (d, 2H, Ar-H), 7.31 (d, 2H, Ar-H), 5.98 (m, 1H, HC=C), 4.69 (t, *J* = 5.2 Hz, 1H, HC-N), 2.43 (s, 3H, H_3C-Ar), 2.05 (s, 3H, H_3CC(N)=N), 2.02-1.72 (m, 4H, alkyl), 1.76 (s, 3H, H_3C-C=C), 1.28 (s, 3H, CH_3), 1.2-1.5 (m, 1H, alkyl, 1.13 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 148.2, 143.7, 140.0, 139.1, 129.7, 127.1, 121.0, 52.9, 52.3, 42.8, 29.9, 28.9, 25.7, 25.0, 23.5, 21.5, 19.7. IR (nujol mull (PSU), ν, cm^{-1}): 2976-2933, 1647, 1341, 1327, 1240, 1148, 1092, 970, 822. $[\alpha]_D^{20}$ = +110 (c = 1 g / 100 mL, MeOH) (Lit. $[\alpha]_D^{25}$ = +93 (c = 1, $CHCl_3$) [17]).

2.2.2. Synthesis of (5aR,9aS)-5,5,8-trimethyl-1-[(4-methyl phenyl)sulfonyl]-2,5,5a,6,7,9a-hexahydro-1H-1,4-benzo diazepine **(14)**

A 100 mL two-necked round bottom flask was oven-dried, fitted with septa, and cooled under N_2. A stir bar, 1.00 mL (0.862 g, 6.33 mmol) of (+)-2-carene (**1**), 1.961 g (1.1 eq.) of chloramine-T trihydrate, and 31.7 mL (0.2 M with respect to compound **1**) of anhydrous acetonitrile were added to the flask and stirred. Finally 0.085 g (0.1 eq.) of *N*-chloro succinimide was added to the flask and left to stir at room temperature. The solution was a heterogeneous slurry which slowly turned yellow. After four days, water was added and the solid dissolved. The mixture was extracted three times

with ethyl acetate. The organic layers were combined and washed with water and then sat. NaCl. The organic was dried over Na_2SO_4 and concentrated *in vacuo*. The crude product was chromatographed on 5 g flash silica gel with mixtures of ethyl acetate and hexanes. Fractions containing compound **14** were combined and concentrated to an oil, not entirely pure (0.332 g). Fractions containing compound **13** were combined and concentrated to solid. The solid was dissolved in a small amount of hot ethyl acetate. Hexanes were added and the solution was allowed to cool. Crystallization began and the flask was allowed to stand in the freezer overnight. Colorless crystals of compound **13** (0.453 g, 20.7%) were isolated and washed twice with cold 30% ethyl acetate:hexanes (*v*:*v*).

(5aR, 9aS)-5,5,8-Trimethyl-1-[(4-methylphenyl)sulfonyl]-2,5, 5a,6,7,9a-hexahydro-1H-1,4-benzodiazepine (**14**): R_f (30% ethyl acetate/hexanes): 0.62. ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm): 7.75 (d, 2H, Ar-H), 7.63 (1H, HC=N), 7.25 (d, 2H, Ar-H), 5.75 (s, 1H, HC=C), 4.62 (m, 1H, H_2C-N), 4.42 (d, *J* = 13 Hz, 1H, N=C-CH_2-N), 3.96 (d, 1H, *J* = 13 Hz, N=C-CH_2-N), 2.35 (s, 3H, H_3C-Ar), 1.67 (s, 3H, H_3C-C=C), 1.24 (s, 3H, CH_3, 1.03 (s, 3H, CH_3), remaining 5 alkyl protons hard to distinguish in the impure sample. ^{13}C NMR (75 MHz, $CDCl_3$, δ, ppm): 146.9, 143.2, 139.5, 136.8, 128.7, 126.2, 118.7, 52.9, 51.2, 44.9, 42.2, 28.9, 27.6, 24.5, 22.5, 20.6, 18.0. IR (ATR, ν, cm^{-1}): 3268, 2969, 2928, 1662, 1597, 1538, 1494, 1432, 1387, 1366, 1329, 1304, 1288, 1153, 1120, 1091, 1033, 1019, 977, 912, 814, 768, 722, 706, 680, 664. MS/MS (*m/z*): 347.2, 253.2, 213.2, 155.1, 135.2, 107.1, 93.1, 90.9. [M+1] of 347.2 is consistent with calculated $[M+H]^+$ of 347.2.

2.2.3. General procedure for reactions of pinenes with chloramine-T trihydrate and phenyltrimethylammonium tribromide in methylene chloride

A 500 mL three-necked round bottom flask was oven-dried, fitted with septa, and cooled under N_2. A stir bar, 36.7 mmol of the pinene (**7**, **11** or **12**), 11.37 g (1.1 eq.) of chloramine-T trihydrate, and 184 mL (0.2 M with respect to the pinene) of methylene chloride (Mallinckrodt) were added to the flask and stirred. Finally 1.38 g (0.1 eq.) of phenyltrimethylammonium tribromide was added to the flask and left to stir at room temperature. After 3-5 days, as determined by TLC, 1 M NaOH was added and the solid dissolved. The mixture was extracted three times with methylene chloride. The organic layers were combined and washed with water and then sat. NaCl. The organic was dried over Na_2SO_4 and concentrated *in vacuo*. The crude product was chromatographed on flash silica gel with mixtures of ethyl acetate and hexanes and then recrystallized as indicated below.

4-Methyl-N-{[(4S)-4-(prop-1-en-2-yl)cyclohex-1-en-1-yl] methyl}benzenesulfonamide (**22**): Color: Off-white crystals. Yield: 1.3074 g (29.2%) after chromatography and recrystallization from ethyl acetate:hexanes. M.p.: 68-69 °C. R_f (30% ethyl acetate/hexanes): 0.51. ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 7.74 (d , 2H, Ar-H), 7.29 (d, 2H, Ar-H), 5.55 (s, 1H, HC=C), 4.72 (m, 1H, NH), 4.70 (d, 2H, H_2C=C), 3.45 (d, 2H, C=C-CH_2-N), 2.41 (s, 3H, H_3C-Ar), 2.04-1.93 (m, 4H, alkyl), 1.77 (m, 1H, alkyl), 1.73 (m, 1H, alkyl), 1.67 (s, 3H, H_3C-C=C), 1.27 (m, 1H, alkyl). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 149.6, 143.4, 137.4, 132.6, 129.7, 127.3, 125.0, 108.8, 49.4, 40.8, 30.5, 27.3, 26.7, 21.6, 20.8. IR (ATR, ν, cm^{-1}): 3260, 2910, 1643, 1596, 1432, 1318, 1156, 1090, 1058, 1040, 889, 846, 808, 664, 614, 539. $[\alpha]_D^{25}$ = -48 (c = 10 g / 100 ml, MeOH). MS/MS (m/z): 306.2, 184.2, 155.1, 135.2, 107.2, 93.1, 91.1, 79.1. [M+1] of 306.2 is consistent with calculated $[M+H]^+$ of 306.2.

4-Methyl-N-[(1R, 5R)-2-methyl-5-(prop-1-en-2-yl)cyclohex-2-en-1-yl]benzenesulfonamide (**16B**) [17,18]: Color: Colorless crystals. Crystals for X-ray crystallography were grown from ethanol by slow evaporation. Yield: 2.9579 g (26.4%) after chromatography and recrystallization from ethyl acetate/ hexanes. A second crop of 0.6173 g (5.5%) was obtained. M.p.: 100-102 °C (lit. 108-110 °C) [18]. R_f (30% ethyl acetate/ hexanes): 0.56. ^{1}H NMR (400 MHz, $CDCl_3$, δ, ppm): 7.77 (d, 2H, Ar-H), 7.29 (d, 2H, Ar-H), 5.52 (s, 1H, HC=C), 4.65 (d, 2H, H_2C=C), 4.51 (d, 1H, HC-N), 3.85 (br s, 1H, NH), 2.42 (s, 3H, H_3C-Ar), 2.15 (m, 1H, alkyl), 2.05 (m, 1H, alkyl), 2.01 (m, 2H, alkyl), 1.63 (s, 3H, CH_3), 1.52 (s, 3H, CH_3), 1.36 (m, 1H, alkyl). ^{13}C NMR (100 MHz, $CDCl_3$, δ, ppm): 148.5, 143.3, 138.6, 133.0, 129.7, 127.1, 125.8, 109.5, 54.5, 40.3, 36.6, 30.5, 21.6, 20.8, 20.1. $[\alpha]_D^{25}$ = -33 (c = 10 g / 100 ml, MeOH) (Lit: $[\alpha]_D^{25}$ = -50.1 (c = 1, $CHCl_3$) [17]; $[\alpha]_D^{20}$ = -3.7 (c = 25.2, THF) [18]). IR (ATR, ν, cm^{-1}): 3298, 2918, 1648, 1597, 1495, 1435, 1382, 1327, 1296, 1265, 1153, 1092, 1062, 1046, 978, 922, 896, 850, 764, 705, 666. MS/MS (m/z): 306.3, 212.2, 172.1, 155.2, 135.2, 107.1, 93.1, 91.0. [M+1] of 306.3 is consistent with calculated $[M+H]^+$ of 306.2.

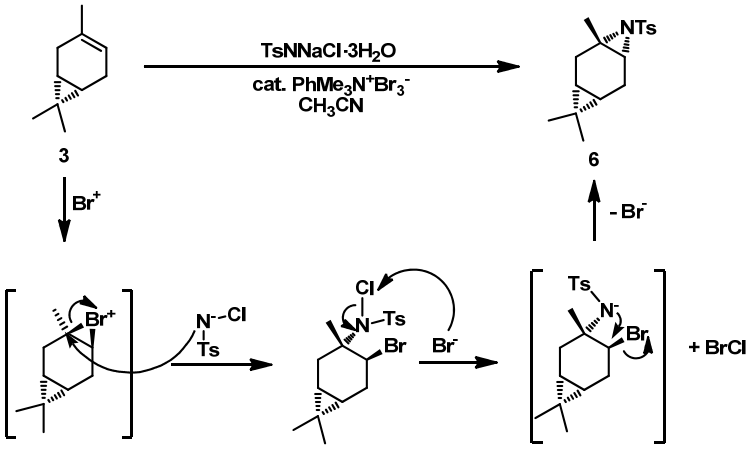
N-[(1R, 5R)-2-(2-Hydroxyethyl)-5-(prop-1-en-2-yl)cyclohex-2-en-1-yl]-4-methylbenzenesulfonamide (**24**): Color: Colorless crystals. Yield on 3.67 mmol scale was 0.1725 g (14.0%) after chromatography and recrystallization from ethyl acetate and hexanes. Yield on 36.7 mmol scale was 1.1013 (8.9%) total after chromatography and recrystallization in three crops. Another 3.6323 g of oil that was still predominantly **24** remained in the mother liquor. M.p.: 122-124 °C. R_f (60% ethyl acetate:hexanes): 0.54. ^{1}H NMR (300 MHz, $CDCl_3$, δ, ppm): 7.79 (d, 2H, Ar-H), 7.29 (d, 2H, Ar-H), 5.65 (s, 1H, HC=C), 5.31 (d, 1H, HC-N), 4.65 (d, 2H, H_2C=C), 3.90 (bs, 1H, NH), 3.58 (m, 2H, H_2C-O), 2.42 (s, 3H, H_3C-Ar), 2.31-1.81 (m, 6H, alkyl), 1.62 (s, 3H, CH_3), 1.38 (q, 1H, alkyl). ^{13}C NMR (75 MHz, $CDCl_3$, δ, ppm): 148.3, 143.4, 138.4, 134.6, 129.8, 128.1, 127.2, 109.7, 62.3, 53.2, 40.1, 36.6, 35.5, 30.5, 21.7, 20.8. $[\alpha]_D^{24}$ = -40 (c = 8.81 g / 100 mL, MeOH). IR (ATR, ν, cm^{-1}): 3353, 3259, 2969, 2918, 2878, 1645, 1597, 1527, 1495, 1436, 1387, 1326, 1289, 1152, 1091, 1067, 1054, 1041, 1018, 925, 887, 815, 705, 666. MS/MS (*m/z*): 336.2, 212.1, 172.2, 165.1, 155.0, 147.2, 121.2, 119.2, 105.2. [M+1] of 336.2 is consistent with calculated $[M+H]^+$ of 336.2.

3. Results and discussion

3.1. 2-Carene and oxygen nucleophiles

Our initial attempts with compound **1** were standard electrophilic additions of halogen electrophiles to alkenes [19]. Reaction with Br_2 in methyl *t*-butyl ether (MTBE) gave an extremely rapid reaction, but the presumed allylic bromide formed appeared by NMR of the product to have also rapidly eliminated. To try to obviate this problem, halohydrin formation was attempted with *N*-chlorosuccinimide (NCS) and water in tetrahydrofuran (THF). Again, volatile products resulting from elimination of the tertiary allylic halide were obtained, but encouragingly, in each case there was evidence by NMR that the presumed cyclopropyl halonium ion was in fact very reactive and the cyclopropane was being opened. It appeared, however, that either cyclopropyl halonium ion would need to be surrounded by a nucleophilic solvent in order to be captured before eliminations to volatile products occur, analogous to what occurred with acid-catalysed reactions of compound **2** [20-22].

Reaction of compound **1** with *N*-bromosuccinimide (NBS) in methanol gave two fractions that were isolated by chromatography. Each was a mixture, but they did appear by NMR to contain a methoxy group. Attempts were then made to prevent elimination by neutralizing the HBr produced with an added base. Reaction of compound **1** with NBS, methanol, and pyridine followed by chromatography gave an impure product whose ^{1}H NMR spectrum showed one methoxy group had been incorporated, but also showed it was a *p*-disubstituted aromatic ring. Similarly, reaction with NBS, ethanol, and pyridine showed a mixture that appeared to contain one ethoxy group.



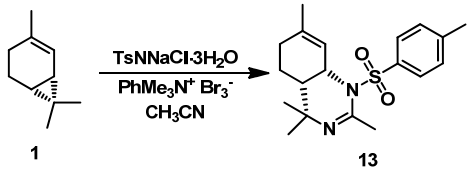
Scheme 6 [27]

Attempts were also made to put on acetate groups by reaction of compound **1** with NBS and acetate ion [23]. Sodium acetate in acetic acid gave very little product of any sort, as did sodium acetate in water.

3.2. 2-Carene and nitrogen nucleophiles

We next turned to nitrogen nucleophiles [16,17,24,25]. One of the better general methods for accomplishing the aziridination of alkenes is Sharpless' reaction, in which a source of Br^+ (phenyltrimethylammonium tribromide, PTAB) catalyses a process using chloramine-T (TsNNaCl) as the nitrogen source [26]. The reaction is believed to proceed through a bromonium ion [26], and has been successfully used by Chandrasekaran for the preparation of tosyl aziridine **6** of (+)-3-carene **3** (Scheme 6) [27]. The intermediate bromonium ion in that case was not adjacent to the cyclopropane ring, and the cyclopropane ring remained unaffected [27].

We performed the reaction of compound **1** according to the procedure of Sharpless [26,27]. The major product **13** was a solid. The ^{1}H NMR spectrum showed a vinyl proton with fine splitting at 5.98 ppm, and a ring junction proton adjacent to a nitrogen as a triplet at 4.69 ppm. However, the ^{13}C NMR spectrum showed 19 carbons (17 signals) instead of the 17 expected if only the *NTs* group was added, and the ^{1}H NMR spectrum showed an extra methyl singlet at 2.06 ppm. We concluded that a 2-carbon, 1-nitrogen unit from acetonitrile must have been incorporated into the structure (Scheme 7). The structure of compound **13** was confirmed by X-Ray Crystallography. As shown in Figure 1, the compound is a six-membered cyclic amidine incorporating one acetonitrile unit and one chloramine-T unit. From 0.5 g of compound **1** (3.67 mmol), 0.314 g (24.7%) of pure **13** was obtained after chromatography followed by recrystallization from MTBE [28].



Scheme 7

In two recent papers, Chandrasekaran and coworkers also reported the reaction of compound **1** and other vinyl cyclopropanes under the conditions of the Sharpless aziridination [16,17]. The same type of heterocycle was obtained (Scheme 8). Chandrasekaran's group appears to have used anhydrous chloramine-T, whereas we used the safer trihydrate [29], which is the commercial form.

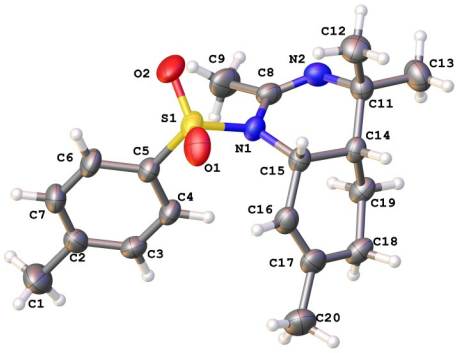
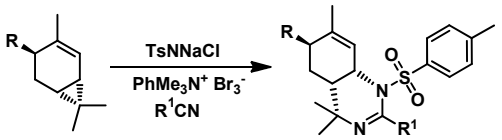


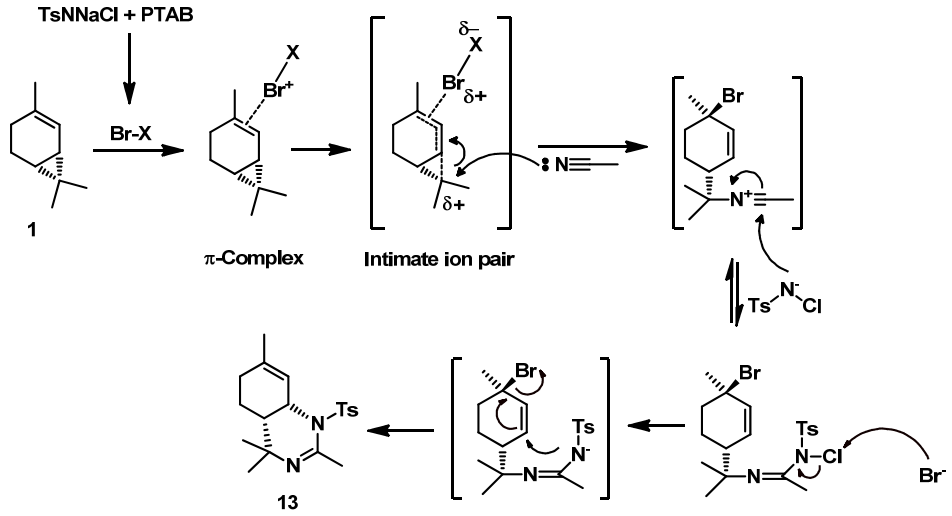
Figure 1. ORTEP drawing of the structure of compound **13**.



Scheme 8 [16,17]

They proposed a mechanism in which the π-bond interacts with Br^+ and the positive charge is delocalized through the cyclopropane ring (Scheme 9), and presented strong experimental and computational evidence of the mechanisms.

To the best of our knowledge, acetonitrile participation has not been otherwise reported in the aziridination reaction under the Sharpless conditions [26]. However, we believe that the involvement of acetonitrile in the reaction of compound **1** under the same conditions can be readily understood in terms of our initial hypothesis. Chloramine-T is a strong nucleophile [26,30], so it is not surprising that it attacks the bromonium ion preferentially in the case of ordinary bromonium ion intermediates. However, if as we expected, the cyclopropyl bromonium ion is delocalized through both three-membered rings, and both rings are opened at the same time, then as we have observed with compounds **2** and **5**, the reactivity would be expected to be much higher than an ordinary bromonium ion.



Scheme 9 [16,17]

This means that the activation energy for reaction of the cation with acetonitrile would be lower, and since acetonitrile is present in much greater concentration than chloramine-T, it is now able to react preferentially. Only after acetonitrile has attacked the cyclopropyl bromonium ion and formed the less reactive nitrilium ion does the chloramine-T attack.

We also note that while the Sharpless aziridination is reported to take 12 hours at room temperature [26,27], the reaction of compound **1** went to completion within 40 minutes at 0 °C. The reaction gave similar results whether run at room temperature or at 0 °C. Results were also the same when the reaction was allowed to stir for six days at room temperature. (Chandrasekaran's group reported running reactions for 5-12 hours at room temperature [16,17]). The faster reaction rate is consistent with the hypothesis of higher reactivity of the cyclopropyl bromonium ion.

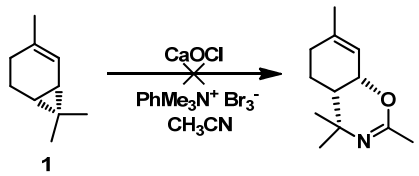
Replacement of CH_3CN with solvents that might participate as CH_3CN does, DMSO and acetone, did not give similar products.

Use of the strong nucleophile chloramine-T was also necessary. Reaction of compound **1** with PTAB, $TsNH_2$ and CH_3CN gave no amidine product. A publication by Yeung and coworkers reported a synthesis of cyclic amidines from an alkene, a nitrile, NBS, and an amine [25]. These reactions involved formation of a bromonium ion and attack by a nitrile, this time followed by attack by an amine on the nitrilium ion, then cyclization by displacement of the bromine. Ordinary alkenes gave a five-membered cyclic amidine, but they also reported the reaction of vinyl cyclobutane α-pinene **11**, which gave opening of the cyclobutane resulting in a seven-membered cyclic amidine [25]. We thus ran the reaction of compound **1** under Yeung's conditions [25]. None of the amidine product **13** was observed, and $TsNH_2$ appeared to be mostly unreacted. We also attempted reactions with $NBS/NH_3/H_2O$ [31] and NBS/NH_3 (*l*) and in each case did not obtain any non-volatile products.

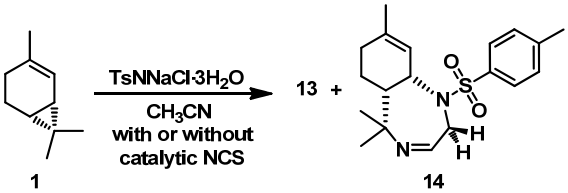
Attempts were also made to capture the nitrilium ion with oxygen nucleophiles. Reaction of compound **1** with $NBS/Na_2CO_3/CH_3CN$ gave many products by TLC. Reactions with $NBS/KOH/CH_3CN$ or NBS in 1:1 CH_3CN/H_2O were also unsuccessful. Attempts to replace chloramine-T with calcium hypochlorite (with PTAB in acetonitrile) in hopes of putting an oxygen into the ring failed as well (Scheme 10).

Chandrasekaran reported trying a number of different sources of Br^+ or I^+ as catalysts for the reaction of compound **1** with chloramine-T/acetonitrile, but did not try any sources of Cl^+ [16,17]. We thus ran the reaction using NCS instead of PTAB, and did in fact get a different result (Scheme 11). Two major products were isolated, amidine **13** (20.7% after chromatography and recrystallization) and new product **14**, a lesser amount of oil, which has resisted all attempts at obtaining pure material. The reaction was significantly slower than with PTAB and was stirred overnight to ensure complete consumption of compound **1**. The reaction was also run without any added catalyst ($TsNNaCl{\cdot}3H_2O/CH_3CN$) and gave the same two products and a similar reaction rate.

The less polar compound **14** displayed ^1H and ^{13}C NMR spectra that were each very similar to compound **13**, but with important differences. The ^{13}C NMR spectrum showed that one of the alkyl carbons had moved from the mid-20s to 44.9 ppm. The ^1H NMR spectrum did not show an amidine CH_3, but did show a pair of one-hydrogen doublets at 4.42 and 3.97 ppm, splitting each other with coupling constant of ~13 Hz. The compound is thus proposed to have structure **14**. The two doublets come from the two methylene protons now in the seven-membered ring.

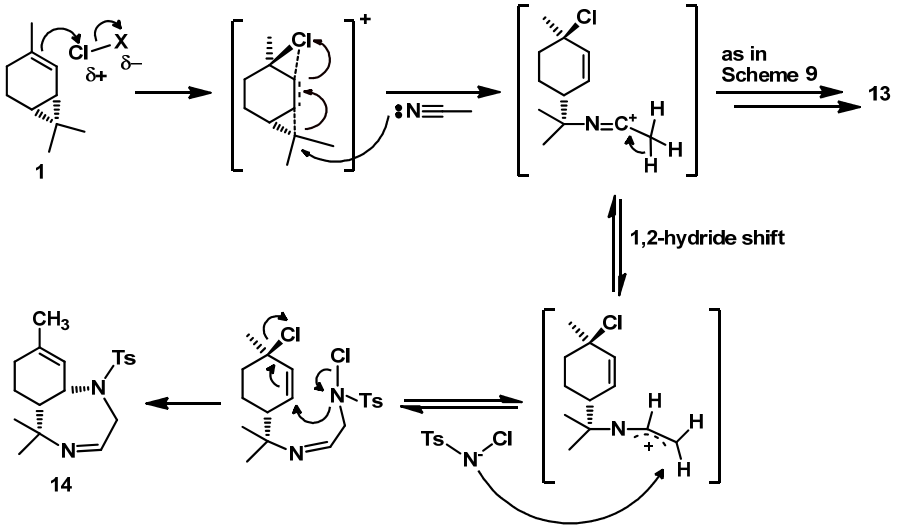


Scheme 10

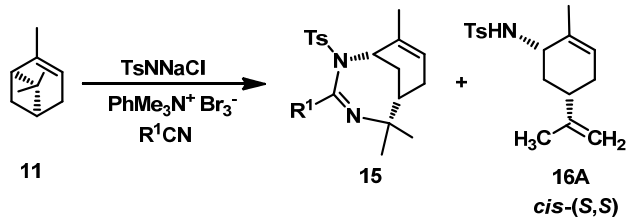


Scheme 11

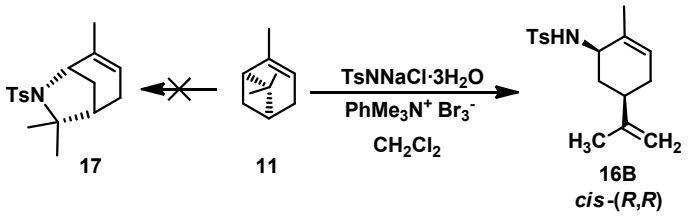
A possible mechanism for the formation of compound **14** is shown in Scheme 12. After formation of the nitrilium ion, a 1,2 hydride shift occurs, producing an α-imino cation, which is stabilized by delocalization [32].



Scheme 12



Scheme 13 [17]



Scheme 14

Since chloride is a poorer leaving group than bromide [33], the final cyclization to compound **13** may have slowed enough to make the hydride shift competitive when NCS or no catalyst was used instead of PTAB.

When the reaction of compound **1** was run with CH_2Cl_2 as solvent instead of CH_3CN, using either PTAB or NCS, mixtures were obtained from which no pure product could be isolated.

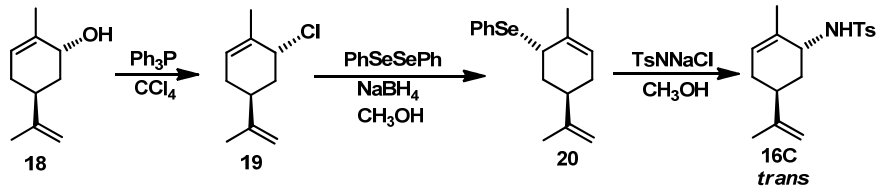
3.3. Pinenes and nitrogen nucleophiles

We initially attempted to use (-)-β-pinene **7** and (-)-α-pinene **11** under the conditions of Sharpless' aziridination reaction [26], but were unsuccessful in isolating any products. However, Chandrasekaran's group also ran the reaction of **11** and was successful [17]. Along with a 45% yield of the expected seven-membered heterocycle **15** (Scheme 13), they reported 15% yield of a compound they identified as **16A**, resulting from elimination prior to attack by acetonitrile.

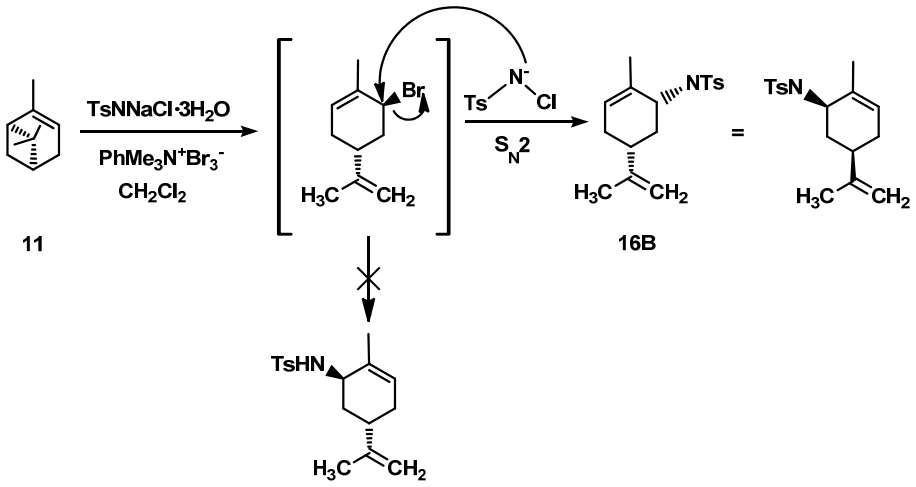
Again, in retrospect the difference in results may have been in our use of the trihydrate. It seemed to us at the time prior to Chandrasekaran's report [17], however, that the problem with our reaction might be that seven-membered rings would have to form from compound **7** or **11** instead of six-membered rings as with compound **1**. Therefore, we replaced acetonitrile with methylene chloride, and it was hoped that five-membered rings might be produced.

The reaction with compound **11** (Scheme 14) did not give the five-membered ring **17**. Instead of the nucleophile attacking at the gem-dimethyl carbon in the cyclobutane ring, elimination occurred, leading to an allylic amine, which X-Ray crystal data showed to be compound **16B** (Figure 2), the enantiomer of what Chandrasekaran proposed (**16A**). The NMR spectra of compound **16B** matched earlier reported NMR data attributed to the *trans* isomer **16C** (Scheme 15) [18] and also matched Chandrasekaran's data [17]. Optical rotation was of the same sign in all three cases as well. Thus it would appear that all three reports were of the *cis*-(*R*,*R*)-isomer **16B**.

The (*R*,*R*)-stereochemistry of compound **16B** suggests that after formation of the intermediate allylic bromide, the bromine is displaced directly at the carbon it is bonded to, with inversion, rather than at the allylic carbon (Scheme 16).



Scheme 15 [18]



Scheme 16

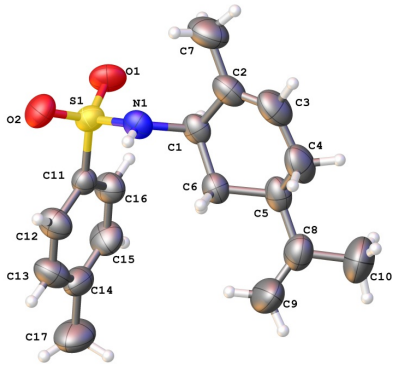


Figure 2. ORTEP drawing of compound **16B**.

A possible mechanism for the reaction of compound **11** is shown in Scheme 17. Formation of a delocalized cyclobutyl bromonium ion is followed by elimination. Displacement of the bromine is proposed to occur through an S_N2 mechanism as discussed above.

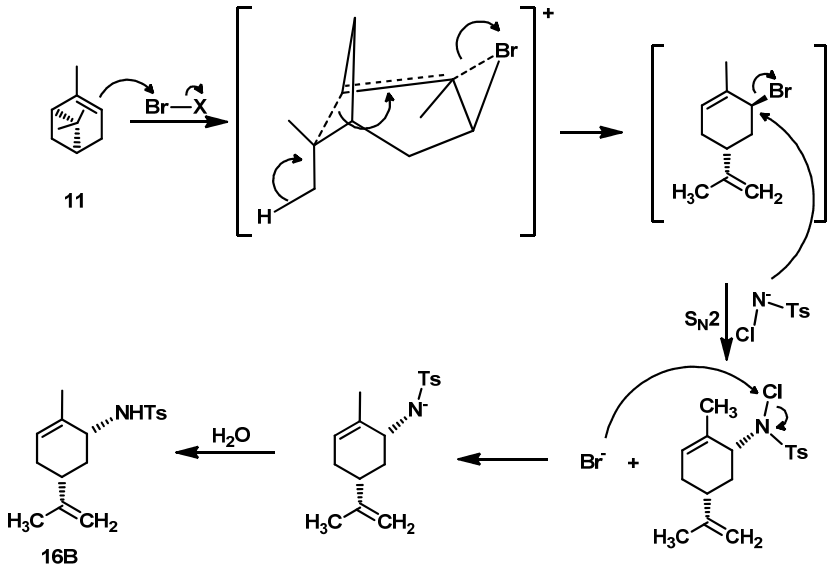
The reaction with compound **7** (Scheme 18) was similar, resulting in a novel compound. The NMR data did not match that reported for the secondary allylic tosylamine **21** [18], and was determined instead to be the primary allylic amine **22**. Thus, as with formation of compound **16B**, the substitution of the tosylamine at the less hindered primary allylic carbon suggests an S_N2 mechanism to the step.

A possible mechanism for the reaction of compound **7** is shown in Scheme 19. Formation of a delocalized cyclobutyl bromonium ion is followed by elimination. Displacement of the allylic bromide occurs through an S_N2 mechanism, yielding the less hindered tosylamine.

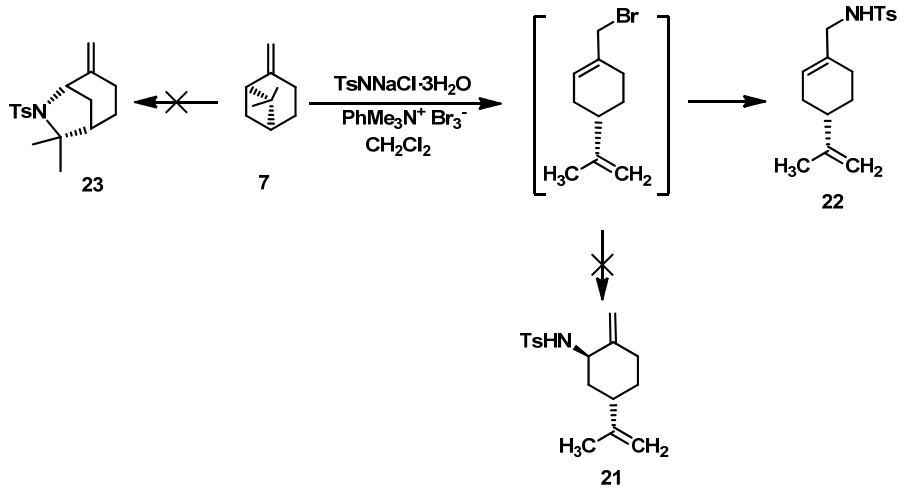
The reaction using (-)-nopol **12**, which has an unprotected primary alcohol, produced the same type of product as compound **11** did (Scheme 20). The stereochemistry has been assigned based on the crystal structure of compound **16B**. Product **24** is a novel molecule that features an unprotected primary alcohol, a secondary allylic tosylamine, a disubstituted alkene, and a trisubstituted alkene, making for a potentially very versatile building block.

4. Calculations

In order to better understand the relative reactivities of the halonium ions included in this report, theoretical investigations were carried out using the Gaussian 09 suite of quantum mechanical programs [34] on the bromonium ions of the following alkenes: methylidene cyclohexane **25**, 1-methylcyclohexene **26**, 2-methyl-cyclohexadiene **27**, the two bromonium ions that can arise from 3-methylidene cyclohexene **28**, 1-methyl-1,3-cyclohexadiene **29**, 2-carene **1**, 3-carene **3**, α-pinene **11** and β-pinene **7**. We will name, for example, the bromonium ion of **25** as **25-Br**$^+$. We will name the two bromonium ions given for **28**, with one having the bromine associated with the methylidene, and the other having the bromine associated with the ring double bond, **28-Br**$^+$**a** and **28-Br**$^+$**b**, respectively. The structures of all these species presented in this report were optimized using Density Functional Theory (DFT), utilizing the B3LYP hybrid functional and the cc-pVDZ correlation-consistent atomic orbital basis set by Dunning [35]. The systems were gas-phase, with no solvent effects included, although depending on the solvent the system is in experimentally, there could be additional effects. The relative reactivities and conjugation of these species were analysed with four criteria. One, the general structure was considered, since conjugation should result in at least partial opening of the three-membered bromonium ring, as well as commensurate opening of the carene cyclopropane and pinene



Scheme 17

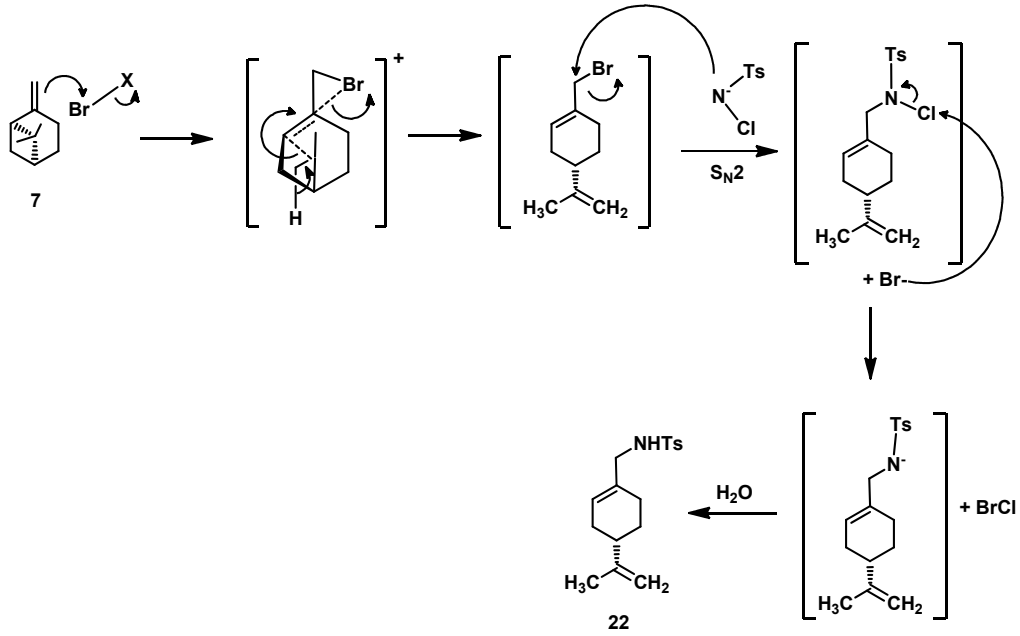


Scheme 18

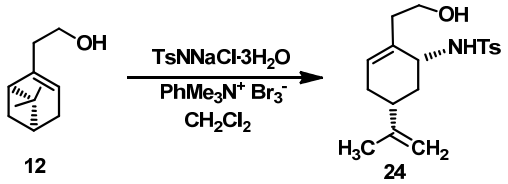
cyclobutane rings, and also creation of new carbon-carbon double bond character. Two, Natural Population Analysis [36] (NPA) partial atomic charges were calculated on the optimized systems using the electron density obtained from Moller-Plessett Second-Order Perturbation Theory (MP2) and the aug-cc-pVDZ basis set. The presence of conjugation relative to a bromonium ion should be translated into positive charge distributing between the Br and select carbons. Three, the absolute hardness, η [37,38], using B3LYP/aug-cc-pVDZ and Hartree-Fock/aug-cc-pVDZ energies for the highest occupied molecular orbital (HOMO) and the lowest unoccupied molecular orbital (LUMO) was calculated for several various bromonium ions of interest. Hardness is the resistance of the chemical potential to change in number of electrons, and is rigorously given by Equation 1. Approximation to easily calculated quantities is also shown in Equation 1.

$$\eta = \frac{1}{2}\left(\frac{\partial^2 E}{\partial N^2}\right) \approx \frac{1}{2}(I - A) \approx \frac{1}{2}(\varepsilon_{LUMO} - \varepsilon_{HOMO}) \quad (1)$$

Here E is the electronic energy, N is the number of electrons, I is the ionization energy, A is the electron affinity, and ε_{LUMO} and ε_{HOMO} are the molecular orbital energies of the lowest unoccupied molecular orbital (LUMO) and the highest occupied molecular orbital (HOMO), respectively. The approximation that hardness is half the HOMO-LUMO energy gap provides a convenient way to calculate hardness from electronic structure methods. Just as increasing conjugation in poly-alkenes both lowers the HOMO-LUMO energy gap and increases the polarizability, thus decreasing hardness, we posit that this index can provide a useful metric for comparing relative conjugation between several model bromonium ion systems. While a comparison of hardness has been made between isomers of otherwise identical systems, such as iron (II) complexes [39], or for comparisons of similar reactants of cycloaddition reactions [40], application of the hardness index to compare reactive intermediates across a range of conjugation and electron density delocalization has to our knowledge not been reported.



Scheme 19



Scheme 20

While the theory of using electronic structure to calculate hardness has been developed using DFT, we have also included the results using Hartree-Fock (HF) theory, since there appears to be nothing in the original derivations that requires that DFT be used to calculate MOs and their energies, and in this study DFT-calculated hardness values had some possibly anomalous results, while HF results seemed to be more accurately descriptive of the systems studied, at least qualitatively.

Figure 3 shows the line structures and the optimized B3LYP/cc-pVDZ structures of bromonium ions formed from the simpler six-membered ring systems to those of the two carene bromonium ions and the two pinene bromonium ions. The structures of the two carenes and the two pinenes are also included, for comparison. Important bond angles, dihedral angles to show degree of planarity of salient carbons, bond lengths, and NPA charges are shown in Figure 3. Partial bonds are shown in the optimized structures with dashed black lines. Figure 3 is arranged in rows of three structures which are related to each other functionally, so the reader can have easier visual comparisons. We will describe the structures and NPA charges mainly in terms of rows of three, but there may be references to structures in other rows important for the particular comparison.

Figure 3 shows in the first row the B3LYP/cc-pVDZ structures of **25-Br⁺, 28-Br⁺a** and **28-Br⁺b**. **26-Br⁺** is in the third row, third panel (l-r). Ions **25-Br⁺** and **26-Br⁺** are both bromonium ions from mono-alkenes, and so might be expected to display classic undistorted 3-member ring bromonium ions. This is the case with ion **26-Br⁺**, with Br-C-C bond angles of 77.7° and 63.2°, and the Br has an NPA charge of +0.32, while the charges on C1 and C2 are +0.17 and -0.18, respectively, with positive charge preferring the tertiary C1. In contrast, ion **25-Br⁺** shows partial ring opening at this level of theory, with a Br-C-C bond angle of 93.1° and an NPA charge on the tertiary carbon of +0.35 (units are *e*), and the Br is carrying a +0.22 charge. The weakened Br-C bond is shown with a dashed black line. The structural and charge differences between these two bromonium ions appear to be a combination of the stability of positive charge on a potentially tertiary carbon and that of a potentially primary bromine. Ion **28-Br⁺a** is the result of bromination of compound **28** on the methylidene C1-C7 bond, and this bromonium ion displays the effects of conjugation into the C2-C3 bond both structurally and in terms of NPA charges. The 3-membered bromonium ring is almost entirely opened, with the Br-C7-C1 bond angle at 99.5°, and the positive charge has been spread out between the Br, C1 and C3 effectively, at +0.15, +0.22, and +0.11, respectively. In contrast, ion **28-Br⁺b** is the result of bromination of compound **28** at the C2-C3 bond, and this bromonium displays significant structural and charge differences compared to ion **28-Br⁺a**. The 3-membered ring of the bromonium ring is less distorted than in ion **28-Br⁺a**, with a Br-C3-C2 bond angle of 83.6°, and while the methylidene C1-C7 bond should in theory be directly conjugated with the 3-membered bromonium ion, this bond is shorter (1.36 Å) than the corresponding C2-C3 bond of ion **28-Br⁺a** (1.38 Å), showing more double bond character. The positive NPA charge in ion **28-Br⁺b** is more localized on the Br, as well, at +0.26, and C2 and C7, the two carbons that could potentially share

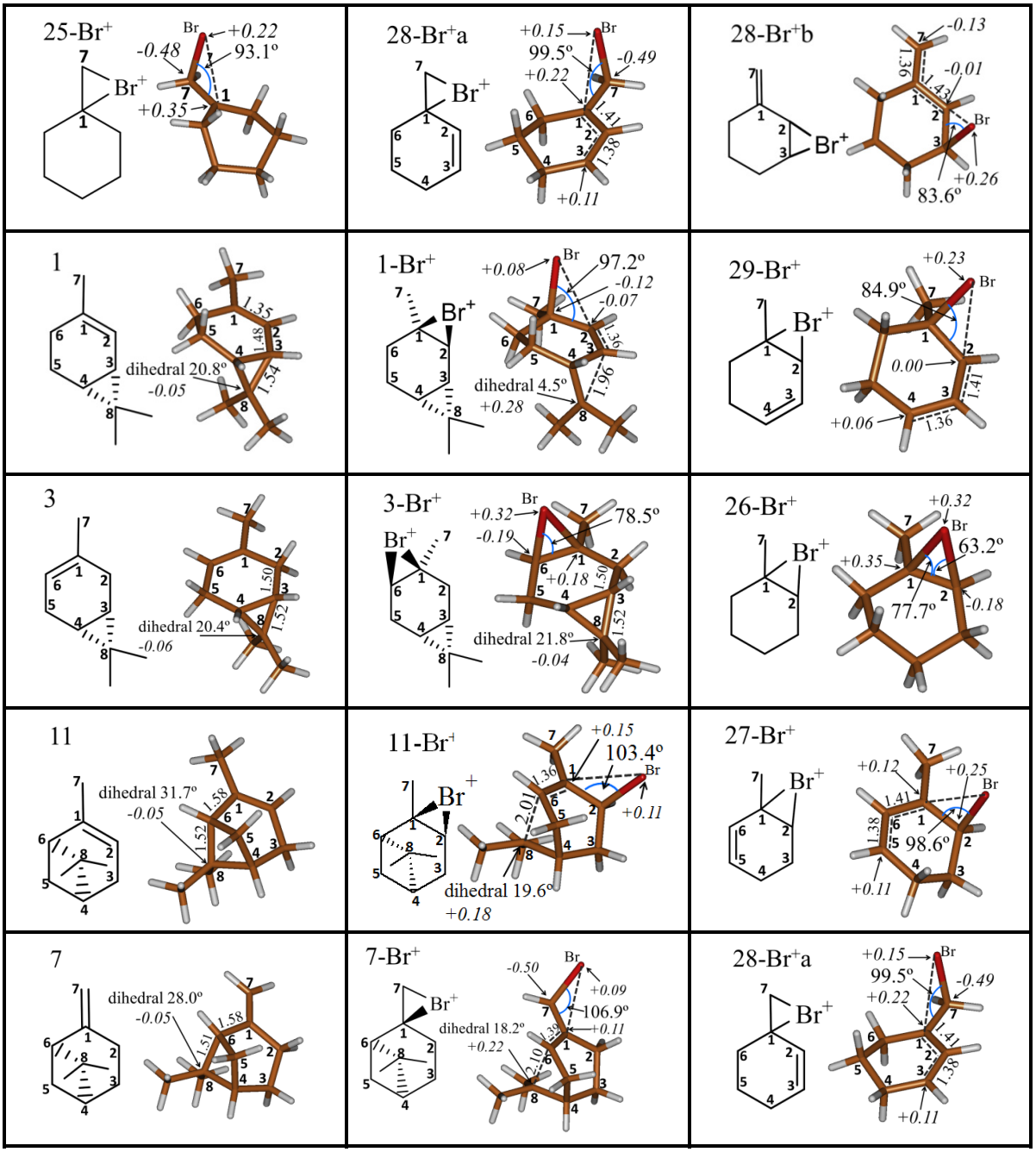


Figure 3. Line structures and optimized B3LYP/cc-pVDZ structures are shown. Carbon atom numbering shown is for discussion purposes only and may not follow IUPAC rules. Bond angles are delineated with a blue arc, and labelled in degrees. Bond lengths are labelled along their particular lines, in Angstroms. NPA charges are italicized and have units of *e*. For the bromonium ions, the Br atom is red, and explicitly labelled. Partial bonds are shown as black dashed lines.

the positive charge of the Br through conjugation, do not at all, displaying charges of -0.01 and -0.13, respectively. Thus, it is shown that while the methylidene is in the correct position for conjugation, the combination of a secondary Br and a potentially primary cation does not support effective resonance in ion **28-Br⁺b**.

Figure 4 shows the B3LYP/aug-cc-pVDZ absolute hardness index values, η, for the bromonium ions in this report, in kcal/mol, and Figure 5 shows the HF/aug-cc-pVDZ results for this index, also in kcal/mol. In both methods, ions **25-Br⁺** and **26-Br⁺** were expected to display the highest hardness values since they have no possibility of conjugation through additional double bonds or, in the cases of the carenes and pinenes, cycloalkane ring openings. Indeed, this was the case using both theoretical methods. This was especially true with the HF hardness values for these two bromonium ions, with energy values of 137.2 and 147.5 kcal/mol, respectively. As expected, the more distorted ion **25-Br⁺** displayed slightly less hardness than ion **26-Br⁺**, but both have hardness values higher than the other potentially conjugated bromonium ions. In the case of the DFT hardness values for these two systems, ion **26-Br⁺** is the highest of all bromonium ions in this report, at 61.9 kcal/mol, but ion **25-Br⁺** is much lower at 51.7 kcal/mol, making it just slightly harder than the two pinene

bromonium ions. We will discuss details of the pinene bromonium ions later, but we would expect both to be softer than the unconjugated ion **25-Br⁺**. Thus, we suspect that either DFT itself or the B3LYP functional is underestimating the hardness for ion **25-Br⁺**. Because hardness is directly related to the HOMO-LUMO energy gap, this could be the result of poorly described virtual orbitals in either DFT or the B3LYP functional for bromonium ions. It should be noted that overall DFT gives lower hardness values than HF, but we are interested in qualitative trends between systems within the results of a method. Both ions **28-Br⁺a** and **28-Br⁺b** show less hardness than ions **25-Br⁺** and **26-Br⁺**, with either method, as expected, but while the hardness of ion **28-Br⁺** is higher than ion **28-Br⁺** using DFT MOs, which could be predicted due to less structural and charge evidence of delocalization, the HF hardness of ion **28-Br⁺a** is greater than that of ion **28-Br⁺b** by about 1.6 kcal/mol, a surprising result which we do not understand, but plan to investigate in the future.

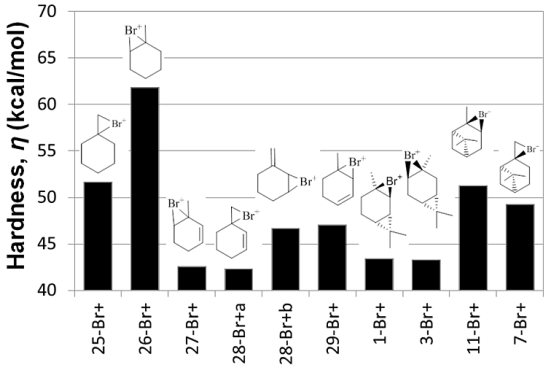


Figure 4. B3LYP/aug-cc-pVDZ absolute hardness index values, η, in kcal/mol, by number as defined in the text, and with line structures of each bromonium ion.

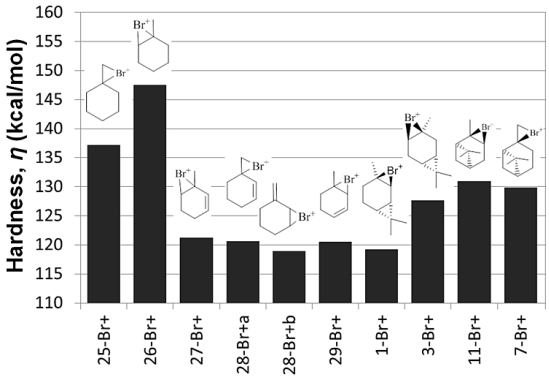


Figure 5. HF/aug-cc-pVDZ absolute hardness index values, η, in kcal/mol, by number as defined in the text, and with line structures of each bromonium ion.

The second row of Figure 3 shows 2-carene, **1**, its bromonium ion, **1-Br⁺**, and ion **29-Br⁺**, which we felt had enough structural similarities to ion **1-Br⁺** to directly compare. Ion **1-Br⁺** shows considerable structural effects remote from the Br compared to compound **1**. In compound **1** the C2-C3 bond length is close to typical single bond length, at 1.48 Å, while in ion **1-Br⁺** this bond has shortened to closer to double bond length, at 1.36 Å. The C3-C8 bond length of the cyclopropyl ring in compound **1** is typical of a C-C single bond, at 1.54 Å, while in ion **1-Br⁺** this bond has stretched to 1.96 Å, implying almost complete ring opening of the cyclopropyl. Indeed, this is also evident with the dihedral angle at C8 with C4 and the two methyl carbons attached to C8, which is 20.8° in compound **1**, but flattens to almost planar in ion **1-Br⁺**, at 4.5°. The 3-membered ring bromonium in ion **1-Br⁺** commensurately distorted to be more open, as well, with Br-C1-C2 bond angle of 97.2°. The NPA charges are quite delocalized away from the Br in ion **1-Br⁺**, with the Br only retaining +0.08 charge, and C8 getting a charge of +0.28. Thus, it is clear that bromination of compound **1** creates significant, almost planar, carbocation character at C8 in ion **1-Br⁺**. This constitutes a somewhat different intermediate structure than what has been proposed previously by Chandrasekaran *et al.* [16,17], which had the Br-C2 bond completely broken in an intimate ion pair between the Br and X^-, and the positive charge delocalized from C1 to the gem-dimethyl carbon of the cyclopropyl moiety (Scheme 11). However, as stated earlier, our interest was in the intrinsic electronic and structural properties of the bromonium ions on their own, without influence of solvent or other species, so their differences could be probed in a rigorous and controlled manner. Therefore, these two pictures should not be viewed as contradictory, but rather as complimentary. Comparing ion **29-Br⁺** to ion **1-Br⁺**, which replaces the cyclopropyl with a C3-C4 double bond, it is interesting that ion **29-Br⁺** does not display nearly the extent of structural and charge effect of resonance as ion **1-Br⁺**. In terms of charges, the Br in ion **29-Br⁺** retains a value of -0.23, which is actually higher than that of ion **25-Br⁺**, which has no potential conjugation at all, but C4 does acquire a charge of +0.06, which while it is much less than C8 in ion **1-Br⁺,** or C3 in ion **28-Br⁺**, one of the previously discussed bromonium ions of a diene, but the charge on C4 is considerably more positive than C7 of ion **29-Br⁺**, the other previously discussed bromonium of a diene. The structure of ion **29-Br⁺** also indicates somewhat limited conjugation. The 3-membered bromonium ring is not very opened, with a Br-C1-C2 bond angle of 84.9°, and its C2-C3 bond length is 1.41 Å, which is less than the typical C-C single bond length, but comparable to C2-C3 in ion **1-Br⁺** (1.36 Å)**,** which is much closer to double bond character.

Commensurate with the structural and charge evidence for delocalization, the hardness for ion **1-Br⁺** is among the lowest of the bromonium ions presented in this report, and at both DFT and HF levels of theory, compared to the others. At the DFT level ion **1-Br⁺** is harder than ion **28-Br⁺a**, but less hard than ions **28-Br⁺b** or **29-Br⁺**, while at the HF level all four of these bromonium ions are calculated to have about equal hardness. This shows that both theories are good at qualitatively predicting hardness of ion **1-Br⁺**, but subtle differences with the two bromonium ions of compounds **28** and **29** are more challenging to understand, and may be the result of differences in how the two levels of theory treat any local hardness of the cyclopropyl. We will see further evidence of this later.

Focusing on compound **3**, where the double bond is more removed from the cyclopropyl, we would predict that bromination of this double bond should have little of the conjugation effects on structure or charge distribution as seen in ion **1-Br⁺**. Indeed, this is what our calculations predict. Compound **3** and ion **3-Br⁺** are shown in the third row of Figure 3. Bromination has little to no effect on the C2-C3 and C3-C8 bond lengths, with both **3** and ion **3-Br⁺** having values of 1.50 and 1.52 Å, respectively, and the C8 dihedral angle of 20.4° for compound **3** and 21.8° for ion **3-Br⁺**. The 3-membered bromonium ring in ion **3-Br⁺** is also not opened, as was predicted, with a Br-C6-C1 bond angle of 78.5°. Likewise, the positive charge is mostly on the Br (+0.32) and C1 (+0.18), with charges of -0.19 at C6, and -0.04 at C8, showing none of the positive charge has delocalized to the cyclopropyl as it does in ion **1-Br⁺**. For comparison, the third panel of the third row of Figure 3 shows ion **26-Br⁺**, which is the bromonium ion of the mono-alkene 1-methylcyclohexene, **26**, and should display no conjugation effects, but still has the bromine and

methyl positioned similarly to ion **3-Br⁺**. Indeed, both ion **26-Br⁺** and ion **3-Br⁺** display undistorted, unopened 3-membered bromonium ion rings. Likewise, the Br in ion **26-Br⁺** carries an NPA charge of +0.32, with C1 having a charge of +0.35 and C2 a charge of -0.18. Thus, it is clear in terms of structure and charge distribution that ion **3-Br⁺** behaves much more like a mono-alkene bromonium ion, with little to no conjugation, than a bromonium ion of a conjugated diene or 2-carene.

The picture is less clear when looking at the DFT or HF absolute hardness index of ion **3-Br⁺** compared to ion **26-Br⁺**. DFT predicts a hardness for ion **3-Br⁺** almost equal to that of ion **1-Br⁺**, which is certainly not supported by either structural features or NPA charge distributions. We are not sure of the reason for this anomalous result, but we suspect it may be in the way DFT treats the orbitals in the cyclopropyl group, and may underestimate its local hardness. The HF hardness of ion **3-Br⁺** makes a bit more sense, with a value greater than ion **1-Br⁺**, but still much less than ion **26-Br⁺**. Thus, like the case of DFT hardness of ion **3-Br⁺**, HF may be treating the local hardness of the cyclopropyl group as erroneously too soft.

Shown in the fourth row of structures in Figure 3 is α-pinene, **11**, its bromonium ion, ion **11-Br⁺**, and, for comparison, the bromonium ion of 2-methyl-1,3-hexadiene, **27-Br⁺**. If the pinene cyclobutyl moiety in **11-Br⁺** is in conjugation with the bromonium 3-membered ring, then one would expect lengthening of the C6-C8 bond, with the C8 dihedral angle to reflect the approach to planarity, compared to the unbrominated compound **11**. Indeed, this is what is seen at the B3LYP/cc-pVDZ level of theory. The C6-C8 bond length in compound **11** is 1.52 Å, typical for a C-C single bond, but it increases to 2.01 Å in ion **11-Br⁺**, and the almost tetrahedral dihedral angle at C8 of 31.7° in compound **11** decreases to 19.6° upon bromination in ion **11-Br⁺**, which while it is not quite planar is more planar than in compound **11**. Additionally, the C1-C6 single-bond length of 1.58 Å decreases to closer to double-bond length in ion **11-Br⁺**, at 1.36 Å. The 3-membered bromonium ring is also essentially completely open at C1, with a Br-C2-C1 bond angle of 103.4°, very close to tetrahedral. Thus, structural effects in ion **11-Br⁺** point to significant conjugation between the bromonium 3-membered ring and the cyclobutyl moiety. The NPA charge distribution in ion **11-Br⁺** also supports this conjugation, with positive charge at the Br, C1 and C8 calculated to be +0.11, +0.15 and +0.18, respectively. Similar structural and charge effects are seen in ion **27-Br⁺**, although the effects are somewhat weaker than in ion **11-Br⁺**. The 3-membered bromonium ring is also quite opened, with a Br-C2-C1 bond angle of 98.6°, and the C1-C6 bond is significantly less than a normal C-C single-bond length, at 1.41 Å, and the C5-C6 bond length a bit longer than a typical double bond, at 1.38 Å. The Br has an NPA charge of +0.25, while C1 and C5 have charges of +0.12 and +0.11, respectively. Thus, in terms of structure and charges, ion **11-Br⁺** displays conjugation effects similar to the analogous diene bromonium ion **27-Br⁺**.

The DFT and HF hardness index values for ions **11-Br⁺** and **27-Br⁺** are shown in Figures 4 and 5. HF gives a hardness of about 131 kcal/mol, putting it between the mono-alkene bromonium ion **25-Br⁺** (137.2 kcal/mol) and diene and 2-carene bromonium ions **28-Br⁺a** and **b**, **29-Br⁺,** and **1-Br⁺**. This is understandable qualitatively, since the structure of ion **11-Br⁺** does not show the extent of cyclobutyl ring opening that ion **1-Br⁺** shows, nor is its positive charge as shifted onto C8 as it is in ion **1-Br⁺**. The DFT hardness index of ion **11-Br⁺**, 51.3 kcal/mol, is also between that of ion **25-Br⁺** (51.7 kcal/mol) and ions **28-Br⁺a** and **b**, **29-Br⁺** and **1-Br⁺** (average η = 43.4 kcal/mol), but the fact that it is almost equal to that of ion **25-Br⁺**, the bromonium ion of a mono-alkene where no conjugation is possible, is a result that needs to be investigated further, and could be a function of functional chosen or basis set.

A similar scenario is observed for β-pinene, **7**, and its bromonium ion, **7-Br⁺**. For comparison and viewing convenience ion **28-Br⁺** is shown again along with compound **7** and ion **7-Br⁺** in the fifth row of Figure 3, since as is the case with ion **7-Br⁺**, conjugation can cause the 3-membered bromonium ion ring to open with the Br being mainly bonded to the primary carbon of the methylidene. As was the case with compound **11** and ion **11-Br⁺**, bromination of the C1-C7 bond in compound **7** leads to a distorted bromonium ion structure, with C7 showing close to pure sp^3 geometry and a Br-C7-C1 bond angle of 106.9°. Also observed upon bromination is the opening of the cyclobutyl ring, with the C8-C6 distance stretching from 1.51 Å in 7 to 2.10 Å in ion **7-Br⁺**, and the C8 dihedral angle decreasing from 28.0° in compound **7** to 18.2° in ion **7-Br⁺**, displaying, like in ion **11-Br⁺**, partial ring opening, but not to the extent that was observed in ion **1-Br⁺**, where C8 becomes almost completely planar. Significant double bond character of the C1-C6 bond also manifests in ion **7-Br⁺** compared to **7**, with this bond shortening from 1.58 Å to 1.39 Å. NPA charges on ion **7-Br⁺** also support conjugation with the bromonium ring. The majority of positive charge is localized on C8 (+0.22), with the Br and C1 having less positive charge, +0.09 and +0.11, respectively. This displays more charge transfer away from the Br than that observed in ion **28-Br⁺a**.

Results of DFT and HF hardness calculations for ion **7-Br⁺** were similar to those of ion **11-Br⁺**, although both methods give values slightly lower for ion **7-Br⁺** than ion **11-Br⁺**. DFT hardness was 49.3 kcal/mol, compared to 51.3 kcal/mol for ion **11-Br⁺**, and the HF hardness was 129.8 kcal/mol, compared to 131.0 kcal/mol for ion **7-Br⁺**. These results correlate well with the slightly greater conjugation effects seen in the distortion and charge distribution of ion **7-Br⁺** compared to ion **11-Br⁺**. The overall greater hardness in ions **7-Br⁺** and **11-Br⁺** compared to ion **1-Br⁺** is probably explained by the lower ring strain of the cyclobutyl moiety compared to the cyclopropyl, and this also can explain the relatively less planar carbocation character of C8 in the pinene bromonium ions, compared to ion **1-Br⁺**. This may also explain the tendency of ion **7-Br⁺** and ion **11-Br⁺** to eliminate, rather than undergo direct nucleophilic attack at C7, as was the case with ion **1-Br⁺**, which displayed higher positive charge and planarity at C8.

5. Conclusion

It has been demonstrated that the reactivity of the cyclopropyl halonium ions of compound **1** is similar to that of the protonated cyclopropyl epoxide **2** [6] and cyclopropyl tosylaziridine **5** [10]. As expected, the cyclopropyl halonium ions were extremely reactive, but acetonitrile was able to trap them, with 1,4-addition occurring, opening the cyclopropane ring, instead of 1,2-addition occurring, as occurs with halonium ions of compound **3** [27]. Furthermore, the reactivity of the cyclopropyl halonium ions of compound **1** was also different than that reported for the acid-catalyzed Prins reaction of compound **1** [2]. This supports the idea that the cyclopropyl halonium ions are delocalized though the cyclopropane.

Similarly, the reactions of the bromonium ions of pinenes involved opening of the cyclobutane ring to give an allylic bromide, which was subsequently displaced by chloramine-T. The cyclobutyl halonium ions could be trapped directly with chloramine-T, unlike the more reactive cyclopropyl halonium ions, which had to first be trapped by acetonitrile solvent. X-Ray crystallography of allylic amine **16b** and the formation of compound **22** suggest that after opening of the cyclobutyl halonium ion, the displacement of the halide occurs by an S_N2 mechanism with displacement directly at the halogenated carbon rather than at the allylic carbon.

The molecular and electronic structures of bromonium ions **1-Br⁺**, **7-Br⁺** and **11-Br⁺** were calculated using various *ab initio* and Density Functional Theory methods, and compared with bromonium ions of select cyclohexenes, and also those of select cyclohexadienes with double bonds in conjugation. In terms of their optimized structures, ions **1-Br⁺** (cyclopropane), **7-Br⁺** and **11-Br⁺** (cyclobutanes) all display partial small alkyl ring opening, as well as bond distortions commensurate with conjugation to the cyclopropane or cyclobutane ring from the bromine, including partial ring opening of the three-membered ring of the bromonium ion moiety. Bond length changes compared to the substrates, in general, were similar with the bromonium ions of the conjugated cyclohexadienes we chose to include. Absolute hardness, using HF/aug-cc-pVDZ and B3LYP/aug-cc-pVDZ, was calculated for all bromonium ions presented in this report. To the best of our knowledge, this method has not been used for analyzing such reactive intermediates, but the results showed that ion **1-Br⁺** displays similar hardness, or the lack thereof, as those of bromonium ions of the conjugated cyclohexenes included in this theoretical study, which was expected, and ions **7-Br⁺** and **11-Br⁺**, while somewhat harder than ion **1-Br⁺**, also displayed hardness values much lower than bromonium ions of non-conjugated mono-alkenes included in this report. Finally, NPA atomic charges on all bromonium ions in this report were calculated from their MP2/aug-cc-pVDZ electron densities, and those of atoms potentially involved in any possible conjugation effects were reported. Ions **1-Br⁺**, **7-Br⁺** and **11-Br⁺** all display delocalization of the positive charge from the Br down into the dimethyl carbon of the cyclopropane (ion **1-Br⁺**) or cyclobutane (ions **7-Br⁺** and **11-Br⁺**), and with values similar to those of the conjugated cyclohexadiene bromonium ions. Thus, taken separately or in combination, structural effects upon bromination, absolute hardness, and NPA charges all support conjugation being present in ions **1-Br⁺**, **7-Br⁺** and **11-Br⁺**. Hardness and NPA charges are simply calculated in Gaussian09, and we believe these can be easily accessible and powerful theoretical probes for researchers studying similar reactive intermediates and their electronic structure.

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Supplementary material

CCDC-831756 and CCDC-1415151 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk /data_request/cif, or by e-mailing data_request@ ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44(0)1223-336033.

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