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Ring Expansions of Alkynyl Cyclopentanols with Iodine and Koser's Reagent.

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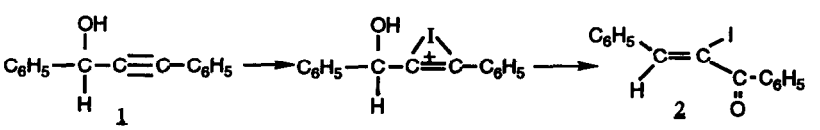
Abstract: Equimolar amounts of iodine, Koser's reagent, and 1-bromoethynylcyclopentanols with none, one or two methyl groups in the α-position lead to ring expansions in acetonitrile at room temperature in yields of 75 to 85%. In the so-formed 2-[bromoiodomethylidene]cyclohexanones, the (Z) isomer was preferred exclusively in the unsubstituted compound. The Z/E ratio was 7.7 for the dimethyl compound and 3.3 for the monomethyl case. The corresponding bromine and Koser's reagent with 1-iodoethynylcyclopentanol afforded a ring expanded product with Z/E ratio of 12:1.

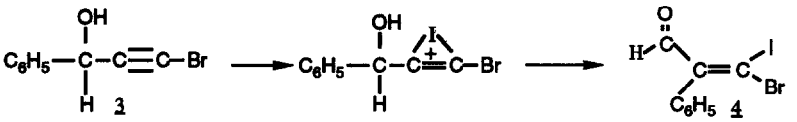
In a series of communications about the reactions of alkynols with iodonium-producing systems, we have reported the formations of β-iodoenones, α-iodoenones, mixed β,β-dihaloenones and mixed β,β-dihaloenals.[1,2,3,4] In the cases of β-iodoenones, phenyl groups migrated from tertiary alkynols or secondary bromoalkynols. Formations of α-iodoenones stemmed from secondary alkyl or aryl alkynols by a process called the "halo-Meyer Schuster" reaction. All of these products were formed with set stereochemistries about the alkene bonds. Such stereospecificities were lost if bromonium-producing species were reacted with iodoalkynols. These products thereby represent attractive starting materials for stereospecific systems since haloalkenes can be templates for numerous metal-catalyzed coupling reactions.

The direction of these reactions would seem to depend on the nature of the alkyne portion of the alkynol. Thus if the secondary alkynol 1 is treated with an iodonium-producing system, the vinyl cation adjacent to the phenyl group might set the course of the reaction to an α-iodoenone 2.[2]



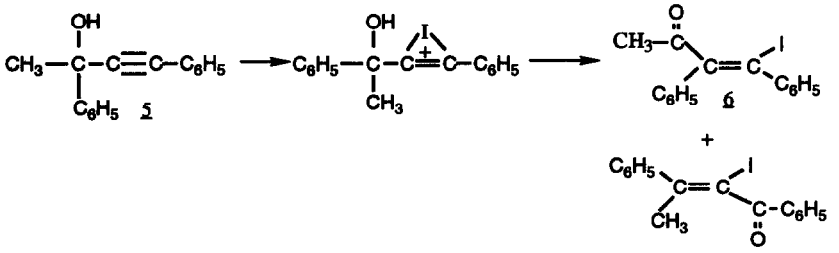
Scheme 1

On the other hand, if the bromoalkynol 3 is treated similarly, the vinyl cation adjacent to the alcoholic carbon would lead to a phenyl shift to the β-enal 4.[4]



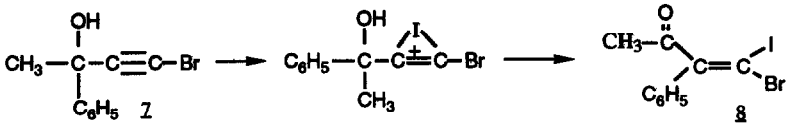
Scheme 2

If the reactants are tertiary alkynols such as compound 5, the vinyl cation might be considered to be bridged and both types are formed with the phenyl shift of 6 predominating.[1] Here too, a bromoalkynol 7 can afford



Scheme 3

exclusively a phenyl shift to 8 by reason of an unsymmetrical vinyl cation.[3]

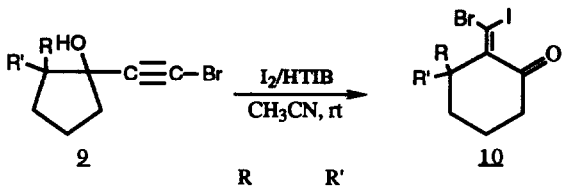


Scheme 4

In cases of mixed products the direction is often a function of the iodonium-producing systems, which extend over a broad range. Originally the systems were iodine and oxides of iodine such as pentoxides, iodic and or periodic acid. Their ratios were usually equimolar or greater with regard to the alkynol. These duos were supplemented with combinations of N-iodosuccinimide and catalytic amounts of Lewis acids or certain protic acids. Prominent among these catalysts were [(hydroxy)p-tosyloxyiodo]benzene (HTIB, Koser's reagent) and p-toluenesulfonic acid.[5] Other catalysts were (diacetoxyiodo)benzene, [bis(trifluoroacetoxy)iodo]benzene and silver tetrafluoroborate. The wide-ranging examination of their effectiveness along with parallel halogenations with N-bromosuccinimide and N-chlorosuccinimide were reported for the halogenations of polyalkylaromatic hydrocarbons.[6,7]

A system used for the iodination of recalcitrant aromatics was the stoichiometric combination of iodine and HTIB in CH_3CN. This system was applied to the aforementioned phenyl shift reaction of haloalkynols when the milder catalytic combination with NIS failed. In this paper we report the applications of this I_2/HTIB system for the ring expansion of cyclopentyl bromoalkynols. These expansions extend greatly the synthetic potential of these methodologies.

Results and Discussion



9a

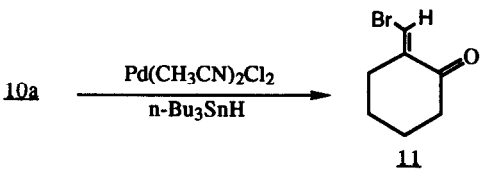
10a

	R	R'
a	H	H
b	CH3	CH3
c	CH3	H

Scheme 5

When 1-bromoethynylcyclopentanol (9a, 1mmol) was treated with iodine (1.22 mmol) and HTIB (1.32 mmol) in acetonitrile (10 mL) at room temperature for twenty hours or at reflux for 1.5 hours, 2-[(Z)-bromoiodomethylidene]cyclohexanone (10a) was formed in 75 to 82% yields as determined by gas chromatography (isolated yields; 10-20% lower). It was isolated by means of silica gel chromatography. The following spectral data are consistent with the assigned structure of 10a: IR 1700 (s) cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.81 (m, 2H, C-4), 1.91 (m, 2H, C-5), 2.48 (t, 6.6Hz, 2H, C-3), 2.73 (t, 6.3Hz, 2H, C-6); ^{13}C-NMR ($CDCl_3$) δ 24.50 (C-4), 25.32 (C-5), 36.39 (C-3), 42.05 (C-6), 54.28 (CBrI), 147.74 (C-2), 201.55 (C-1); GC/MS m/e (rel. int.) 314/316 (M^+, 3), 286/288 (M^+-CO, 3), 159/161 (M-CO-I, 2), 80 (M-CO-I-Br, 26), 79 (100).

The assignment of the geometry about the alkene was based on a conversion of 10a to 11 by means of $Pd(CH_3CN)_2Cl_2$ and Bu_3SnH whereby the vinyl iodine atom was exchanged with a hydrogen atom.



11

Scheme 6

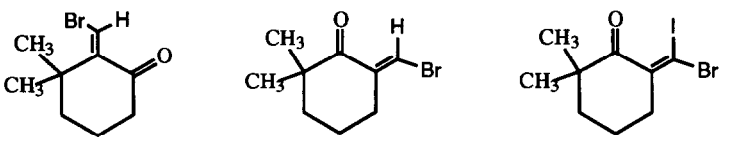
The product, 2-[(E)-bromomethylidene]cyclohexanone, had a ^{1}H-NMR that features a resonance at 7.40 ppm (t, J = 2.25Hz). According to the reports of Piers on cyclic and acyclic enones, haloenones with protons syn to a carbonyl carbon had resonances between 7.35 and 7.70 ppm.[8] Those protons anti to the carbonyl had values between 6.28 and 6.96 ppm. A value of 7.3 ppm (t, J = 2Hz) was reported by Russell and Herold for bromo methylidenecyclohexanone formed by the thermal dehydrobromination of 2-(dibromomethyl)cyclohexanone.[9] The infrared spectrum and the GC/Ms data of that product match those of 11.

No conversions of 9a to 10a took place with efforts to replace HTIB with other polyiodinated compounds such as iodosylbenzene, (diacetoxyiodo)benzene and [bis(trifluoroacetoxy)iodo]benzene. The use of half-molar quantities of I_2 and HTIB with 9a in acetonitrile at room temperature for 24 hours led to a conversion of 42% and a selectivity to 10a of 54%. Admixed with 10a was a cyclopentenyl structure with two iodines and a bromine. This latter compound was a major product if these combinations of reagents were refluxed in acetonitrile. The use of NIS and catalytic quantities of HTIB in methanol, N-methylpyrrolidinone or ethyl acetate gave no reactions.[10]

Catalytic quantities of p-toluenesulfonic acid in acetonitrile or methanol did give 10a mixed with the cyclopentenyl product as well as other uncharacterized compounds.

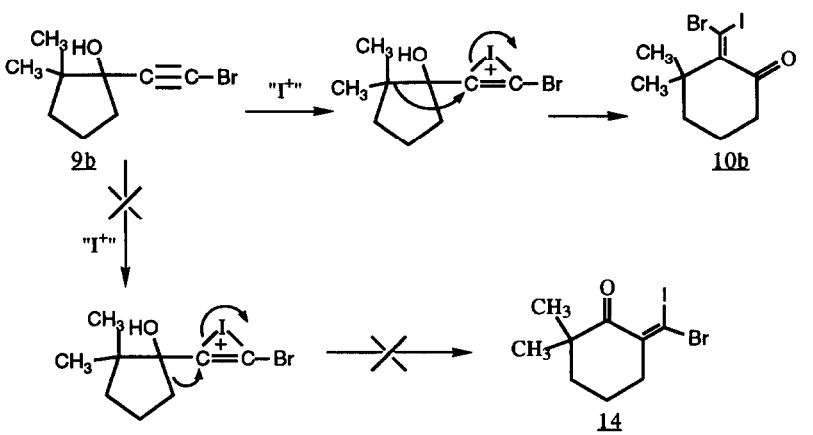
An analogous equimolar experiment with I_2/HTIB was carried out to convert 1-bromoethynyl-2,2-dimethylcyclopentanol (9b) to 2-[(Z)-bromoiodomethylidene]-3,3-dimethylcyclohexanone (10b) in 85% yield. Selected spectral data were as follows: IR 1705 (s) cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.16 (s, 6H, CH_3's), 1.75 (m, 4H, C-4 and C-5), 2.71 (m, 2H, C-6); ^{13}C-NMR ($CDCl_3$) δ 20.98 (CH_3's), 23.85 (C-4), 37.47 (C-5), 40.68 (C-3), 46.68 (C-6), 58.73 (CBrI), 149.50 (C-2), 206.85 (C-1); GC/MS m/e (rel. int.) 342/344 (M^+, 13) 314/316 (M-CO, 13), 235 (M^+-Br, 20), 187/189 (M-CO-I, 18), 136 (M-I-Br, 14), 108 (M-CO-I-Br, 42), 107 (62), 41 (100). The display in the ^{1}H-NMR spectrum of a multiplet at 2.71 should be compared to the multiplets at 2.48 and 2.73 of 10a. The values at 2.73 were indicative of protons alpha to the carbonyls. The values of 2.48 for 10a indicated the allylic hydrogens. Since the products of 9b had no peak arond 2.48, it would follow that structure 10b without allylic hydrogens was reasonable. Thus in the ring expansion of 9b, the quaternary carbon (C-2) of the cyclopentanol ring migrated rather than the secondary carbon (C-5). If the secondary carbon (C-5) had migrated, the product would have been 2-[(Z)-bromoiodomethylidene]-6,6-dimethylcyclohexanone (14) and its ^{1}H-NMR would have a multiplet at about 2.48ppm but none around 2.73ppm.

The (Z)-isomerism was demonstrated as before for 10a. When 10b was treated with $Pd(CH_3CN)_2Cl_2$ and Bu_3SnH, the product's ^{1}H-NMR spectrum possessed a singlet at 7.2ppm and was assigned the structure 2-[(E)-bromomethylidene]-3,3-dimethylcyclohexanone (12). The lack of splitting of the 7.2 signal was also consistent with this assignment rather than structure 13, the putative product of 14, the result of a shift of C-5



12 13 14

Scheme 7



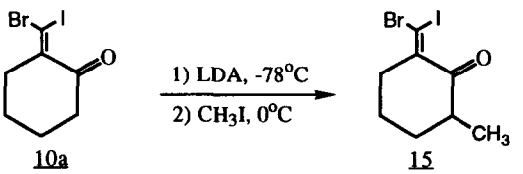
9b 10b 14

Scheme 8

of the cyclopentanol compound 9b. According to GC and GC/Ms data such a product was not detected. An unisolated product formed in 11% yield was presumed to be the (E)-isomer of 10b on the basis of its GC/MS, which featured a mass at 215/217 corresponding to the loss of anti-iodine just as the GC/MS of 10a displayed a 235 mass corresponding to the loss of an anti-bromine. The mass spectrum of this (E) isomer was as follows: 342/344 (M^+, 8), 215/217 (M-I, 22), 187/189 (M-CO-I, 7), 136 (M-I-Br, 14), 127 (I, 12), 108 (M-CO-I-Br, 38), 107 (32), 41 (100).

The possibility of competitive shifts was examined with the ring expansion of 1-bromoethynyl-2-methylcyclopentanol (9c). Its reaction with I_2/HTIB did not lead to a yield of 2-[(Z)-bromoiodomethylidene]-3-methylcyclohexanone (10c) high enough for a clean separation from another isomer. Gas chromatographic results indicated no starting material in the reaction products and only two products in a ratio of 77/23 after a silica gel chromatography. The GC/MS cracking patterns are similar to those for the (E) and (Z) isomers of 10b with the (Z) isomer assigned to the 77% isomer. Thus this latter isomer had the following MS pattern: 328/330 (M^+, 20), 300/302 (M-CO, 9), 221 (M-CO-Br, 6), 173/175 (M-CO-I, 9), 127 (11), 94 (M-CO-I-Br, 42), 93 (100), 79 (51), 77 (33), 65 (22), 55 (47), 51 (38), 41 (44). The (E)-isomer had the following mass spectrum: 328/330 (M^+, 4), 201/203 (M-I, 4), 127 (13), 122 (M-I-Br, 7), 94 (M-CO-I-Br, 42), 93 (100), 79 (65), 77 (54), 65 (33), 55 (49), 51 (80), 41 (73). The ^{1}H-NMR of this mixture was not helpful. Only a pair of doublets at 1.11/1.13ppm and 1.03/1.01ppm signaled similar methyl hydrogens. The splittings in the 1.5-2.0 and 2.3-2.5 region could be assigned to the diastereomeric mixture of the starting material 9c. That mixture may be the source of the lower Z/E ratio of 3.3 for 10c versus 7.7 for 10b. The ^{13}C-NMR provided a clearer picture of this mixture. The resonances due to 10c were as follows: 14.91 (CH_3), 23.93 (C-4), 34.71 (C-5), 37.29 (C-3), 46.35 (C-6), 51.65 (CBrI), 149.64 (C-2), 204.77 (C-1). Those resonances due to the (E)-isomer of 10c, 2-[(E)-bromoiodomethylidene]-3-methylcyclohexanone, had these values: 17.15 (CH_3), 21.20 (C-4), 30.96 (C-5), 40.84 (C-3), 42.40 (C-6), 52.26 (CBrI), 153.34 (C-2), 202.96 (C-1). Thus it would seem there was no evidence for any major product corresponding to a compound formed by a shift of C-5 of 9c. The E/Z mixture of 10c was formed by a shift of the tertiary carbon at C-3.

To further be sure of this lack of shift from C-5 of 9c, the other possible methylcyclohexanone was prepared. The product of 9a's ring expansion, 10a, was treated with LDA followed by CH_3I to afford compound 15, 2-[(E)-bromoiodomethylidene]-6-methylcyclohexanone. The GC/MS data for this compound were as follows: m/e (rel. int.) 328/330 (2), 300/302 (2), 221 (3), 179 (3), 173/175 (5), 144/146 (3), 131/133 (8), 128 /130 (3), 127 (24) 117/119 (17), 93 (100), 79 (79), 77 (48), 65 (30), 58 (60), 51 (65), 41 (71). These data do not match those of 10c or its (E)-isomer.



10a 15

Scheme 9

Table 1.

Mass spectral cracking patterns for ring-expanded products *

	(Z)-isomers**				(E)-isomers**		
	10a	10b	10c	15***	10a	10b	10c
M^+	314/316(22)	342/344(13)	328/330(21)	328/330(2)	314/316(1)	342/344(8)	328/330(3)
M-CO	286/288(14)	314.316(13)	300/302(9)	300/302(1)	----	----	----
M-I	----	----	----	----	187/189(22)	215/217(22)	201/203(4)
M-CO-I	159/161(3)	187/189(18)	173/175(9)	173/175(5)	----	----	----
M-I-CH_2CO	----	----	----	----	145/147(100)	173/175(3)	159/161(4)
P	79	41	93	93	145	41	93

* Hewlett Packard 5992 with an OV-1 column (0.25mm x 15m) operated with the following conditions: injection temperature (250°C), initial temperature (80°C), ramp rate (16°C/min.) and solvent elution time (60 seconds).

** m/e (relative intensity)

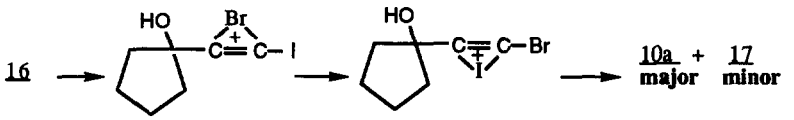
*** Formed by treatment of 10a with LDA/CH_3I.

Additionally, the ^{13}C-NMR of compound 15 had these values: δ 16.24 (CH_3), 25.27 (C-4), 36.07 (C-5), 36.72 (C-3), 38.74 (C-6), 47.72 (CIBr), 141.67 (C-2), 206.05 (C-1). Again, there was no match with the products of 9c. On the basis of the cracking pattern in the GC/MS, which featured an initial loss of CO prior to a loss of iodine, it was assigned the Z-configuration. Since it had been prepared from the (Z)-isomer, 10a, this suggested that there was no isomerization in the LDA/CH_3I procedures and work-ups. These mass spectral patterns are summarized in Table 1. In general, the (Z)-isomers' initial losses from M^+ peaks are CO, whereas the (E)-isomers' initial peaks are the losses of iodine.

Since, the route to mixed β,β-dihaloenones could be approached by the bromination of iodoalkynyl cyclopentanols, the iodoalkynol 16 was treated with bromine and HTIB (1:1).

Scheme 10

If the bromination were as stereospecific as the iodination, the expected product would be 17. When 16 was treated with equimolar amounts of Br_2 and HTIB in acetonitrile at room temperature for two hours, the major product was 10a in 80% yield. Compound 17 was detected with the GC/MS and its ratio to 10a was 1:12. The rationale for this isomer would be that the bromonium ion intermediate was converted to a more stable iodonium species prior to the ring expansion.



Scheme 11

A similar effect had been noticed in the formation of β,β-bromoiodoenones from linear halogenated tertiary alkynols.[3] If the Br_2/HTIB molar ratios to 16 were lowered to 0.5 and the acetonitrile reaction solution was refluxed for 2.5 hours, the yield of 10a fell to 20%. The other products were the iodo-analogues of those cyclopentenyl compounds mentioned as side products in the reactions of 9a with half-molar quantities of I_2/HTIB.

Despite the synthetic limitation of the E/Z mixture of 10c, the mixed halogens of 10a and 10b represent admirable building blocks for multi-ringed system such as steroids and terpenes

Experimental Section

IR spectra were obtained with a Mattson Polaris FT-IR spectrophotometer and a 137 Perkin-Elmer spectrophotometer. ^{1}H-NMR and ^{13}C-NMR were recorded of $CDCl_3$ solutions containing tetramethylsilane as

an internal standard on a GE-300 spectrometer, operated in the Fourier transform mode at 300 or 75.5 MHz. GC analyses were carried out on a Perkin-Elmer Sigma 3B gas chromatograph with a methyl silicone column (0.25mm x 50m). GC/MS analyses were performed with a Hewlett-Packard 5992 with an OV-1 column (0.25mm x 15m). Products were purified by silica gel chromatography on J.T. Baker silica gel (40-140mesh). Alkynols were purchased from Farchan Laboratories. Other reagents were obtained from the Aldrich Chemical Co. and solvents were received from the J.T. Baker Co. Elemental analyses were performed by Schwarzkopf Microanalytical Laboratory of Woodside NY.

Preparations of 1-bromoethynylcyclopentanol (9a), 1-bromoethynyl-2,2-dimethylcyclopentanol (9b), 1-bromoethynyl-2-methylcyclopentanol (9c) and 1-iodoethynylcyclopentanol (16).

Compounds 9a, 9b, 9c and 16 were prepared according to the procedure of Hofmeister[11] and had the following spectral data:

1-Bromoethynylcyclopentanol (9a): ^{1}H-NMR ($CDCl_3$) δ 1.72-1.84 (m, 4H), 1.91-1.96 (m, 4H); IR (neat) 3413 (vs), 3021 (vs), 2242 (w), 1439 (s), 1302 (s), 1203 (s), 1072 (s), 1038 (s), 989 (s), 940 (m), 909 (m), 875 (s) cm^{-1}; GC/MS m/e (rel.int.) 190/188 (M^+, 1), 161/159 (15), 133/131 (14), 81 (100), 79 (43), 77 (5), 67 (17), 55 (23), 53 (47), 41 (32); Anal. calcd for C_7H_9BrO: C, 44.45; H, 4.81. Found: C, 44.11; H, 5.01.

1-Bromoethynyl-2,2-dimethylcyclopentanol (9b): ^{1}H-NMR ($CDCl_3$) δ 1.02 (s, 3H), 1.06 (s, 3H), 1.22-1.27 (m, 2H), 1.72-1.78 (m, 2H), 2.16-2.24 (m, 2H); IR (neat) 3436 (vs), 3003 (vs), 2283 (w), 1443 (s), 1370 (s), 1277 (m), 1072 (s), 987 (m), 907 (s), 875 (m) cm^{-1}; GC/MS m/e (rel. int.) 218/216 (M^+, 1), 203/201 (6), 161/159 (11), 148/146 (30), 137 (23), 133/131 (20), 109 (60), 95 (28), 93/91 (22), 81 (37), 79 (22), 77 (16), 67 (63), 55 (62), 41 (100); Anal. calcd for $C_9H_{13}BrO$: C, 49.79; H, 6.04. Found: C, 50.40; H, 6.18.

1-Bromoethynyl-2-methylcyclopentanol (9c): ^{1}H-NMR ($CDCl_3$) δ 1.04 (d, 6.6Hz, 3H), 1.23 (d, 8.7Hz, 3H), 1.67-2.12 (m, 7H); IR (neat) 3497 (vs), 3067 (vs), 2257 (w), 1460 (m), 1374 (m), 1300 (m), 1200 (m), 1083 (s), 1038 (s), 997 (m), 952 (m), 911 (m), 870 (m) cm^{-1}; GC/MS m/e (rel. int.) 204/202 (M^+, 1) 189/187 (2), 161 (17), 160 (18), 148/146 (44), 133/131 (23), 123 (17), 95 (100), 81 (31), 79 (25), 77 (17), 67 (80), 55 (73), 53 (41), 41 (62); Anal. calcd for $C_8H_{11}BrO$: C, 47.29; H, 5.47. Found: C, 46.85; H, 5.70.

1-Iodoethynylcyclopentanol (16): ^{1}H-NMR ($CDCl_3$) δ 1.74-1.83 9m, 4H), 1.92-2.00 (m, 4H); IR (nujol) 3521 (s), 2994 (s), 2203 (w), 1451 (s), 1372 (s), 1284 (m), 1199 (m), 1064 (m), 986 (m), 906 (w)cm^{-1}; Anal. calcd for C_7H_9IO: C, 35.58; H, 3.85. Found: C, 35.90; H, 3.60.

Preparation of 2-[(Z)-bromoiodomethylidene]-3-methylcyclohexanone (10c) and 2-[(E)-bromoiodomethylidene]-3-methylcyclohexanone.

To a solution of 1-bromoethynyl-2-methylcyclopentanol, 9c (280mg, 1.38mmol) in acetonitrile (10mL), iodine (369mg, 1.45mmol) and HTIB (586mg, 1.49mmol) were added together at room temperature. The solution was stirred overnight. The solution was diluted with 75mL of ether and washed with 5% $Na_2S_2O_3$ and then with 3x100mL of H_2O. The ether layer was dried with $MgSO_4$. The solvent was evaporated under vacuum. The resulting residue was then applied to a silica gel chromatography column. Iodobenzene was first washed off with CCl_4. The solvent was then changed to CH_2Cl_2/CCl_4 (1:1) to elute the products 10c and its (E)-isomer as green oil in yields of 60% (267mg).

2-[(Z)-bromoiodomethylidene]-3-methylcyclohexanone (10c): ^{13}C-NMR ($CDCl_3$) δ 14.91 (CH_3), 23.93 (C-4), 34.71 (C-5), 37.29 (C-3), 46.35 (C-6), 51.65 (CBrI), 149.64 (C-2), 204.77 (C-1); GC/MS m/e (rel. int.) 328/330 (M^+, 20), 300/302 (M-CO, 9), 221 (M-CO-Br, 6), 173/175 (M-CO-I, 9), 127 (11), 94 (M-CO-I-Br, 42), 93 (100), 79 (51), 77 (33), 65 (22), 55 (47), 51 (38), 41 (44).

2-[(E)-bromoiodomethylidene]-3-methylcyclohexanone: ^{13}C-NMR ($CDCl_3$) δ 17.15 (CH_3), 21.20 (C-4), 30.96 (C-5), 40.84 (C-3), 42.40 (C-6), 52.26 (CBrI), 153.34 (C-2), 202.96 (C-1); GC/MS m/e (rel. int.) 328/330 (M^+, 4), 201/203 (M-I, 4), 127 (13), 122 (M-I-Br, 7), 94 (M-CO-I-Br, 42), 93 (100), 79 (65), 77 (54), 65 (33), 55 (49), 51 (80), 41 (73).

2-[Bromoiodomethylidene]-3-methylcyclohexanone: IR (nujol) 2930 (s), 1690 (s), 1570 (m), 1450 (s), 1380 (m), 1220 (w), 1180 (w), 1130 (m), 1070 (w), 1000 (m), 850 (m), 780 (m) cm^{-1}; Anal. calcd for $C_8H_{10}BrIO$: C, 29.18; H, 3.07. Found: C, 29.24; H, 2.77.

Preparation of 2-[(Z)-bromoiodomethylidene]cyclohexanone (10a).

1-Bromoethynylcyclopentanol, 9a (1.40g, 7.42mmol) was dissolved in 25mL of acetonitrile. To this solution iodine (1.88g, 7.41mmol) and HTIB (2.94g, 7.50mmol) were added with an ice-bath cooling. The reaction became exothermic upon the addition of I_2 and HTIB. The solution was stirred for 2 hours and then worked up as described above for the preparation of 10c and its (E)-isomer. The product 10a was isolated by silica gel chromatography column as described previously. The second fraction (CH_2Cl_2/CCl_4, 1:1 as eluant) yielded 1.42g of 10a (61%).

2-[(Z)-bromoiodomethylidene]cyclohexanone (10a): IR (neat) 2950 (s), 1700 (s), 1570 (m), 1500 (m), 1440 (m), 1300 (w), 1250 (s), 1225 (s), 1140 (s), 1120 (s), 1060 (m), 820 (m), 770 (s) cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.81 (m, 2H, C-4), 1.91 (m, 2H, C-5), 2.48 (t, 6.6Hz, 2H, C-3), 2.73 (t, 6.3Hz, 2H, C-6); ^{13}C-NMR ($CDCl_3$) δ 24.50 (C-4), 25.32 (C-5), 36.39 (C-3), 42.05 (C-6), 54.28 (CBrI), 147.74 (C-2), 201.55 (C-1); GC/MS m/e (rel. int.) 314/316 (M^+, 3), 286/288 (M^+-CO, 3), 159/161 (M-CO-I, 2), 80 (M-CO-I-Br, 26), 79 (100); Anal. calcd for C_7H_8BrIO: C, 26.67; H, 2.57. Found: C, 27.22; H, 2.69.

Preparation of 2-[(Z)-bromoiodomethylidene]-3,3-dimethylcyclohexanone (10b).

Iodine (306mg, 1.21mmol) and HTIB (487mg, 1.24mmol) were added together to a solution of 1-bromoethynyl-2,2-dimethylcyclopentanol, (9b) (245mg, 1.13mmol) in 10mL of acetonitrile. The solution was stirred overnight and it was diluted with ether and worked up as previously described in the preparation of 10c and its (E)-isomer. Isolation of 10b was achieved by silica gel chromatography column using CH_2Cl_2/CCl_4 (1:1) as eluant. Iodobenzene was first washed off the column using CCl_4. 10b was next eluted as a green oil weighing 213mg (55%).

2-[(Z)-bromoiodomethylidene]-3,3-dimethylcyclohexanone (10b): IR (nujol) 2940 (s), 1705 (s), 1570 (m), 1460 (s), 1375 (m), 1250 (w), 1175 (w), 1150 (w), 1100 (w), 1050 (w), 990 (m), 850 (w), 775 (m) cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.16 (s, 6H, CH_3's), 1.75 (m, 4H, C-4 and C-5), 2.71 (m, 2H, C-6); ^{13}C-NMR ($CDCl_3$) δ 20.98 (CH_3's), 23.85 (C-4), 37.47 (C-5), 40.68 (C-3), 46.68 (C-6), 58.73 (CBrI), 149.50 (C-2), 206.85 (C-1); GC/MS m/e (rel. int.) 342/344 (M^+, 13) 314/316 (M-CO, 13), 235 (M^+-Br, 20), 187/189 (M-CO-I, 18), 136 (M-I-Br, 14), 108 (M-CO-I-Br, 42), 107 (62), 41 (100); Anal. calcd for $C_9H_{12}BrIO$: C, 31.49; H, 3.53. Found: C, 31.02; H, 3.27.

Procedure for preparation of 2-[(Z)-bromoiodomethylidene]-6-methylcyclohexanone (15).

LDA was prepared in situ in THF at -78°C from diisopropylamine (0.7mmol) and t-butyllithium (0.6mmol). To the LDA solution 10a (0.6mmol) was added via syringe at -78°C under N_2 and the solution was allowed to warm up to 0°C in 1 hour. Excess CH_3I (3mmol) was added via syringe and stirred at ice-bath temperature for a further 2 hours. The solution was poured into a cooled saturated solution of NH_4Cl and extracted with ether. Compound 15 was isolated by preparative silica gel TLC (Rf = 0.4) using CH_2Cl_2/CCl_4, 1:1 as eluant. The conversion to 15 from 10a was 60%.

2-[(Z)-bromoiodomethylidene]-6-methylcyclohexanone (15): ^{1}H-NMR ($CDCl_3$) δ 1.14 (d, 6.3Hz, 3H), 1.53-2.57 (m, 7H); ^{13}C-NMR ($CDCl_3$) δ 16.24 (CH_3), 25.27 (C-4), 36.07 (C-5), 36.72 (C-3), 38.74 (C-6), 47.72 (CIBr), 141.67 (C-2), 206.05 (C-1); IR (nujol) 2994 (s), 1704 (s), 1567 (m), 1443 (s), 1366 (m), 1175 (w), 1121 (m), 994 (w), 845 (m) cm^{-1}; GC/MS m/e (rel. int.) 328/330 (2), 300/302 (2), 221 (3), 179 (3), 173/175 (5), 144/146 (3), 131/133 (8), 128 /130 (3), 127 (24) 117/119 (17), 93 (100), 79 (79), 77 (48), 65 (30), 58 (60), 51 (65), 41 (71).

General procedure for preparations of 2-[(E)-bromomethylidene]cyclohexanone (11) and 2-[(E)-bromomethylidene]-3,3-dimethylcyclohexanone (12).

Compounds 10a and 10b were used on a 0.8 to 0.2 mmol scale, respectively. The following procedure applies to both 10a and 10b. Either 10a or 10b was injected via syringe into a THF (3mL) solution containing $Pd(CH_3CN)_2Cl_2$[12] (half-molar equivalent) at room temperature under N_2. After stirring for 5 minutes, 1 molar equivalent of n-Bu_3SnH was added at room temperature. The deposition of Pd was immediate. The solution was diluted with ether and filtered to remove Pd. The solvent was evaporated in vacuo and the residue was applied to preparative silica gel TLC. Compounds 11 and 12 were isolated in the above fashion (R_f of 11 = 0.45 and R_f of 12 = 0.50) using CH_2Cl_2/CCl_4, 1:1 as eluant.

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