Synthesis of 7a-Aryl-5-*t*-butyl-3-methyleneoctahydrobenzofuran Possessing Partial Skelotons of Some Santonin Analogue and Furanolignans by Intramolecular Radical Cyclisation Reaction

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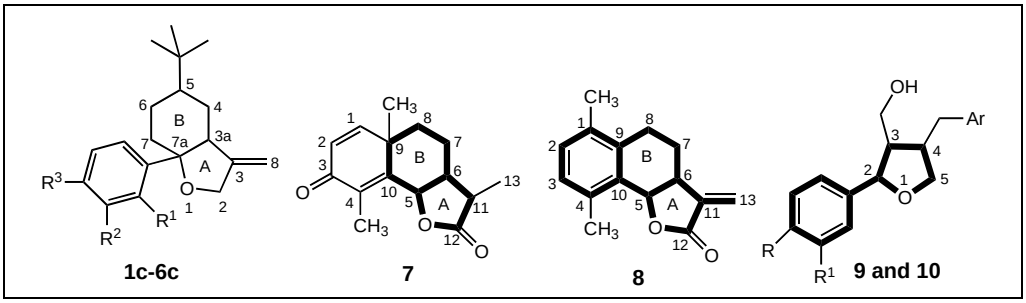

Bicyclic octahydrobenzofuran derivatives (**1c-6c**) possessing the partial skeletons of santonin (**7**), 11,13–dehydroisohyposantonin (**8**), dihydrosesamin (**9**) and lariciresinol (**10**) have been synthesised by intramolecular radical cyclisation in good yield *via* the precursors *viz*., the *trans* diaxial bromopropynyl ethers (**1b-6b**) obtained in highly regio/stereoselective manner.

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INTRODUCTION

The use of radical reactions in organic synthesis has increased over the last few decades [1]. Intramolecular radical cyclisation is an especially useful synthetic protocol for the construction of five- and six-membered carbocyclic and heterocyclic rings [2] and oxygen containing compounds commonly related to natural products and pharamacologically active substances [3]. One of the classical methods for carbon-carbon bond formation involving radical chemistry consists of the reactions of bromopropynyl compounds in the presence of tributyltin hydride (n-Bu_3SnH) and α,α'-azobis(isobutyronitrile) (AIBN).

The tin hydride method relies on the ability of the tin radical to act as a mediator and the tin hydride to act as a hydrogen atom donor for the removal of the final product radical. It has turned out to be one of the most powerful and extensively used radical chain methods and can be applied to both inter and intramolecular radical reactions.

Tetrahydrofuran derivatives are versatile precursors for the synthesis of naturally occurring cytotoxic or anti-tumour agents [3] and also for the construction of a variety of other natural products [4]. Santonin (**7**), a pharmaceutically important sesquiterpenoid, has assumed significance as potential parent compound for anti-tumour drugs [5]. On the other hand, dihydrosesamin (**9**), a tetrahydrofuran lignan isolated from Daphane tangutica Maxim has been used as an abortifacient, anti-oxidant, PAF inhibitors, stress compounds in plants [6], and a medicine for rheumatism and toothache [7]. Another tetrahydrofuran lignan, lariciresinol (**10**) is well known for its activity against lymphocytic leukaemia [8]. Hence, the synthesis of these compounds and their analogues has gained importance. While **7** and one of its analogues *viz*., 11,13-dehydroisohyposantonin (**8**) [9] possess a tetrahydrofuran ring (**A**) attached to an alicyclic six membered ring (**B**) as their partial skeletons, **8, 9** and **10** contain 2-aryltetrahydrofuran as their partial skeletons. These partial skeletons are indicated by bold lines in the corresponding structures (Figure 2). We herein report the synthesis of tetrahydrofuran derivatives (**1c-6c**, Figure 1), that are bicyclic with an aryl ring placed in one of the bridgehead carbons, by intramolecular radical cyclisation of bromopropynyl ethers (**1b-6b**) using n-Bu_3SnH and AIBN (catalyst) in refluxing benzene. Compounds **1c-6c** possess all the above said partial skeletons of **7-10** (Figure 2).

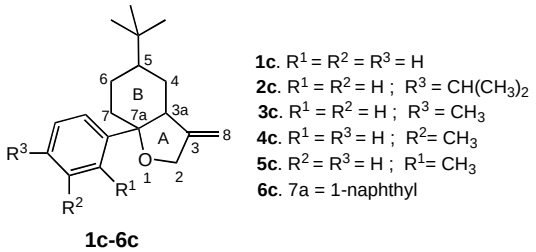


Figure 1.

RESULTS AND DISCUSSION

The hitherto unknown radical precursors, **1b-6b** were prepared by a procedure similar to that reported [10] earlier from the corresponding 4-t-butyl-1-arylcyclo-

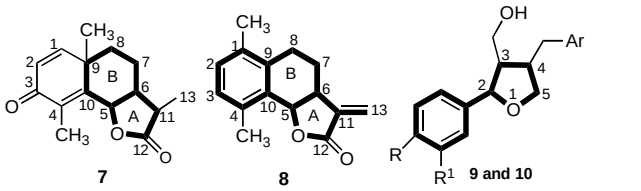
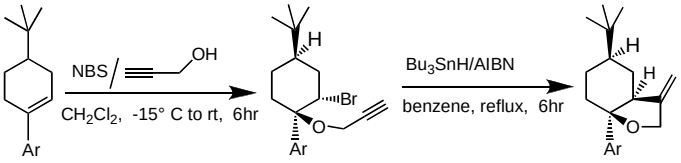


Figure 2. Bold bonds indicating the partial skeletons of santonin (**7**), 11, 13 – dehydroisohyposantonin (**8**), dihydrosesamin (**9**) and lariciresinol (**10**) that are possessed by **1c-6c**.

hexenes (**1a-6a**) by treatment with *N*-bromosuccinimide and propargyl alcohol at –15°C to room temperature in good yield (Table 1) (Scheme 1). The bromopropynyl ethers, **1b-6b** were isolated as the major products by PTLC and were found to be of high analytical purity. Regio/Stereochemistry of **1b-6b** has been interpreted [11] as the *trans* diaxial Markovnikov type product, indicating the high regio/stereoselectivity in propargyloxy bromination of **1a-6a**.

Scheme 1

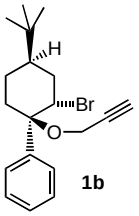
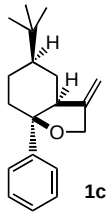
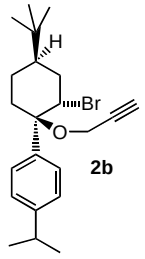
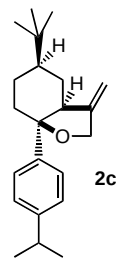
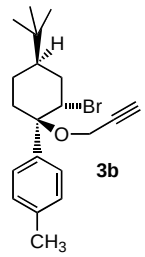
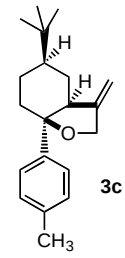
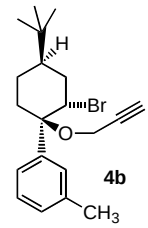
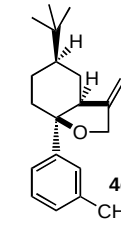
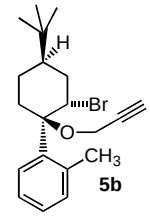
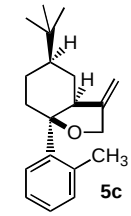
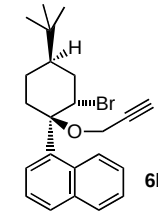
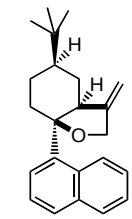


Ar = phenyl,
4-isopropylphenyl,
4-methylphenyl,
3-methylphenyl,
2-methylphenyl,
1-naphthyl

Treatment of the above bromopropynyl ethers, **1b-6b** with n-Bu_3SnH in presence of catalytic amount of AIBN in refluxing benzene for 6 hrs furnished the corresponding tetrahydrofuran derivatives (**1c-6c**) (Scheme 1). The crude residue of the reaction was contaminated with the tri-butyl tin hydride residue as evident from its ^1H NMR spectra. However, PTLC of the crude mixture with silica gel as a stationary phase and ethyl acetate:petroleum ether (2:98) resulted in easy isolation of the cyclised product. Thus, a series of bromopropynyl ethers were subjected to radical cyclisation reaction and the results are summarized in Table 1.

The ring junction in the bicyclic compounds, **1c-6c** has been interpreted as *cis* fused by analogy with structurally related compounds [9,13]. This is supported by the fact that the doublet of doublet pattern of the signal, around 2.88 ppm (J_{aa} = 10.5 Hz, J_{ae} = 6.6 Hz), is confirmed to be due to the methine proton attached to C-3a. Thus the structure of the octahydrobenzofuran derivatives (**1c-6c**) is as shown in Figure 3.

Table 1. Radical cyclisation of bromopropynyl ethers with n-Bu_3SnH/AIBN

Entry	Substrate [a]	Yield (%) [b]	Product [a]	Yield (%) [b]
1	 **1b**	86	 **1c**	78
2	 **2b**	80	 **2c**	75
3	 **3b**	87	 **3c**	80
4	 **4b**	81	 **4c**	72
5	 **5b**	76	 **5c**	66
6	 **6b**	71	 **6c**	61

[a] products are characterized by 1D and 2D NMR (^1H & ^{13}C) analysis [12]. [b] Yields refer to pure isolated products.

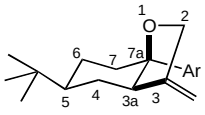


Figure 3

CONCLUSION

Tetrahydrofuran derivatives possessing the partial skeletons of santonin (**7**), 11,13–dehydroisohyposantonin (**8**), dihydrosesamin (**9**) and lariciresinol (**10**) have been prepared in good yield by intramolecular radical cyclisation.

EXPERIMENTAL

All solvents and reagents were of commercial grade available (Merck) and used without further purification. The ^{1}H and ^{13}C NMR of **1b-6b** and **1c-6c** were acquired in $CDCl_3$ on a Bruker Avance 300 spectrometer; the ^{1}H (frequency: 300 MHz) NMR spectra were internally referenced to TMS signal and the ^{13}C NMR (frequency: 75 MHz) spectra to the $CDCl_3$ signal (77.00 ppm). The abbreviations used for the multiplicity pattern of the peaks in the NMR spectra are: m, multiplet; t, triplet; s, singlet; b, broad; d, doublet; $W_{1/2}$, width at half height. Elemental analysis of **1b-6b** and **1c-6c** were found to be satisfactory as expected. All 4-*t*-butyl-1-arylcyclohexenes *viz*., 4-*t*-butyl-1-phenylcyclohexene (**1a**), 4-*t*-butyl-1-(4-isopropylphenyl)cyclohexene (**2a**), 4-*t*-butyl-1-(4-methylphenyl)cyclohexene (**3a**), 4-*t*-butyl-1-(3-methylphenyl)cyclohexene (**4a**), 4-*t*-butyl-1-(2-methylphenyl)cyclohexene (**5a**), 4-*t*-butyl-1-(1-naphthyl)cyclohexene (**6a**) were prepared following the procedure of Garbisch's method [14] in good yield.

Typical procedure for the preparation of the bromopropynyl ethers (1b-6b)

2a-Bromo-4e-*t*-butyl-1a-propargyloxy-1e-phenylcyclohexane (1b). To a stirred solution of 4-*t*-butyl-1-phenylcyclohexene, **1a** (750 mg, 3.50 mmol) in propargyl alcohol (15 ml), maintained at temperature below -15°C to start with, *N*-bromosuccinimide (850 mg, 3.97 mmol) was added in small portions over a period of 10-20 minutes. The stirring was continued for 5-6 hrs allowing the reaction mixture to reach the room temperature. The reaction mixture was then poured into water (50 ml), and extracted with ether (3x25ml). The organic layer was separated, solvent evaporated over water bath and the residue was subjected to PTLC using silica gel as a stationary phase and petroleum ether of boiling range 60-80°C as the mobile phase. The most intense band was extracted with chloroform using soxhlet to afford bromopropynyl ether, **1b** (820 mg, 86%) as a viscous oil. ^{1}H NMR: δ 0.93 (s, 9H, $C(CH_3)_3$), 1.51-2.52 (m, 7H, alicyclic protons), 2.36 (t, 1H, 9-H, J (allylic) = 2.1 Hz), 3.61 (d, 1H, 7-H, J = 11.4 Hz), 3.81 (d, 1H, J = 11.4 Hz), 4.52 (b, 1H, 2-H, $W_{1/2}$ ≈ 7-8 Hz), 7.15-7.45 (m, 5H, Ar-H); ^{13}C NMR: 21.50, 25.06, 27.75, 31.78, 32.13, 40.60, 51.78, 60.60, 70.79, 74.76, 80.48, 126.65, 128.04, 128.24, 141.99. Anal. Calcd. for $C_{19}H_{25}BrO$: C, 65.33%; H, 7.21%. Found: C, 65.29%; H, 7.19%.

2a-Bromo-4e-*t*-butyl-1a-propargyloxy-1e-(4-isopropylphenyl)cyclohexane (2b). Compound **2b** (835 mg, 80%, viscous oil) was prepared from **2a** (740 mg, 2.90 mmol) by following the same procedure as described for **1b.** ^{1}H NMR: δ 0.93 (s, 9H, $C(CH_3)_3$) 1.25 (d, 6H, $(CH(CH_3)_2$), 1.43-2.62 (m, 7H, alicyclic protons), 2.36 (t, 1H, 9-H, J (allylic) = 2.1 Hz), 2.91 (septet, 1H, $(CH(CH_3)_2$), 3.60 (d, 1H, 7-H, J = 11.4 Hz), 3.80 (d, 1H, 7-H, J = 11.4 Hz), 4.57 (b, 1H, 2-H, $W_{1/2}$ ≈ 7-8 Hz), 7.20-7.60 (m, 4H, Ar-H); ^{13}C NMR: 21.64, 24.01, 25.15, 27.74, 31.67, 31.83, 33.45, 40.70, 51.75, 60.83, 70.68, 74.68, 80.96, 126.24, 126.74, 137.04, 142.02. Anal. Calcd. for $C_{22}H_{31}BrO$: C, 67.51%; H, 7.98%. Found: C, 67.55; H, 7.96%.

2a-Bromo-4e-*t*-butyl-1a-propargyloxy-1e-(4-methylphenyl)-cyclohexane (3b). Compound **3b** (875 mg, 87%, viscous oil) was prepared from **3a** (800 mg, 3.50 mmol) by following the same procedure as described for **1b.** ^{1}H NMR: δ 0.93 (s, 9H, $C(CH_3)_3$), 1.43-2.62 (m, 7H, alicyclic protons), 2.38 (s, 3H, Ar-CH_3), 2.43 (t, 1H, 9-H, J (allylic) = 2.1 Hz), 3.60 (d, 1H, 7-H, J = 11.4 Hz), 3.80 (d, 1H, 7-H, J = 11.4 Hz), 4.56 (b, 1H, 2-H, $W_{1/2}$ ≈ 7-8 Hz), 7.12-7.61 (m, 4H, Ar-H); ^{13}C NMR: 21.07, 21.65, 25.10, 27.74, 31.81, 31.84, 40.70, 51.73, 60.98, 70.74, 74.75, 81.15, 126.72, 125.63, 136.65, 139.09. Anal. Calcd. for $C_{20}H_{27}BrO$: C, 66.11%; H, 7.49%. Found: C, 66.15%; H, 7.52%.

2a-Bromo-4e-*t*-butyl-1a-propargyloxy-1e-(3-methylphenyl)-cyclohexane (4b). Compound **4b** (875 mg, 81%, viscous oil) was prepared from **4a** (800 mg, 3.50 mmol) by following the same procedure as described for **1b.** ^{1}H NMR: δ 0.94 (s, 9H, $C(CH_3)_3$), 1.50-2.62 (m, 7H, alicyclic protons), 2.36 (s, 3H, Ar-CH_3), 2.50 (t, 1H, 9-H, J (allylic) = 2.1 Hz), 3.55 (d, 1H, 7-H, J = 11.4 Hz), 3.77 (d, 1H, 7-H, J = 11.4 Hz), 4.55 (b, 2-H, $W_{1/2}$ ≈ 7-8 Hz), 7.10-7.40 (m, 4H, Ar-H); ^{13}C NMR: 21.50, 21.59, 25.06, 27.60, 31.78, 32.09, 40.60, 51.78, 60.60, 70.79, 74.76, 80.48, 123.74, 127.32, 128.01, 128.82, 137.62, 141.99. Anal. Calcd. for $C_{20}H_{27}BrO$: C, 66.11%; H, 7.49%. Found: C, 66.08%; H, 7.48%.

2a-Bromo-4e-*t*-butyl-1a-propargyloxy-1e-(2-methylphenyl)-cyclohexane (5b). Compound **5b** (1.02 g, 76%, viscous oil) was prepared from **5a** (850 mg, 3.70 mmol) by following the same procedure as described for **1b.** ^{1}H NMR: δ 0.91 (s, 9H, $C(CH_3)_3$), 1.53-2.56 (m, 7H, alicyclic protons), 2.59 (s, 3H, Ar-CH_3), 2.47 (t, 1H, 9-H, J (allylic) = 2.1 Hz), 3.57 (d, 1H, 7-H, J = 11.4 Hz), 3.80 (d, 1H, 7-H, J = 11.4 Hz), 5.07 (b, 1H, 2-H, $W_{1/2}$ ≈ 7-8 Hz), 7.00-7.42 (m, 4H, Ar-H); ^{13}C NMR: 21.05, 21.72, 26.82, 27.47, 31.35, 31.82, 40.55, 51.40, 60.20, 73.60, 75.28, 81.28, 125.09, 126.48, 127.75, 128.62, 136.40, 140.35. Anal. Calcd. for $C_{20}H_{27}BrO$: C, 66.11%; H, 7.49%. Found: C, 66.16%; H, 7.50%.

2a-Bromo-4e-*t*-butyl-1a-propargyloxy-1e-(1-naphthyl)-cyclohexane (6b). Compound **6b** (847 mg, 71%, viscous oil) was prepared from **6a** (800 mg, 3.0 mmol) by following the same procedure as described for **1b**. ^{1}H NMR: δ 0.96 (s, 9H, $C(CH_3)_3$), 1.44-2.40 (m, 7H, alicyclic protons), 2.31 (t, 1H, 9-H, J (allylic) = 2.1 Hz), 3.60 (d, 1H, 7-H, J = 11.4 Hz), 3.81 (d, 1H, 7-H, J = 11.4 Hz), 5.31 (b, 1H, 2-H, $W_{1/2}$ ≈ 7-8 Hz), 7.20-7.92 (m, 6H, Ar-H), 8.90 (s, 1H, peri-H); ^{13}C NMR: 21.92, 27.15, 27.54, 31.51, 31.98, 40.93, 52.05, 58.37, 73.64, 76.05, 82.42, 124.29, 125.31,126.23, 127.01, 128.16, 128.36, 129.64, 136.16, 136.43, 140.17. Anal. Calcd. for $C_{23}H_{27}BrO$: C, 69.17%; H, 6.81%. Found: C, 69.22%; H, 6.84%.

Typical procedure for the preparation of bicyclic octahydrobenzofuran derivatives (1c-6c).

5-*tert*-Butyl-octahydro-3-methylene-7a-phenylbenzofuran (1c). Tributyltin hydride (200 mg, 0.54 mmol) was added dropwise over 10 min to a stirred solution of the bromopropynyl ether **1b** (150 mg, 0.431 mmol) and AIBN (20 mg) in refluxing benzene (15 ml) under nitrogen atmosphere for 6 h. After

completion of the reaction (monitoring by TLC), the reaction mixture was allowed to reach room temperature and diluted with ether (50 ml). The organic part was separated, solvent removed under reduced pressure and the residue obtained was subjected to PTLC using silica gel as stationary phase and 2% ethyl acetate:petroleum ether (boiling range 60-80 ºC) as the mobile phase. The most intense band was extracted with chloroform using soxhlet to afford the cyclised product **1c**, (91 mg, 78%) as a viscous oil. ^{1}H NMR: δ 0.91(s, 9H, C(CH_3)$_3$), 1.17-2.39 (m, 7H, alicyclic protons), 2.88 (dd, 1H, 3a-H, J_{aa} = 10.5 Hz, J_{ae} = 6.6 Hz), 4.18 (d, 1H, 2-H, J = 13.5 Hz), 4.53 (d, 1H, 2-H, J = 13.5 Hz), 4.60 (s, 1H, 8-H), 4.81 (s, 1H, 8-H); 7.20-7.37 (m, 5H, Ar-H); ^{13}C NMR: 23.04, 27.48, 31.59, 32.39, 38.73, 46.36, 49.76, 68.02, 85.07, 103.05, 125.03, 126.46, 128.12, 146.73, 153.12. Anal. Calcd. for $C_{19}H_{26}O$: C, 84.39%; H, 9.69%. Found: C, 84.45%; H, 9.68%.

5-*tert*-Butyl-octahydro-7a-(4-isopropylphenyl)-3-methylenebenzofuran (2c). Compound **2c** (83 mg, 75%, viscous oil) was prepared from **2b** (138 mg, 0.355 mmol) by following the same procedure as described for **1c**. ^{1}H NMR: δ 0.90 (s, 9H, -C(CH_3)$_3$), 1.20-2.41 (m, 7H, alicyclic protons), 1.25 (d, 6H, CH(C*H*$_3$)$_2$), 2.87 (m, 1H, C*H*(CH_3)$_2$), 2.87 (dd, 1H, 3a-H, J_{aa} = 10.5 Hz, J_{ae} = 6.6 Hz), 4.18 (d, 1H, 2-H, J = 13.5 Hz), 4.51 (d, 1H, 2-H, J = 13.5 Hz), 4.61 (s, 1H, 8-H), 4.82 (s, 1H, 8-H), 7.14-7.27 (m, 4H, Ar-H); ^{13}C NMR: 23.08, 23.95, 27.49, 31.72, 32.39, 33.54, 38.83, 46.34, 49.62, 68.00, 84.96, 102.88, 124.90, 126.16, 143.97, 146.78, 153.47. Anal. Calcd. for $C_{22}H_{32}O$: C, 84.56%; H, 10.32%. Found: C, 84.60%; H, 10.30%.

5-*tert*-Butyl-octahydro-3-methylene-7a-4-tolylbenzofuran (3c). Compound **3c** (94 mg, 80%, viscous oil) was prepared from **3b** (150 mg, 0.414 mmol) by following the same procedure as described for **1c**. ^{1}H NMR: δ 0.90 (s, 9H, -C(CH_3)$_3$), 1.21-2.19 (m, 7H, alicyclic protons), 2.31 (s, 3H, Ar-CH_3), 2.87 (dd, 1H, 3a-H, J_{ae} = 6.6 Hz, J_{aa} = 10.5 Hz), 4.17 (d, 1H, 2-H, J = 13.5 Hz), 4.52 (d, 1H, 2-H, J = 13.5Hz), 4.61 (s, 1H, 8-H), 4.82 (s, 1H, 8-H), 7.10-7.26 (m, 4H, Ar-H); ^{13}C NMR: 20.99, 23.05, 31.58, 27.47, 32.37, 38.79, 46.34, 49.73, 67.97, 84.94, 102.99, 124.94, 128.87, 135.97, 143.73, 153.27. Anal. Calcd. for $C_{20}H_{28}O$: C, 84.45%; H, 9.92%. Found: C, 84.40%; H, 9.89%.

5-*tert*-Butyl-octahydro-3-methylene-7a-3-tolylbenzofuran (4c). Compound **4c** (79 mg, 72%, viscous oil) was prepared from **4b** (140 mg, 0.390 mmol) by following the same procedure as described for **1c**. ^{1}H NMR: δ 0.90(s, 9H, -C(CH_3)$_3$), 1.13-2.20 (m, 7H, alicyclic protons), 2.34 (s, 3H, Ar-CH_3), 2.88 (dd, 1H, 3a-H, J_{ae} = 6.6 Hz, J_{aa} = 10.5 Hz), 4.18 (d, 1H, 2-H, J = 13.5 Hz), 4.52 (d, 1H, 2-H, J = 13.5 Hz), 4.61 (s, 1H, 8-H), 4.82 (s, 1H, 8-H), 7.00-7.26 (m, 4H, Ar-H); ^{13}C NMR: 21.65, 23.04, 27.48, 31.63, 32.39, 38.77, 46.36, 49.74, 67.99, 85.08, 103.02, 122.02, 125.75, 127.26, 128.01, 137.60, 146.70, 153.21. Anal. Calcd. for $C_{20}H_{28}O$: C, 84.45%; H, 9.92%. Found: C, 84.41%; H, 9.93%.

5-*tert*-Butyl-octahydro-3-methylene-7a-2-tolylbenzofuran (5c). Compound **5c** (75 mg, 66%, viscous oil) was prepared from **5b** (145 mg, 0.400 mmol) by following the same procedure as described for **1c**. ^{1}H NMR: δ 0.91 (s, 9H, -C(CH_3)$_3$), 1.20-2.18 (m, 7H, alicyclic protons), 2.50 (s, 3H, Ar-CH_3), 3.14 (dd, 1H, 3a-H, J_{ae} = 6.6 Hz, J_{aa} = 10.5 Hz), 4.13 (d, 1H, 2-H, J = 13.5 Hz), 4.51 (d, 1H, 2-H, J = 13.5 Hz), 4.60 (s, 1H, 8-H), 4.83 (s, 1H, 8-H), 7.10-7.41 (m, 4H, Ar-H); ^{13}C NMR: 21.78, 22.99, 27.44, 31.86, 32.42, 35.65, 45.78, 48.48, 67.42, 85.83, 102.71, 125.76, 126.03, 126.76, 132.51, 134.47, 143.28, 153.41. Anal. Calcd. for $C_{20}H_{28}O$: C, 84.45%; H, 9.92%. Found: C, 84.39%; H, 9.95%.

5-*tert*-Butyl-octahydro-3-methylene-7a-(naphthalene-1-yl)-benzofuran (6c). Compound 6**c** (74 mg, 61%, viscous oil) was prepared from **6b** (153 mg, 0.380 mmol) by following the same procedure as described for **1c**. ^{1}H NMR: δ 0.96 (s, 9H, -C(CH_3)$_3$), 1.30-2.24 (m, 7H, alicyclic protons), 3.46 (dd, 1H, 3a-H, J_{ae} = 6.6 Hz, J_{aa} = 10.5 Hz), 4.57 (s, 2H, 2-H), 4.61 (s, 1H, 8-H), 4.74 (s, 1H, 8-H), 7.39-7.76 (m, 6H, Ar-H), 8.34 (s, peri-H); ^{13}C NMR: 23.17, 27.48, 32.02, 32.56, 36.19, 45.73, 49.44, 67.20, 86.03, 103.05, 123.80, 124.79, 125.05, 128.18, 129.35, 134.86, 140.89, 153.32. Anal. Calcd. for $C_{23}H_{28}O$: C, 86.20%; H, 8.81%. Found: C, 86.27%; H, 8.80%.

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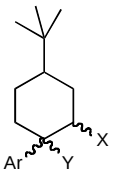
[11a] Of the two possible regiostructures (Markonikov's (**M**) & contra-Markonikov's (**CM**)), for bromopropynyl ethers **1b-6b,** the regiostructure was interpreted to be **M**. This was based on (i) the solvolytic reaction and (ii) comparison of the ^{1}H and ^{13}C NMR of ethers with that of the structurally related compounds.



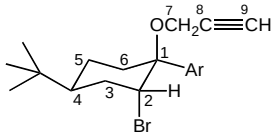
1b-6b

M (Markovnikov's adduct) X = Br ; Y = 

CM (contra-Markovnikov's adduct) Y = Br ; X = 

(iii) Solvolytic reaction: **1b-6b**, when allowed to stand in ethanol: water (4:1) for several hours and the aqueous solution tested for the presence of bromide, it shows negative result. It is to be noted that under this condition a tertiary bromide as in the case of the contra-Markonikov's adduct (**CM**) should have given a positive result for

the presence of bromide ion in the aqueous solution. Hence, it ruled out the contra-Markonikov's (**CM)** structure for **1b-6b** with a tertiary bromo function. Thus, the regiochemistry of bromo-propynyl ethers, **1b-6b** is assigned as 1-aryl-2-bromo-4-t-butyl-1-propargyloxycyclohexane. [b] The peak corresponding to CHBr of **1b-6b** in ^{1}H NMR appears as a broad signal with $W_{1/2}$ (width at half height) ≈ 7-8 Hz, which is characteristic of the equatorial hydrogen in cyclohexyl systems. Thus, the bromo function is axially oriented. With regard to the stereochemistry at tertiary carbon of **1b-6b,** it has been reported (Garbisch, Jr., E. W.; Patterson, B. *J. Am. Chem. Soc*. **1963**, *85*, 3228) that phenyl group has a substantially greater preference for the equatorial position in cyclohexane than do the methyl, ethyl and isopropyl groups. Also, this is supported by the fact in analogous compounds the phenyl group takes over an equatorial orientation (Huitric, A. C.; Carr, J. B. *J. Org. Chem.* **1961**, *26*, 2648; Crotti, P.; Chini, M.; Uccello-Barretta, G.; Macchia, F. *J. Org. Chem.* **1989**, *54*, 4525. Hence, it is concluded that the **1b-6b** are 1e-aryl-2a-bromo-4e-t-butyl-1a-propargyloxy-cyclohexane.



1b-6b

The 2D NMR data obtained from H,H-COSY, C,H-COSY, HMBC and various DEPT experiments were consistent with the above structural assignment.

[12] In ^{1}H NMR spectra of **1b-6b** and **1c-6c**, the allylic coupling could not be observed in all occasions. But signals due to protons experiencing such coupling shows fine splitting and broadening.

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