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Cyclopropane-shift type reaction of diaryl(2-halogenocyclopropyl)methanols promoted by Lewis acids

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Abstract

Novel cyclopropane-shift type reaction of diaryl(2-halogenocyclopropyl)methanols **2b** and **7** proceeded by using $BF_3{\cdot}OEt_2$ and $TiCl_4$, respectively. Utilizing these reactions, 1-aryl-3-chloro-1,2-methanoindans **5** and **9**, 1-aryl-3-methylnaphthalenes **6**, and 1,2-methano-1-arylindens **10** were constructed.

Utilization of cyclopropylmethyrinium cationic intermediates has attained versatile synthetic transformations, for example, for the precursor of homoallylic compounds and cyclobutanes.[1] Concerning readily available *gem*-dihalogenocyclopropanes, the Nazarov-type annulation[1d] and benzannulations have been exploited.[1e,f] The driving force of these transformations is derived from the variation from the unstable cyclopropanes into thermodynamically stable products. Therefore, the reconstruction of cyclopropanes is quite rare and to the best of our knowledge there has only been a single study on cationic cyclopropane-shift reactions of humulene derivatives.[2] Along with our continuing interest in the synthetic utilization of *gem*-dihalocyclopropanes from many sided cationic,[1e] radical[3] and anionic[4] type approaches, we report here a novel, unique Lewis acid-promoted cyclopropane-shift reaction using monohalogenocyclopropanes **2b** to construct 1-aryl-3-halogeno-1,2-methanoindans **5**, which are the precursors of 1-aryl-3-methylnaphthalenes **6**.

Other cyclopropane-shift reactions of 3-methyl monochloro substrates **7a** and **7b** were performed to give 1-aryl-3-chloro-1,2-methanoindans **9**, which are the precursors of 1,2-methano-1-arylindens **10**.

Monohalogeno substrates [(1*R**,2*R**)-**2a** and its diastereomer (1*R**,2*S**)-**2b**] were prepared by the reduction of esters **1** using *t*-BuMgCl/cat. $CoCl_2$(dppe),[4] followed by addition of 2LiPh-(*p*-R)

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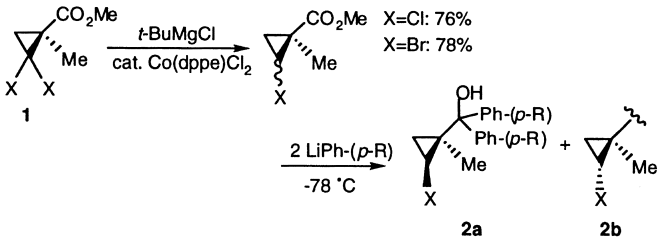
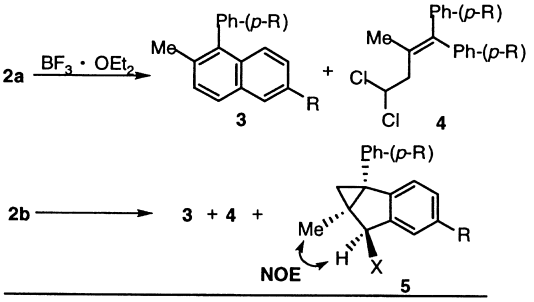
(Scheme 1).[5] Diastereomers **2a** and **2b** were easily separated by column chromatography. Precursors **2b** were prepared with moderate to good selectivities, particularly in the cases of bromo analogs **2b-5** to **-8**.



X	R	Yield / %			X	R	Yield / %		
Cl	H	**2a-1** 35	**2b-1** 63		Br	H	**2a-5** 12	**2b-5** 65	
	Me	**2a-2** 32	**2b-2** 62			Me	**2a-6** 13	**2b-6** 69	
	OMe	**2a-3** 29	**2b-3** 61			OMe	**2a-7** 18	**2b-7** 65	
	Cl	**2a-4** 33	**2b-4** 61			Cl	**2a-8** 17	**2b-8** 66	

Scheme 1.

Benzannulation of chloro compounds **2a-1** to **-4** using $BF_3{\cdot}OEt_2$ proceeded through *normal mode* to give the corresponding 1-aryl-2-methylnaphthalenes **3** along with open chain compounds **4** (Scheme 2). In clear contrast, the reaction of **2b-1** to **-3** resulted in the main formation of

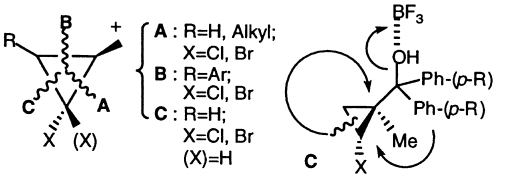


Substrate	X	R	Temp. / °C	Yield / % 3	4	5
2a-1	Cl	H	rt	50	0	0
			50	26	49	0
2a-2	Cl	Me	rt	56	46	0
			50	50	37	0
2a-3	Cl	OMe	rt	55	40	0
2a-4	Cl	Cl	rt	40	41	0
2b-1	Cl	H	rt	30	38	0
			50	14	0	71 (**5-1**)
2b-2	Cl	Me	rt	14	46	0
			50	15	0	77 (**5-2**)
2b-3	Cl	OMe	50	28	0	69 (**5-3**)
2b-4	Cl	Cl	50	59	0	0
2b-5	Br	H	50	trace	0	90 (**5-5**)
2b-6	Br	Me	50	trace	0	84 (**5-6**)
2b-7[b)]	Br	OMe	50	trace	0	89 (**5-7**)

a) Carried out in 1,2-dichloroethane for 0.5 h. Molar ratio of **2** : $BF_3{\cdot}OE_2$ = 1 : 1. b) High dilution (0.01 mol/L)

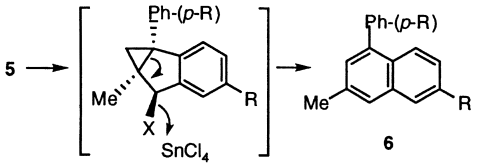
Scheme 2.

tricyclic compounds **5-1** to **-3** at 50°C, i.e. the cyclopropane-shift reaction occurred except for *p*-Cl analog **2b-4**.[6] Reactions of bromo substrates **2b-5** to **-8** proceeded in higher yields compared with chloro substrates **2b-1** to **-3**. The structure of **5-1** was determined by ^{1}H, ^{13}C NMR, IR, GC–MS and NOE experiments.[7] Despite a number of acid-catalyzed ring openings of the *gem*-dihalogenocyclopropylmethylinium cation, this is the first example of bond C fission across the cation (Scheme 3).



Scheme 3.

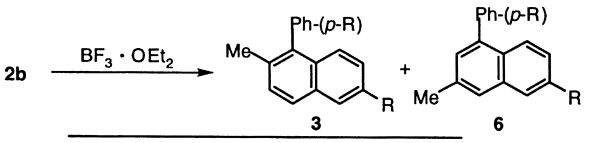
Treatment of tricyclic compounds **5-1** to **-3** (X = Cl) with a strong Lewis acid, $SnCl_4$, furnished 1-aryl-3-methylnaphthalenes **6-1** to **-3**,[8] which is regarded as the cyclopropane-shift type benzannulation (Scheme 4). $BF_3{\cdot}OEt_2$ did not promote the benzannulation of **5-1** to **-3** (X = Cl); in clear contrast, **5-5** to **-7** (X = Br) underwent smooth cyclopropane-shift type benzannulation at 80°C. Thus, isomeric naphthalenes were alternatively prepared from diastereomers **2a** and **2b**. Encouraged by the results, direct cyclopropane-shift type benzannulation of **2b-5** to **-7** (X = Br) were performed in excellent yields (Scheme 5).



Substrate	X	R	Conditions	Yield / %
5-1	Cl	H	$SnCl_4$ 80 °C	78 (**6-1**)
5-2		Me		80 (**6-2**)
5-3		OMe		50 (**6-3**)
5-5	Br	H	$BF_3{\cdot}OEt_2$ 80 °C	92 (**6-1**)
5-6		Me		91 (**6-2**)
5-7		OMe		87 (**6-3**)

Scheme 4.

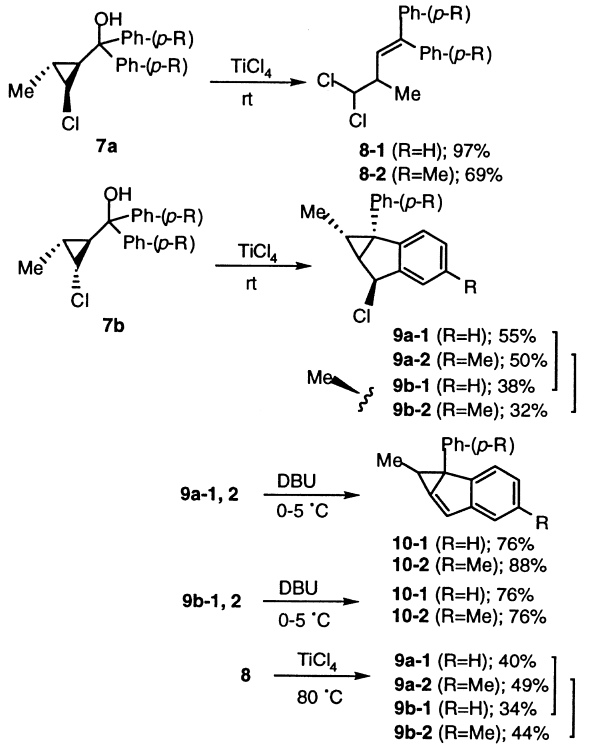
On the other hand, $TiCl_4$-promoted reaction of 3-methyl monochloro substrates **7a** and diastereomers **7b** showed another different mode. Compounds **7a** were exclusively transformed into open chain product **8**, whilst compounds **7b** gave exclusively cyclopropane-shift tricyclic product **9** as diastereomeric mixtures in good yields (Scheme 6).[9] Several attempts to transform **9** into naphthalenes failed (no reaction); however, treatment with DBU was found to give uniquely fused cyclopropanes **10** in good yields. The structure of **10-1** was determined by ^{1}H NMR and GC–MS measurements.[10] It should also be noted that open chain product **8** was converted to cyclopropane-shift tricyclic product **9** using $TiCl_4$ at 80°C. Eventually, both substrates **7a** and **7b** were converted into **9** in good yields.



Substrate	X	R	Yield / % (3 : 6)
2b-5	Br	H	97 (1 : 20)
2b-6		Me	88 (1 : 32)
2b-7[b)]		OMe	92 (1 : 40)

a) Carried out in 1,2-dichloroethane at 80 °C for 10 h. Molar ratio of **2b** : $BF_3{\cdot}OE_2$ = 1 : 2. b) High dilution (0.01 mol/L)

Scheme 5.



Scheme 6.

The mechanistic reasoning for the present cyclopropane-shift reaction would be rationally supported by the calculation.[11]

Acknowledgements

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5. Compound **2a-1**: colorless crystals; mp 115.5–117.0°C; ^{1}H NMR (400 MHz) $\delta = 0.89$ (1H, dd, $J_{gem} = 6.1$ Hz, $J = 7.8$ Hz), 0.92 (3H, s), 1.95 (1H, dd, $J_{gem} = 6.1$ Hz, $J = 4.6$ Hz), 2.82 (1H, s, OH), 3.40 (1H, dd, $J = 7.8$ Hz, 4.6 Hz), 7.22–7.42 (8H, m), 7.57–7.62 (2H, m); ν_{max} (KBr)/cm^{-1} 3536, 3084, 1447, 972, 957, 762, 702. Compound **2b-1**: colorless crystals; mp 79.5–80.5°C; ^{1}H NMR (400 MHz) $\delta = 0.63$ (1H, dd, $J_{gem} = 6.1$ Hz, $J = 4.4$ Hz), 1.23 (3H, s), 1.49 (1H, dd, $J_{gem} = 6.1$ Hz, $J = 7.8$ Hz), 2.06 (1H, s, OH), 3.52 (1H, dd, $J = 7.8$ Hz, 4.4 Hz), 7.26–7.41 (10H, m); ν_{max} (KBr)/cm^{-1} 3569, 3084, 1445, 949, 752, 700, 679. Compound **2b-5**: colorless crystals; mp 60.0–61.0°C; ^{1}H NMR (400 MHz) $\delta = 0.70$ (1H, dd, $J = 4.6$ Hz, $J_{gem} = 6.1$ Hz), 1.28 (3H, s), 1.58 (1H, dd, $J_{gem} = 6.1$ Hz, $J = 8.3$ Hz), 2.05 (1H, s, OH), 3.48 (1H, dd, $J = 4.6$ Hz, 8.3 Hz), 7.25–7.48 (10H, m); ν_{max} (KBr)/cm^{-1} 3578, 3057, 1445, 1005, 770, 702, 644.
6. Typical procedure is as follows. $BF_3{\cdot}OEt_2$ (0.046 ml, 0.37 mmol) was added to a stirred solution of **2a-1** (100 mg, 0.37 mmol) in 1,2-dichloroethane (0.5 ml) at 50°C under Ar atmosphere, and the mixture was stirred at the same temp. for 30 min. Aqueous satd $NaHCO_3$ solution was added to the mixture, which was extracted with ether. The organic phase was washed with water, brine, dried (Na_2SO_4) and concentrated. The obtained crude oil was subjected to flash column chromatography on SiO_2 using hexane to give the products **3-1** (R = H; 11 mg, 14%) and **5-1** (R = H; 66 mg, 71%).
7. Compound **5-1**: colorless crystals; mp 35.5–36.5°C; ^{1}H NMR (400 MHz) $\delta = 1.52$ (3H, s), 3.55 (1H, d, $J_{gem} = 10.7$ Hz), 3.77 (1H, d, $J_{gem} = 10.7$ Hz), 6.49 (1H, s), 7.11–7.62 (9H, m); ^{13}C NMR (100 MHz) $\delta = 20.21$, 52.02, 52.85, 121.06, 122.44, 125.73, 127.66, 127.95, 128.07, 129.19, 133.93, 135.23, 139.00, 142.48, 150.04; ν_{max} (KBr)/cm^{-1} 3061, 1445, 833, 781, 756, 698. Relative stereochemistry was determined by NOE measurement between 1-H and 2-CH_3. GC–MS (70 eV) *m*/*e* 254 (M^+). Compound **5-5**: colorless crystals; mp 42.5–43.5°C; ^{1}H NMR (400 MHz) $\delta = 1.54$ (3H, s), 3.44 (1H, d, $J_{gem} = 9.8$ Hz), 3.68 (1H, d, $J_{gem} = 9.8$ Hz), 6.47 (1H, s), 7.12–7.61 (9H, m); ^{13}C NMR (100 MHz) $\delta = 21.24$, 41.25, 52.06, 121.03, 122.19, 125.67, 127.51, 127.61, 127.90, 128.54, 135.09, 139.63, 142.32, 143.37, 149.98; ν_{max} (neat)/cm^{-1} 3061, 1445, 1238, 947, 779, 758, 698.
8. Compound **6-1** (R = H): colorless oil; ^{1}H NMR (400 MHz) $\delta = 2.72$ (3H, s), 7.28-7.54 (9H, m), 7.91 (1H, d, $J = 8.5$ Hz), 8.04 (1H, d, $J = 8.1$ Hz); ν_{max} (neat)/cm^{-1} 1443, 980, 910, 833, 764, 702.
9. Typical procedure: $TiCl_4$ (1.0 M solution in CH_2Cl_2, 1.00 ml, 1.00 mmol) was added to a stirred solution of **7b-1** (273 mg, 1.00 mmol) in CH_2Cl_2 (2.0 ml) at 0–5°C under Ar atmosphere, and the mixture was stirred at the same temp. for 1 h. After usual work up and flash column chromatography on SiO_2 using hexane, the products **9a-1** (R = H; 139 mg, 55%) and **9b-1** (R = H; 96 mg, 38%) were obtained. Reactions using $BF_3{\cdot}OEt_2$ and $SnCl_4$ were a little sluggish. Compound **9a-1**: brown oil; ^{1}H NMR (400 MHz) $\delta = 1.23$ (3H, d, $J = 6.6$ Hz), 4.01 (1H, dd, $J = 1.9$ Hz, 5.1 Hz), 4.63 (1H, m), 6.65 (1H, d, $J = 1.9$ Hz), 7.15–7.65 (9H, m); ν_{max} (neat)/cm^{-1} 3063, 1447, 867, 774, 747, 700. Compound **9a-2**: brown crystals; mp 39.5–40.5°C; ^{1}H NMR (400 MHz) $\delta = 1.54$ (3H, d, $J = 6.6$ Hz), 3.92 (1H, dd, $J = 2.2$ Hz, 4.2 Hz), 4.57 (1H, m), 6.49 (1H, d, $J = 2.2$ Hz), 7.22–7.75 (9H, m); ν_{max} (neat)/cm^{-1} 3063, 1443, 810, 774, 743, 696. Relative stereochemistries of **9a-1** and **9b-1** were determined by NOE measurements. The reaction of aryl(*gem*-dihalocyclopropyl)-methanols without the 1-Me group gave substantial amounts of the open chain product.[1e] This fact coincides with the reaction of **9a**.
10. Compound **10-1**: yellow oil; ^{1}H NMR (400 MHz) $\delta = 2.22$ (3H, d, $J = 7.3$ Hz), 6.73 (1H, m), 6.91 (1H, s), 7.20-7.70 (9H, m); ν_{max} (neat)/cm^{-1} 3061, 3027, 1445, 748, 737, 700. GC–MS (70 eV) *m*/*e* 218 (M^+). Halton, B.; Banwell, M. G. In *The Chemistry of the Cyclopropyl Group*; Patai, S.; Rappoport, Z., Eds.; Wiley: London, 1987; p. 1223.
11. We propose two mechanistic speculations. One is that bond C not of **2a-1** but of **2b-1** is located in a transannular position toward the leaving OH group and bond C of **2b-1** is longer than bonds A and B; therefore, this bond C is

weakened and so inclined to cleave. The other is that cationic intermediate **11** after the cyclopropane-shift is significantly stable compared with *normal* open chain intermediate **12**. These are supported by calculations [SPARTAN version 5.0 (Wavefunction, Inc., Irvine, CA), semiempirical, AM1].