Reaction of Phenyl-Substituted Allyllithiums with *tert*-Alkyl Bromides. Remarkable Difference in the Alkylation Regiochemistry between a Polar Process and the One Involving Single-Electron Transfer

Jiro Tanaka, Masatomo Nojima,* and Shigekazu Kusabayashi

Contribution from the Department of Applied Chemistry, Faculty of Engineering, Osaka University, Suita, Osaka 565, Japan. *Received September 2, 1986*

Abstract: The reaction of phenyl-substituted allyllithiums **1a–h** with *tert*-alkyl bromides was investigated systematically. The alkylation regiochemistry was influenced in a complicated fashion by various factors including substituent effects, both steric and electronic, solvents, and the presence of strongly coordinating additives, tetramethylethylenediamine and hexamethylphosphoramide. On the basis of the cyclizable probe experiments, the observed regiochemistry was interpreted as follows. (a) The reaction proceeds by two alternative pathways, a polar one and single electron transfer (SET), the extent of each path being influenced by the variable factors and (b) a polar pathway favors coupling at the phenyl-substituted site (C-1), while in the case of SET the C–C bond formation occurs predominantly at the site far from the phenyl substituent (C-3).

Allylic organometallic species have two reaction sites, and, therefore, their reaction with alkyl halides often gives a mixture of two alkylation products. The product composition is a function of various factors[1] including substituent effects, both electronic[2] and steric,[3] electrophiles,[4] the nature of the cation,[5] solvents,[6] and the presence of strongly co-ordinating additives, e.g. tetramethylethylenediamine (TMEDA), hexamethylphosphoramide (HMPA), and crown ether.[6] In principle, the reaction could proceed by two or more alternative pathways, different reaction pathways leading to different product compositions.[7,8]

In the light of these results, we systematically investigated the reactions of phenyl-substituted allyllithiums **1a–h** with *tert*-alkyl bromides and discovered that two reaction pathways, a polar one and a single-electron transfer (SET), participate in these reactions, the extent of each path being a marked function of variable factors. Moreover, a polar pathway favored attack at the phenyl-substituted site (C-1), whereas coupling at the alternative site (C-3) occurred predominantly in the case of SET.

Results and Discussion

Synthesis and Electronic Spectra of Phenyl-Substituted Allyllithiums. Phenyl-substituted allyllithiums **1a–h** were prepared by treating the corresponding hydrocarbon precursors with BuLi in ether or tetrahydrofuran (THF) in the presence or absence of additives, TMEDA and HMPA. Workup with D_2O gave the corresponding monodeuteriated products, **4-*d*$_1$** and **5-*d*$_1$** (around 70% yield) (eq 1–3).

Table I. Electronic Spectra of Phenyl-Substituted Allyllithiums[a]

Li compd	solvent	additive[b]	absorptn λ_{max}, nm
1a	Et_2O		387
1a	Et_2O	TMEDA	390
1a	Et_2O	HMPA	423
1a	THF		400 (395[c])
1a	THF	TMEDA	395
1a	THF	HMPA	432 (430[c])
1d	Et_2O		395
1d	Et_2O	TMEDA	395
1d	Et_2O	HMPA	436
1d	THF		418
1d	THF	TMEDA	418
1e	Et_2O		331
1e	Et_2O	TMEDA	338
1e	Et_2O	HMPA	428
1e	THF		398
1e	THF	TMEDA	394
1f	Et_2O		423
1f	Et_2O	TMEDA	422
1f	Et_2O	HMPA	488
1f	THF		486
1f	THF	TMEDA	484
1f	THF	HMPA	490
1g	THF/hexane[f]		563, 510 (510[d])
1g	THF		570 (560[d,e])
1h	pentane		338
1h	Et_2O		362
1h	THF		388

[a] The lithium compound **1** was prepared by treating **4** with 0.8 equiv of BuLi at 20 °C unless otherwise noted. The electronic spectra were measured at 20 °C. [b] TMEDA: the reaction in the presence of 1.2 equiv of TMEDA. HMPA: the reaction in the presence of 10 equiv of HMPA at −45 °C. [c] Reference 10a. [d] Fox, M. A.; Voynick, T. A. *Tetrahedron Lett.* **1980**, *21*, 3943. [e] Burley, J. W.; Young, R. N. *J. Chem. Soc. C* **1971**, 3780. [f] 1:1 v/v.

To obtain information for the ion pair states of these lithium compounds,[9] the electronic spectra were measured under various conditions. As the data in Table I demonstrate, intermediates **1a–e** exist in ether as contact ion pairs as evidenced by $\lambda_{max} <$ 395 nm while solvent-separated ion pairs are important in the presence of HMPA as evidenced by $\lambda_{max} >$ 423 nm. Absorption falling in between these limits, as frequently observed in THF, may be attributed to either loosened ion pairs or mixtures of contact and solvent-separted ion pairs. This conclusion is consistent with that from the ^1H and ^{13}H NMR spectroscopies.[10]

(1) (a) Guthrie, R. D. *Comprehensive Carbanion Chemistry*; Buncel, E., Durst, T., Eds.; Elsevier: Amsterdam, 1980; Part A, Chapter 5. (b) Magid, R. M. *Tetrahedron* **1980**, *36*, 1901. (c) Bates, R. B.; Ogle, C. A. *Carbanion Chemistry*; Springer-Verlag: Berlin, 1983. (d) Biellmann, J. F.; Ducep, J. *Organic Reactions*; Wiley: 1982; Vol. 27, p 1.

(2) Bushby, R. J.; Ferber, G. J. *J. Chem. Soc., Perkin Trans. 2*, **1976**, 1688.

(3) Evans, D. A.; Andrews, G. C. *Acc. Chem. Res.* **1974**, *7*, 147.

(4) (a) Murphy, W. S.; Wattanasin, S.; *Tetrahedron Lett.* **1979**, 1827. (b) Seyferth, D.; Simon, R. M.; Sepelak, D. J.; Klein, H. A. *J. Am. Chem. Soc.* **1983**, *105*, 4634. (c) Hayashi, T.; Hori, I.; Oishi, T. *Ibid.* **1983**, *105*, 2909.

(5) (a) Schlosser, M. *Angew. Chem., Int. Ed. Engl.* **1974**, *13*, 701. (b) Beak, P.; Hunter, J. E.; Jun, Y. M. *J. Am. Chem. Soc.* **1983**, *103*, 6350. (d) Hoppe, D.; Krämer, T. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 160.

(6) (a) Atlani, P. M.; Biellmann, J. F.; Dube, S.; Vicens, J. J. *Tetrahedron Lett.* **1974**, 2665. (b) Binns, M. R.; Haynes, R. K. *J. Org. Chem.* **1981**, *46*, 3790. (c) Hua, D. H.; Sinai-Zingde, G.; Venkataraman, S. *J. Am. Chem. Soc.* **1985**, *107*, 4088.

(7) Kornblum, N. *Angew. Chem., Int. Ed. Engl.* **1975**, *14*, 734.

(8) (a) A part of this work was previously reported. Tanaka, J.; Nojima, M.; Kusabayashi, S. *J. Chem. Soc., Chem. Commun.* **1986**, 242. (b) Muraoka, M.; Nojima, M.; Kusabayashi, S.; Nagase, s. *J. Chem. Soc., Perkin Trans. 2*, **1986**, 761. (c) Hirabe, T.; Takagi, M.; Muraoka, K.; Nojima, M.; Kusabayashi, S. *J. Org. Chem.* **1985**, *50*, 1797. (d) Takagi, M.; Nojima, M.; Kusabayashi, S. *J. Am. Chem. Soc.* **1983**, *105*, 4676. (e) Takagi, M.; Nojima, M.; Kusabayashi, S. *Ibid.* **1982**, *104*, 1636.

(9) Buncel, E.; Menon, B. *Comprehensive Carbanion Chemistry*; Buncel, E., Durst, T., Eds., Elsevier: Amsterdam, 1980; Part A, Chapter 3.

0002-7863/87/1509-3391$01.50/0

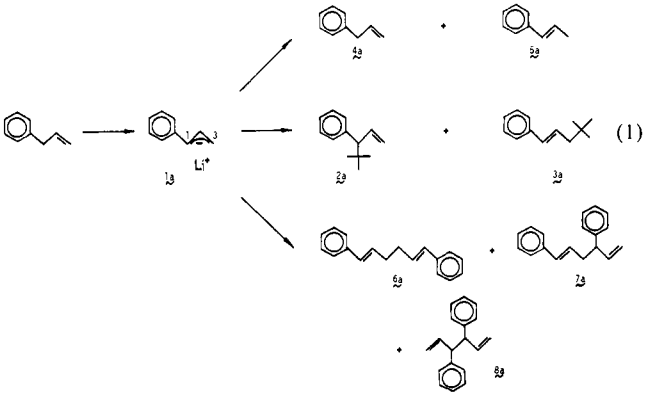
Table II. Reaction of Phenyl-Substituted Allyllithiums with *tert*-Butyl Bromide[a]

			products					
			alkylation		reduction		dimerization	
Li compd	solvent	additive	% yield	**2:3**	% yield	**4:5**	% yield	**6:7:8**
1a	Et_2O		55	28:72	9	81:19	11	25:57:18
1a	Et_2O	TMEDA	47	39:61	12	69:31	8	33:50:17
1a	Et_2O	HMPA	52	73:27	8	44:56		
1a	THF	TMEDA	48	82:18	8	52:48		
1a	THF	HMPA	50	77:23	5	42:58		
1b	Et_2O	TMEDA[c]	46	26:74			15	18:63:19
1b	Et_2O	HMPA	51	79:21				
1c	Et_2O	TMEDA	48	82:18	4	49:51		
1c	Et_2O	HMPA	43	82:18	10	51:49		
1d	Et_2O	TMEDA[c]	47	40:60	23	61:39	21	55:41:4
1d	Et_2O	HMPA	43	100:0	47	49:51		
1e	Et_2O	TMEDA[c]	36	46:54	15	89:11	17	9:69:22
1e	Et_2O	HMPA	54	81:19				
1e	THF	TMEDA[c]	59	79:21				
1f	Et_2O		32	40:60	53	50:50	10	78:22:0
1f	Et_2O	TMEDA	10	50:50	50	45:55	10	81:19:0
1f	Et_2O	HMPA	20	50:50	50	40:60	6	80:20:0
1f	THF	TMEDA	16	50:50	48	45:55	8	80:20:0
1f	THF	HMPA	21	47:53	63	40:60	14	100:0:0
1g	THF	TMEDA	96					
1g	THF	HMPA	74					
1h[d]	pentane		32	67:33	61	0:100		
1h[d]	Et_2O		22	73:27	26	0:100		
1h[d]	THF		19	82:18	75	0:100		

[a] The reaction with 5 equiv of *tert*-butyl bromide at 20 °C for 1 h unless otherwise noted. [b] TMEDA: The lithium compound was prepared by treating the hydrocarbon precursor **4** with 1.2 equiv of BuLi in the presence of 1.2 equiv of TMEDA unless otherwise noted. HMPA: The lithium compound was prepared by treating the hydrocarbon precursor **4** with 1.2 equiv of BuLi in the presence of 10 equiv of HMPA at −45 °C. [c] The lithium compound was prepared by treating the hydrocarbon precursor with 2 equiv of BuLi in the presence of 2 equiv of TMEDA. [d] The reaction with *tert*-butyl bromide was undertaken at 20 °C for 2.5 h.

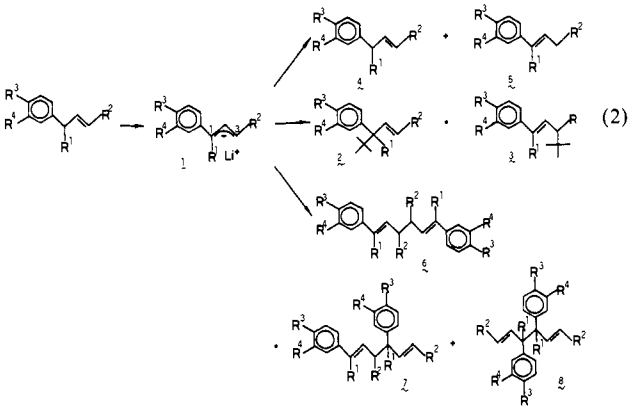
1,1-Diphenylallyllithium (**1f**) forms a contact ion pair in ether in the presence or absence of TMEDA but a solvent-separated ion pair upon addition of HMPA. The well-delocalized 1,3-diphenylallyllithium (**1g**) is known to exist as a solvent-separated ion pair in THF.[10a] The data in Table I would demonstrate that even in THF/hexane **1g** exists as an equilibrium mixture of contact and solvent-separated ion pairs.

Reaction with *tert*-Alkyl Bromides. The reaction of 1-phenylallyllithium (**1a**) with *tert*-butyl bromide in ether in the presence of HMPA gave a mixture of two alkylation products, **2a** and **3a** (about 50%), the **2a**/**3a** ratio being 7:3 (eq 1 and Table II). When the reaction of **1a** was undertaken in ether in the



(1)

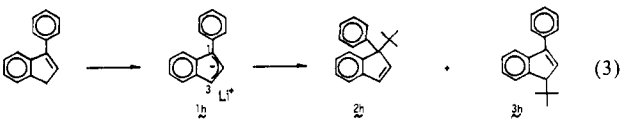
presence or absence of TMEDA, however, dimers **6a–8a** were obtained in around 10% yield together with alkylation products, **2a** and **3a** (about 50%). Moreover, the C-3 attack product **3a** was the major isomer; the **2a**/**3a** ratio being around 3:7. For the reaction of *p*-anisylallyllithium (**1b**), 1-phenyl-1-methylallyllithium (**1d**), and 1-phenyl-3-methylallyllithium (**1e**) also, the same dependence of the product composition on the polarity of the solvent system was observed (eq 2 and Table II).



(2)

compound	R^1	R^2	R^3	R^4
b	H	H	OMe	H
c	H	H	H	Cl
d	Me	H	H	H
e	H	Me	H	H
f	Ph	H	H	H
g	H	Ph	H	H

In the case of the relatively more stable carbanion **1c**,**h**, however, the C-1 attack product **2c**,**h** was the major isomer irrespective of the identity of the solvent systems (the **2**/**3** ratio is ca. 4:1). Another characteristic was the absence of the corresponding dimers **6–8** (eq 2 and 3 and Table II).



(3)

(10) (a) Ahlbrecht, H.; Zimmermann, K.; Boche, G.; Decher, G. *J. Organomet. Chem.* **1984**, *262*, 1. (b) Sandel, V. R.; McKinley, S. V.; Freedman, H. H. *J. Am. Chem. Soc.* **1968**, *90*, 495. (c) Cox, R. H.; Terry, H. W., Jr.; Harrison, L. W. *Ibid.* **1971**, *93*, 3297. (d) Heiszwolf, G. J.; Kloosterziel, H. *Recl. Trav. Chim. Pays-Bas* **1967**, *86*, 1345. (e) Van Dongen, J. P. C. M.; Van Dijkman, H. W. D.; De Bie, M. J. A. *Ibid.* **1974**, *93*, 29.

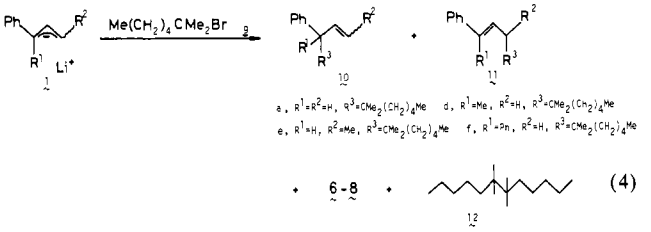
Table III. Reaction of Phenyl-Substituted Allyllithiums with 2-Bromo-2-methylheptane in Et_2O[a]

Li compd	additive[b]	products: alkyltn % yield	alkyltn 10:11	dimerztn[d] % yield	others (% yield)
1a	TMEDA	43	31:69	15	**12** (7)
1a	HMPA	35	90:10		
1d	TMEDA[c]	40	51:49	16	**12** (25)
1d	HMPA	58	90:10		
1e	TMEDA[c]	44	56:44	11	**12** (19)
1e	HMPA	60	90:10		
1f	TMEDA	12	50:50	15	**4** + **5** (68) **12** (14)
1f	HMPA	17	50:50	10	**4** + **5** (71) **12** (8)

[a] The reaction with 2.5 equiv of 2-bromo-2-methylheptane (**9**) at 20 °C for 1 h. [b,c] See the footnotes in Table II. [d] The composition was not determined.

A remarkably different trend was observed in the reaction of 1,1-diphenylallyllithium (**1f**) (eq 2 and Table II). Under all the conditions an equimolar mixture of two alkylation products, **2f** and **3f**, was obtained in a low yield of around 10%, together with dimers, **6f** and **7f**.

The reaction of lithium compounds **1a,d–f** with relatively bulkier 2-bromo-2-methylheptane (**9**) was also undertaken in ether in the presence of TMEDA or HMPA (eq 4 and Table III). In the



(4)

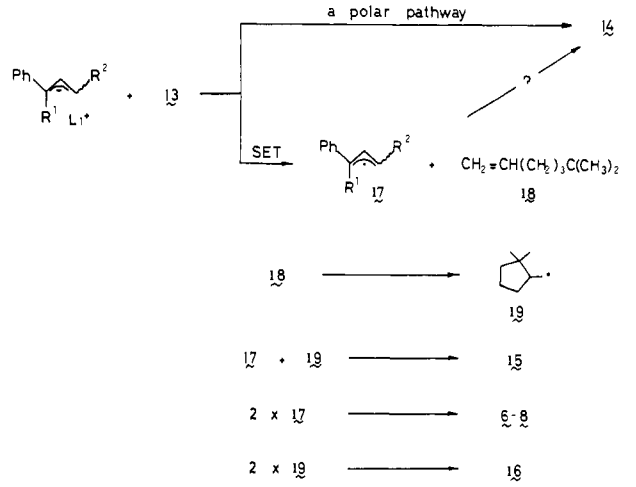
case of **1a,d,e** the composition of alkylation products, **10** and **11**, was a marked function of the identity of the additive. The reaction in the presence of HMPA favored the formation of the C-1 attack product **10**, whereas a roughly 1:1 mixture of **10** and **11** was obtained in the reaction in the presence of TMEDA. Under the latter conditions, dimers **6–8** and 6,6,7,7-tetramethyldodecane (**12**) were also produced in considerable amounts. These trends were exactly the same as those observed in the reaction with *tert*-butyl bromide.

In the case of 1,1-diphenylallyllithium (**1f**), however, the nature of the additive did not exert a meaningful influence on the product composition. From the reaction in both ether/TMEDA and ether/HMPA, an equimolar mixture of **10f** and **11f** was obtained in a poor yield of around 15%. The byproducts were dimers **6f** and **7f** and 6,6,7,7-tetramethyldodecane (**12**).

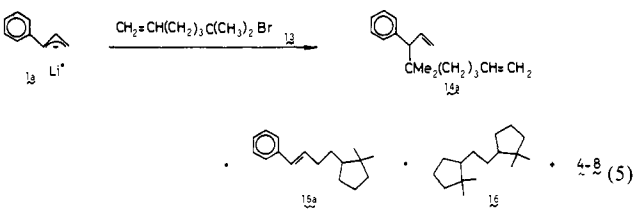
Reaction with 6-Bromo-6-methyl-1-heptane, a Tertiary Cyclizable Probe. Thus, a systematic survey on the reaction of lithium compounds **1a–h** with *tert*-alkyl bromides revealed that the composition of alkylation products is a marked function of various factors including the structure of the carbanions, solvents, and additives. In addition, it is noted that there exists an apparent correlation between dimer formation and alkylation regiochemistry: The formation of dimers **6–8** is observed characteristically in the reaction in which the production of the C-3 attack product **3** predominates. From the reaction, in which the formation of dimers **6–8** is not observed, however, the C-1 attack product **2** is obtained predominantly.

Since dimers **6–8** are most likely to be produced by dimerization of phenyl-substituted allyl radicals, we next undertook the reaction of the lithium compounds **1a–h** with 6-bromo-6-methyl-1-heptene (**13**), a tertiary cyclizable probe (Table IV).[11] When the reaction

Scheme I



of **1a** with **13** was performed in ether in the presence or absence of TMEDA, a mixture of two alkylation products, **14a** (a straight chain product formed by coupling at the more hindered C-1) and **15a** (a cyclized product formed by coupling at C-3), was obtained in around 50% yield, **14a**/**15a** ratio being 17:83. Dimers **6a–8a** and 1,2-bis(2,2-dimethylcyclopentyl)ethane (**16**) were also produced in yields of 10% and 8%, respectively. The reaction of **1a** in ether in the presence of HMPA, however, gave mainly a straight chain product **14a**, as did the reaction in THF in the presence of TMEDA or HMPA (eq 5). Another characteristic of this reaction was the absence of **6a–8a** and **16**. In the case of lithium compounds **1d,e** also the same trends for the effects of solvent systems on the product compositions were observed.



(5)

It is surprising that of the two possible cyclized products, only one isomer **15** is isolated. This would imply that (a) a SET process is certainly involved in the reaction of lithium compounds **1a,d,e** with *tert*-alkyl bromides and (b) 2,2-dimethylcyclopentylmethyl radical (**19**), formed from bromide **13** by SET followed by cyclization, couples with phenyl-substituted allyl radical **17** at the less hindered C-3 exclusively (Scheme I).[12,13]

Then, a question may arise whether the straight chain product **14** is also formed by a process involving SET of alternatively by a polar process. To differentiate these mechanistic alternatives, the reaction of lithium compound **1a** with a cyclizable probe **13** was undertaken in the presence of 1,4-cyclohexadiene (CHD), a radical scavanger[14] (Table IV). In the reaction in ether/TMEDA the additive CHD exerted a remarkable influence on the product composition; the yield of a cyclized product **15a** decreased significantly (46% → 10%), whereas no meaningful influence was observed in the case of a straight chain product **14a** (12% → 10%). In addition, the formation of 1,2-bis(2,2-dimethylcyclopentyl)ethane (**16**) was completely suppressed, sug-

(11) (a) Griller, D.; Ingold, K. U. *Acc. Chem. Res.* **1980**, *13*, 317. (b) Ashby, E. C.; DePriest, R. N. *J Am. Chem. Soc.* **1982**, *104*, 6144. (c) Ashby, E. C.; DePriest, R. N.; Goel, A. B.; Wenderoth, B.; Pham, T. N. *J. Org. Chem.* **1984**, *49*, 3545.

(12) For the formation of the cross-coupling product **15**, the $S_{RN}1$ pathway involving coupling between 2,2-dimethylcyclopentylmethyl radical (**19**) and phenyl-substituted allyllithium **1** would operate instead of the radical–radical coupling between **17** and **19**. To differentiate between these mechanistic alternatives, the reaction of **1** with *tert*-alkyl bromide was undertaken in the presence of nitrobenzene, a good quencher of radical anion.[7] However, only dimers **6–8** were obtained quantitatively, suggesting that electron transfer between **1** and nitrobenzene is extremely fast. Light was found to exert no meaningful influence on the reaction of **1** with *tert*-alkyl bromide.

(13) (a) Bunnett, J. F. *Acc. Chem. Res.* **1978**, *11*, 413. (b) Saveant, J. M. *Ibid.* **1980**, *13*, 323.

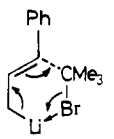
(14) (a) Ashby, E. C.; DePriest, R. N.; Su, W. *Organometallics* **1984**, *3*, 1718. (b) Ashby, E. C.; Argyropoulos, J. N. *J. Org. Chem.* **1985**, *50*, 3274.

Table IV. Reaction of Phenyl-Substituted Allyllithiums with 6-Bromo-6-methylhept-1-ene[a]

			products					
			alkylation		dimerization		redctn	**16**
Li compd	solvent	additive[b,e]	% yield	**14:15**	% yield	**6:7:8**	% yield[f]	% yield
1a	Et_2O		45	16:84	10	22:59:19		8
1a	Et_2O	TMEDA	68	18:82	10	20:60:20		7
1a	Et_2O	TMEDA, CHD	20	51:49	8	31:62:7	40	
1a	Et_2O	HMPA	35	73:27				
1a	Et_2O	HMPA, CHD	33	84:16			30	
1c	Et_2O	TMEDA	17	77:23				
1c	Et_2O	HMPA	30	88:12				
1d	Et_2O	TMEDA[c]	53	28:72	17	20:80:0		12
1d	Et_2O	TMEDA, CHD[c]	23	48:52	8	31:69:0	30	
1d	Et_2O	HMPA	46	92:8				
1d	Et_2O	HMPA, CHD	33	94:6			59	
1e	Et_2O	TMEDA[c]	43	16:84	19	7:73:20		22
1e	Et_2O	TMEDA, CHD[c]	12	68:32	29	6:74:20	37	
1e	Et_2O	HMPA	37	80:20				
1e	Et_2O	HMPA, CHD	29	90:10				
1e	THF	TMEDA	28	88:12				
1f	Et_2O	TMEDA	12	0:100	22	78:22:0	50	24
1f	Et_2O	TMEDA, CHD	11	85:15	12	76:24:0	72	
1f	Et_2O	HMPA	9	0:100	8	81:19:0	70	
1f	Et_2O	HMPA, CHD	10	58:42	5	80:20:0	82	
1f	THF	TMEDA	4	0:100	9	100:0:0	70	
1f	THF	HMPA	15	0:100	6	100:0:0	65	
1g	THF/pentane		12	100:0			50	
1g	THF	TMEDA	40	100:0			20	
1h	pentane[d]		20	100:0			35	
1h	Et_2O[d]		14	100:0			50	

[a] The reaction with 2.5 equiv of 6-bromo-6-methyl-1-heptane (**13**) at 20 °C for 1 h unless otherwise noted. [b,c] See the footnotes in Table II. [d] The reaction with **13** at 20 °C for 2.5 h. [e] CHD (1,4-cyclohexadiene): the reaction in the presence of 3 equiv of CHD. [f] The composition was not determined.

Chart I



gesting that CHD can effectively capture the radical **19**.[14] In the reaction in ether/HMPA, however, CHD exerted a relatively smaller effect on both the yield (35% → 33%) and the composition (the **14a**/**15a** ratio; 73:27 → 84:16) of alkylation products, **14a** and **15a**. Exactly the same trends were observed for **1d**,**e** also (Table IV).

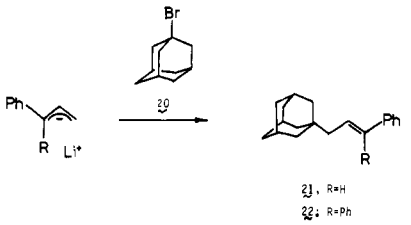
The observed effect of the additive CHD leads us to deduce that a cyclized product **15** is formed by a SET pathway, CHD retarding the formation of **15**. In contrast, a polar pathway predominates for the formation of a straight chain product **14**, and, consequently, the additive CHD does not exert meaningful effects on the production of **14**.[15]

A brief comment is made here on the "polar pathway" for the *tert*-alkylation. It would be useful to stress that it does not need to be an S_N2 displacement with inversion as is the reaction for secondary bromides.[1,16] Rather a cyclic mechanism involving bromide abstraction by unsufficiently solvated lithium cation would be more probable (Chart I). In the extreme case, the carbocation intermediate would be formed first from *tert*-alkyl bromide,[17] followed by coupling with a carbanion to give the alkylation products.[18] In connection with this, the reaction with 1-bromoadamantane (**20**), having poor susceptibility to S_N processes,[19] would be suggestive (eq 6 and Table V). The reaction

Table V. Reaction with 1-Bromoadamantane (**20**) in Et_2O[a]

Li compd	additive	alkyltn (% yield)	% yield	**6:7:8**
1a	TMEDA	**21** (16)	36	42:55:3
1f	TMEDA[b]	**22** (8)	16	100:0:0
1f	HMPA[b]	**22** (21)		

[a] For the reaction conditions, see the Experimental Section. [b] Reduction products, **4f** and **5f**, were also isolated in a yield of 50%.



(6)

of **1a** with **20** in ether/TMEDA gave 1-phenyl-3-(1-adamantyl)-1-propene (**21**) in 16% yield together with dimers **6a**–**8a** (36% yield), while the bromide **20** was completely inert in the reaction in ether/HMPA. In direct constrast, the reaction of 1,1-diphenylallyllithium (**1f**) in ether in the presence of HMPA yielded the corresponding alkylation product **22** (21% yield), as did the reaction in ether/TMEDA. The reaction of **1a** with a mixture of *tert*-butyl bromide and 1-bromoadamantane in ether in the presence of TMEDA or HMPA, however, gave only the *tert*-butylated products **2a** and **3a**, suggesting that the more bulky bromide **20** has a much less reactivity than *tert*-butyl bromide. Consistent with this, isopropyl bromide was found to be much more reactive than *tert*-butyl bromide in the competitive reaction with

(15) As a referee has suggested, the reaction of allyllithium **1** with tertiary cyclizable probe **13** in the presence or absence of CHD would give only the information about the behavior of radicals **17** and **18** escaped from the cage, since the rate constant for hexenyl cyclization [10^5/s] precludes intercepting a cage process [10^{10}/mol·s].[11] Likewise a CHD trap will only scavenge radicals which have diffused outside the cage.[14] Consequently, we cannot completely exclude the possibility that at least a part of a straight chain product **14** is produced by cross-coupling between allyl radical **17** and a straight chain radical **18** in the cage.

(16) The reaction of **1a** with optically active *sec*-butyl bromide in ether in the presence of TMEDA or HMPA yields predominantly the C-1 attack product with complete inversion. The details will be published elsewhere.

(17) Schlosser, M. *Structure and Reactivity of Polar Organometallics*; Springer: Berlin, 1973.

(18) We appreciate the comments from both referees that in the "polar process" lithium cation assistance would be important.

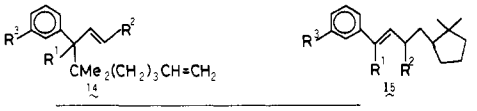
(19) Carey, F. A.; Sundberg, R. J. *Advanced Organic Chemistry*; Plenum Press: New York, 1984; Part A, Chapter 5.

Table VI. Physical Properties of Products

compd	*m/e* (M^+)	^{1}H NMR (δ)	elemental analysis
2b	204	0.85 (s, 9 H), 2.89 (d, J = 10.0 Hz, 1 H), 3.65 (s, 3 H), 5.0 (m, 2 H), 6.1 (m, 1 H), 6.9 (m, 4 H)	($C_{14}H_{20}O$) C, H
(*E*)-**3b**	204	0.92 (s, 9 H), 2.00 (d, J = 7.0 Hz, 2 H), 3.62 (s, 3 H), 5.95 (d × d, J = 15.0 and 7.0 Hz, 1 H), 6.22 (d, J = 15.0 Hz, 1 H), 6.9 (m, 4 H)	($C_{14}H_{20}O$) C, H
2c	208, 210	0.89 (s, 9 H), 2.99 (d, J = 10.0 Hz, 1 H), 5.0 (m, 2 H), 6.2 (m, 1 H), 7.2 (m, 4 H)	($C_{13}H_{17}Cl$) C, H
3c	208, 210	0.94 (s, 9 H), 2.05 (d, J = 7.0 Hz, 2 H), 6.2 (m, 2 H), 7.1 (m, 4 H)	($C_{13}H_{17}Cl$) C, H
2d	188	0.84 (s, 9 H), 1.45 (s, 3 H), 5.1 (m, 2 H), 6.67 (d × d, J = 10.5 and 16.5 Hz, 1 H), 7.2 (m, 5 H)	($C_{14}H_{20}$) C, H
3d	188	0.96 (s, 9 H), 2.00 (s, 3 H), 2.1 (m, 2 H), 5.7 (m, 1 H), 7.2 (m, 5 H)	($C_{14}H_{20}$) C, H
(*E*)-**2e**	188	0.85 (s, 9 H), 1.68 (d, J = 6.0 Hz, 3 H), 2.92 (d, J = 9.6 Hz, 1 H), 5.41 (d × q, J = 15.0 and 6.0 Hz, 1 H), 5.84 (d × d, J = 15.0 and 9.0 Hz, 1 H), 7.2 (m, 5 H)	
(*E*)-**3e**	188	0.88 (s, 9 H), 1.03 (d, J = 7.0 Hz, 3 H), 2.0 (m, 1 H), 6.02 (d × d, J = 15.0 and 7.0 Hz, 1 H), 6.24 (d, J = 15.0 Hz, 1 H), 7.1 (m, 5 H)	($C_{14}H_{20}$) C, H
2f	250	1.14 (s, 9 H), 4.35 (d, J = 16.8 Hz, 1 H) 5.2 (m, 1 H), 6.75 (d × d, J = 10.8 and 16.8 Hz, 1 H), 7.2 (m, 10 H)	($C_{19}H_{22}$) C, H
3f	250	0.90 (s, 9 H), 2.20 (d, J = 7.5 Hz, 2 H), 6.20 (t, J = 7.5 Hz, 1 H), 7.2 (m, 10 H)	($C_{19}H_{22}$) C, H
2g	250	0.89 (s, 9 H), 3.08 (d, J = 9.6 Hz, 1 H), 6.5 (m, 2 H), 7.2 (m, 10 H), 0.95 (s, 9 H), 6.70 (d, J = 5.4 Hz, 1 H), 6.98 (d, J = 5.4 Hz, 1 H), 7.5 (m, 9 H)	($C_{19}H_{20}$) C, H
2h			($C_{19}H_{20}$) C, H
3h	248	1.08 (s, 9 H), 3.27 (d, J = 2.7 Hz, 1 H), 6.45 (d, J = 2.7 Hz, 1 H), 7.3 (m, 9 H)	($C_{19}H_{20}$) C, H
10d	244	0.81 (s, 6 H), 1.2 (m, 11 H), 1.43 (s, 3 H), 5.0 (m, 2 H), 6.65 (d × d, J = 11.4 and 16.5 Hz, 1 H), 7.2 (m, 5 H)	($C_{18}H_{28}$) C, H
11d	244	0.90 (s, 6 H), 1.1 (m, 11 H)8 1.98 (s, 3 H), 5.70 (t, J = 6.9 Hz, 1 H)	($C_{18}H_{28}$) C, H
10e	244	0.79 (s, 3 H), 0.87 (s, 3 H), 1.1 (m, 11 H), 1.65 (d, J = 5.4 Hz, 3 H), 3.04 (d, J = 9.9 Hz, 1 H), 5.4 (m, 2 H), 7.1 (m, 5 H)	($C_{18}H_{28}$) C, H
(*E*)-**11e**	244	0.82 (s, 6 H), 1.01 (d, J = 6.9 Hz, 3 H), 1.1 (m, 11 H), 2.14 (q, J = 6.9 Hz, 1 H), 6.05 (d × d, J = 15.0 and 6.9 Hz, 1 H), 6.27 (d, J = 15.0 Hz, 1 H), 7.1 (m, 5 H)	($C_{18}H_{28}$) C, H
10f	306	1.09 (s, 9 H), 4.35 (d, J = 16.5 Hz, 1 H), 5.20 (d × d, J = 9.9 and 1.2 Hz, 1 H), 6.82 (d × d, J = 16.5 and 9.9 Hz, 1 H), (m, 10 H)	($C_{23}H_{30}$) C, H
11f	306	0.87 (s, 6 H), 1.1 (m, 11 H), 2.01 (d, J = 7.0 Hz, 2 H), 6.09 (t, J = 7.0 Hz, 1 H), 7.2 (m, 10 H)	($C_{23}H_{30}$) C, H
14a	228	0.76 (s, 3 H), 0.87 (s, 3 H), 1.7 (m, 6 H), 3.03 (d, J = 10.0 Hz, 1 H), 5.0 (m, 2 H), 6.0 (m, 2 H), 7.1 (m, 5 H)	($C_{17}H_{24}$) C, H
(*E*)-**15a**	228	0.73 (s, 3 H), 0.97 (s, 3 H), 1.4 (m, 7 H), 2.1 (m, 2 H), 6.09 (d × d, J = 15.0 and 7.0 Hz, 1 H), 6.36 (d, J = 15.0 Hz, 1 H), 7.2 (m, 5 H)	($C_{17}H_{24}$) C, H
14c	262, 264	0.80 (s, 3 H), 0.87 (s, 3 H), 1.6 (m, 6 H), 3.05 (d, J = 10.0 Hz, 1 H), 5.0 (m, 4 H), 6.0 (m, 2 H), 7.0 (m, 4 H)	($C_{17}H_{23}Cl$) C, H
15c	262, 264	0.72 (s, 3 H), 0.96 (s, 3 H), 1.4 (m, 7 H), 2.0 (m, 4 H), 6.0 (m, 2 h), 7.1 (m, 4 H)	($C_{17}H_{23}Cl$) C, H
14f	304	1.09 (s, 6 H), 2.1 (m, 6 H), 4.25 (d × d, J = 16.5 and 1.5 Hz, 1 H), 4.9 (m, 2 H), 5.21 (d × d, J = 9.6 and 1.5 Hz, 1 H), 5.56 (t × d × d, J = 6.9, 9.9, and 16.5 Hz, 1 H), 6.78 (d × d, J = 16.5 and 9.6 Hz, 1 H)	($C_{23}H_{28}$) C, H
15f	304	0.71 (s, 3 H), 0.95 (s, 3 H), 1.7 (m, 11 H), 6.00 (t, J = 7.0 Hz, 1 H), 7.2 (m, 10 H)	($C_{23}H_{28}$) C, H
(*E*)-**14g**	304	0.88 (s, 3 H), 0.90 (s, 3 H), 1.6 (m, 6 H), 3.22 (d, J = 9.0 Hz, 1 H), 4.9 (m, 2 H), 5.7 (m, 1 H), 6.27 (d, J = 15.0 Hz, 1 H)8 6.57 (d × d, J = 15.0 and 9.0 Hz, 1 H) 7.1 (m, 10 H)	($C_{23}H_{28}$) C, H
14h	302	0.97 (s, 6 H), 1.6 (m, 6 H), 4.9 (m, 2 H), 5.7 (m, 1 H), 6.77 (d, J = 5.4 Hz, 1 H), 7.12 (d, J = 5.4 Hz, 1 H), 7.6 (m, 9 H)	($C_{23}H_{26}$) C, H

lithium compound **1a** in ether/TMEDA.

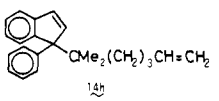
The reaction of the relatively more stable 1,3-diphenylallyllithium (**1g**) with a tert cyclizable probe **13** resulted in exclusive formation of a straight chain product **14g**. In the case of 1-phenylindenyllithium (**1h**) also, a straight chain product **14h**,



14

15

compound	R^1	R^2	R^3
c	H	H	Cl
d	Me	H	H
e	H	Me	H
f	Ph	H	H
g	H	Ph	H



14h

formed by coupling at the more hindered C-1, was the sole cross-coupling product under all the conditions. These results would imply that stable allylic carbanions are prone to react by a polar pathway even with bulky *tert*-alkyl bromides. In this framework the predominant formation of a straight chain product **14c** from the *m*-chloro derivative **1c** even in ether/TMEDA would be understood.

Thus, the increase in stability of carbanions and the increase in donicity of the solvent systems seems to enhance the contribution of a polar pathway.[20] Inconsistent with this, 1,1-diphenylallyllithium (**1f**), an allyl anion stabilized by two phenyl groups, seems to proceed by a SET pathway irrespective of the intensity of the solvent systems. From the reaction with a cyclizable probe **13**, only the cyclized product **15f** was obtained in a low yield of around 10%. A possible explanation would be as follows. A polar pathway is extremely disfavored since attack by bulky *tert*-alkyl bromide at the 1-position is very slow from steric reasons. Thus, although SET is also expected to be a slow process due to the enhanced stability of **1f**, the participation of only this process can be observed in the reaction with *tert*-alkyl bromides. Alternatively, 1,1-diphenylallyl anion would have an abnormally low ionization potential, and, as a result, the SET process would be extremely favored.

In summary, the systematic survey on the reaction of phenyl-substituted allyllithiums **1a–h** with *tert*-alkyl bromides has revealed that the product regiochemistry observed in the reaction proceeding by SET would be remarkably different from that proceeding by a polar pathway. The concept itself is, however, not particularly novel. About 30 years ago Kornblum[21] and Russell[22] demonstrated that treatment of the salt of an aliphatic

(20) (a) Alnajjar, M. S.; Kuivila, H. G. *J. Am. Chem. Soc.* **1985**, *107*, 416. (b) Troughton, E. B.; Molter, K. E.; Arnett, E. M. *Ibid.* **1984**, *106*, 6726. (c) Bordwell, F. G.; Clemens, A. H. *J. Org. Chem.* **1981**, *46*, 1035.

(21) Kornblum, N.; Michel, R. E.; Kerber, R. C. *J. Am. Chem. Soc.* **1966**, *88*, 5660, 5662.

nitro compound with an alkyl halide may result in alkylation at carbon or oxygen, the $S_{RN}1$ process being important for carbon alkylation, and in direct contrast, the oxygen alkylation product is obtained by a polar process. Our contribution would be the finding that even for the simple allylic carbanions having two reaction sites with apparent similar reactivities different pathways would lead to notably different product regiochemistries. This leads us to deduce that as an approach to perform regioselective C–C bond formation, the control of reaction pathways would be attractive.

Experimental Section

^{1}H NMR spectra were obtained with a JNM-PS-100 spectrometer in CCl_4. Mass spectral data were obtained with a Hitachi RMU-6H spectrometer and electronic spectra with a Hitachi 220A spectrometer. GLC analysis was carried out on a Hitachi 164 gas chromatograph.

The starting materials **4a**,[23] **4b**,[23] **4c**,[23], **4d**[24] **4f**,[24] **4g**,[25] and **4h**[26] were prepared by the reported methods. 1-Phenyl-2-butene (**4e**) was purchased from Tokyo Kasei.

Preparation and Electronic Spectra of Phenyl-Substituted Allyllithiums 1a–h. 1-Phenylallyllithium (**1a**) was prepared under five conditions. (i) In ether in the absence of additive: In a 50-mL flask, equipped with a magnetic stirrer and maintained under argon, an ether solution of 3-phenylpropene (**4a**) (4.2 mmol) was syringed. To this soltuion was syringed a hexane solution of BuLi (8.4 mmol) at 0 °C, and then the mixture was stirred for 2 h under reflux. (ii) In ether in the presence of TMEDA: To an ether solution of **4a** (4.2 mmol) and TMEDA (5.0 mmol) was syringed a hexane solution of BuLi (5.0 mmol) at 0 °C, and then the mixture was stirred at 20 °C for 2 h. (iii) In ether in the presence of HMPA: To an ether solution of **4a** (4.2 mmol) and HMPA (42 mmol) was syringed a hexane solution of BuLi (5.0 mmol) at −45 °C, and then the mixture was stirred at −45 °C for 10 min. (iv) In THF in the presence of TMEDA: To a THF solution of **4a** (4.2 mmol) and TMEDA (5.0 mmol) was syringed a hexane solution of BuLi (5.0 mmol) at 0 °C, and then the mixture was stirred at 20 °C for 1 h. (v) In THF in the presence of HMPA: To a THF solution of **4a** (4.2 mmol) and HMPA (42 mmol) was syringed a hexane solution of BuLi (5.0 mmol at −45 °C, and then the mixture was kept with stirring at −45 °C for 10 min.

Under similar conditions other lithium compounds **1b–h** were prepared (see the footnotes in Table I–IV).

The electronic spectra were measured by diluting aliquots of a solution of the lithium compound **1** with dry ether or THF in a quartz cell maintained under nitrogen.

Reaction of 1-Phenylallyllithium (1a) with *tert*-Butyl in Ether in the Presence of TMEDA. To an ether–hexane solution of **1a** (prepared from 4.2 mmol of **4a**, 5.0 mmol of BuLi, and 5.0 mmol of TMEDA) was injected an ether solution of *tert*-butyl bromide (21 mmol), and then the mixture was kept at 20 °C for 1 h. The reaction mixture was then quenched with water, and the ether layer was separated and dried over anhydrous Na_2SO_4. After evaporation of the ether, the crude products were column chromatographed on silica gel. The first fraction contained a mixture of *tert*-butylation products **2a** and **3a**, the physical properties being identical with those of authentic samples prepared from the reaction of 1-phenyl-3-chloropropene with *tert*-butylmagnesium bromide.[8b]

From the second fraction were obtained dimers **6a–8a**.[8b] The compositions of both alkylation products and dimers were determined by ^{1}H NMR spectroscopy and GLC analysis. The errors in composition of alkylation products and dimers were around 2% and 5%, respectively. The errors in yields of both alkylation products and dimers were around 7%.

Reaction of 1-Phenylallyllithium (1a) with 2-Methyl-2-bromoheptane (9) in Ether/TMEDA. To an ether–hexane solution of **1a** (prepared from 4.2 mmol of **4a**, 5.0 mmol of BuLi, and 5.0 mmol of TMEDA) was injected an ether solution of **9** (10 mmol) in 1 portion, and then the reaction was continued with stirring at 20 °C for 1 h. After conventional workup, the crude products were column chromatographed on silica gel. The first fraction contained 6,6,7,7-tetramethyldodecane (**12**): an oil; *m/e* 226 (M^+); ^{1}H NMR δ 0.75 (s, 12 H), 0.81 (t, *J* = 7.4 Hz, 6 H), 1.2 (m, 16 H). Anal. Calcd for $C_{16}H_{34}$: C, 84.96, H, 15.04. Found: C, 84.60; H, 15.14. From the second fraction a mixture of two alkylation products, **11a** and **10a**, was isolated. (**E**)-**11a**: an oil; *m/e* 230 (M^+); ^{1}H NMR δ 0.90 (s, 6 H), 1.1 (m, 11 H), 2.06 (d, *J* = 5.7 Hz, 2 H), 6.01 (dxt, *J* = 15.0 and 5.7 Hz, 1 H), 6.12 (d, *J* = 15.0 Hz, 1 H), 7.2 (m, 5 H). Anal. Calcd for $C_{17}H_{26}$: C, 88.70; H, 11.30. Found: C, 88.35; H, 11.30. **10a**: an oil; *m/e* 230 (M^+); ^{1}H NMR δ 0.78 (s, 3 H), 0.85 (s, 3 H), 1.1 (m, 11 H), 3.03 (d, *J* = 8.7 Hz, 1 H), 4.9 (m, 2 H), 6.2 (m, 1 H), 7.1 (m, 5 H). Anal. Calcd for $C_{17}H_{26}$: C, 88.70; H, 11.30. Found: C, 88.91; H, 11.22. The third fraction contained dimers **6a–8a**.

Reaction of 1-Phenyl-1-methylallyllithium (1d) with 6-Bromo-6-methyl-1-heptene (13) in Ether/HMPA. To an ether–hexane solution of **1d** (prepared from 4 mmol of **4d**, 8 mmol of BuLi, and 8 mmol of TMEDA) was injected an ether solution of **13** (10 mmol) in 1 portion, and then the reaction was continued with stirring at 20 °C for 1 h. After conventional workup, the products were isolated by column chromatography on silica gel. The first fraction contained bromide **13**. From the second fraction was isolated 1,2-bis(2,2-dimethylcyclopentyl)ethane (**16**): an oil; *m/e* 222 (M^+); ^{1}H NMR δ 0.71 (s, 6 H), 0.95 (s, 6 H), 1.4 (m, 18 H). Anal. Calcd for $C_{16}H_{30}$: C, 86.49; H, 13.51. Found: C, 86.50; H, 13.50. The third fraction contained 2-phenyl-5-(2,2-dimethylcyclopentyl)-2-pentene (**15d**): an oil; *m/e* 242 (M^+); ^{1}H NMR δ 0.74 (s, 3 H), 0.98 (s, 3 H), 1.7 (m, 11 H), 2.00 (s, 3 H), 5.72 (t, *J* = 7.0 Hz, 1 H), 7.2 (m, 5 H). Anal. Calcd for $C_{18}H_{26}$: C, 89.26; H, 10.74. Found: C, 89.30; H, 10.70. From the fourth fraction was isolated 3,4,4-trimethyl-3-pehnyl-1,8-nonadiene (**14d**): an oil; *m/e* 242 (M^+); ^{1}H NMR δ 0.82 (s, 6 H), 1.7 (m, 6 H), 1.44 (s, 3 H), 5.3 (m, 5 H), 6.66 (d × d, *J* = 15.0 and 11.4 Hz, 1 H), 7.2 (m, 5 H). Anal. Calcd for $C_{18}H_{26}$: C, 89.26; H, 10.74. Found: C, 89.50; H, 10.80. The final fraction contained dimers **6d–8d**. **6d**: an oil; *m/e* 262 (M^+); ^{1}H NMR δ 2.03 (s, 6 H), 2.4 (m, 4 H), 5.8 (m, 2 H), 7.4 (m, 10 H). **7d**: an oil; *m/e* 262 (M^+); ^{1}H NMR δ 1.42 (s, 3 H), 2.10 (s, 3 H), 2.63 (d, *J* = 6.9 Hz, 2 H), 5.1 (m, 2 H), 5.53 (t, *J* = 6.9 Hz, 1 H), 6.06 (d × d, *J* = 15.0 and 9.6 Hz, 1 H), 7.2 (m, 10 H). Anal. Calcd for $C_{20}H_{22}$: C, 91.60; H, 8.40. Found: C, 91.90; H, 8.35. **8d**: an oil; *m/e* 262 (M^+); ^{1}H NMR δ 1.44 (s, 6 H), 5.1 (m, 4 H), 6.54 (d × d, *J* = 17.4 and 10.8 Hz, 2 H), 7.2 (m, 10 H). Anal. Calcd for $C_{20}H_{22}$: C, 91.60; H, 8.40. Found: C, 91.75; H, 8.41.

Reaction of 1-Phenyl-3-methylallyllithium (1e) with 13 in Ether/TMEDA in the Presence of 1,4-Cyclohexadiene (CHD). To an ether–hexane solution of **1e** (prepared from 4 mmol of **4e**, 8 mmol of BuLi, and 8 mmol of TMEDA) was injected an ether solution of **13** (10 mmol) and CHD (12 mmol) in 1 portion, and then the reaction was continued at 20 °C for 1 h. After conventional workup, the products were column chromatographed on silica gel. The first fraction contained 1-phenyl-4-(2,2-dimethylcyclopentyl)-3-methyl-1-butene ((**E**)-**15e**): an oil; ^{1}H NMR δ 0.72 (s, 3 H), 0.93 (s, 3 H), 1.07 (d, *J* = 6.9 Hz, 3 H), 1.8 (m, 9 H), 5.9 (m, 1 H), 6.26 (d, *J* = 15.0 Hz, 1 H), 7.2 (m, 5 H). Anal. Calcd for $C_{18}H_{26}$: C, 89.26; H, 10.74. Found: C, 89.00; H, 10.83. From the secnd fraction was obtained 6,6-dimethyl-7-phenyl-1,8-decadiene (**14e**): an oil; *m/e* 242 (M^+); ^{1}H NMR δ 0.77 (s, 3 H), 0.85 (s, 3 H), 1.66 (d, *J* = 5.4 Hz, 3 H), 1.7 (m, 6 H), 3.03 (d, *J* = 9.6 Hz, 1 H), 5.0 (m, 2 H), 5.7 (m, 3 H), 6.7 (m, 5 H). Anal. Calcd for $C_{18}H_{26}$: C, 89.26; H, 10.74. Found: C, 89.55; H, 10.71.

The final fraction contained dimers. **6e**: an oil; *m/e* 262 (M^+); ^{1}H NMR δ 1.11 (d, *J* = 6.9 Hz, 6 H), 2.3 (m, 2 H), 6.1 (m, 4 H), 7.2 (m, 10 H). **7e**: an oil; *m/e* 262 (M^+); ^{1}H NMR δ 1.02 (d, *J* = 6.6 Hz, 3 H), 1.6 (m, 3 H), 2.6 (m, 1 H), 3.1 (m, 1 H), 5.5 (m, 2 H), 6.1 (m, 2 H), 7.2 (m, 10 H). Anal. Calcd for $C_{20}H_{22}$: C, 91.60 H, 8.40. Found: C, 91.85; H, 8.30. **8e**: an oil; *m/e* 262 (M^+); ^{1}H NMR δ 1.6 (m, 6 H), 3.4 (m, 2 H), 5.5 (m, 4 H), 7.0 (m, 10 H). Anal. Calcd for $C_{20}H_{22}$: C, 91.60; H, 8.40. Found: C, 91.35; H, 8.55.

Reaction of 1,1-Diphenylallyllithium (1f) with *tert*-Butyl Bromide in Ether/TMEDA in the Presence of Nitrobenzene. To an ether–hexane solution of **1f** (prepared from 4 mmol of **4f**, 4.8 mmol of BuLi, and 4.8 mmol of TMEDA) was syringed an ether solution of *tert*-butyl bromide (20 mmol) and nitrobenzene (10 mmol) in 1 portion. and then the reaction was continued at 20 °C for 1 h. By column chromatography on silica gel were isolated 1,1,6,6-tetraphenyl-1,5-hexadiene (**6f**) and 1,1,4,4-tetraphenyl-1,5-hexadiene (**7f**) in yields of 62% and 14%, respectively. **6f**: a solid; mp 104–108 °C (from hexane); ^{1}H NMR δ 2.2 (m, 4 H), 6.1 (m, 2 H), 7.3 (m, 20 H). Anal. Calcd for $C_{30}H_{26}$: C, 93.26; H, 6.74. Found: C, 93.20; H, 6.60. **7f**: an oil; *m/e* 386 (M^+); ^{1}H NMR δ 3.09 (d, *J* = 6.9 Hz, 2 H), 4.79 (d, *J* = 16.5 Hz, 1 H), 5.23 (d, *J* = 11.1 Hz, 1 H), 5.95 (t, *J* = 6.9 Hz, 1 H), 6.47 (d × d, *J* = 16.5 and 11.4 Hz, 1 H), 7.2 (m, 20 H).

Reaction with 1-Bromoadamantane (20). The reaction of **1a** (2.5 mmol) with 20 (12.5 mmol) in ether in the presence of TMEDA (3.1 mmol) was undertaken at 45 °C for 4 h. By column chromatography on silica gel, 1-phenyl-3-(1-adamantyl)-1-propene (**21**) was isolated in 16% yield, together with dimers **6a–8a** (36% yield). **21**: an oil; ^{1}H NMR δ 1.8 (m, 17 H), 6.3 (m, 2 H), 7.2 (m, 5 H). Anal. Calcd for $C_{19}H_{24}$:

(22) (a) Russell, G. A.; Danen, W. C. *J. Am. Chem. Soc.* **1966**, *88*, 5663. (b) Russell, G. A.; Ros, F. *Ibid.* **1985**, *107*, 2506.

(23) Fujimoto, Y.; Suzuki, Y.; Tanaka, Y.; Tominaga, T.; Takeda, H.; Sekine, H.; Morito, N.; Miyaoka, Y. *Heterocycles* **1977**, *6*, 1604.

(24) Walling, C.; Bollyky, L. *J. Org. Chem.* **1964**, *29*, 2699.

(25) Bamford, W. R.; Stevens, T. S. *J. Chem. Soc.* **1952**, 4735.

(26) Miura, M.; Nojima, M.; Kusabayashi, S.; McCullough, K. J. *J. Am. Chem. Soc.* **1984**, *106*, 2932.

C, 90.48; H, 9.52. Found: C, 90.70; H, 9.50.

The reaction of **1f** (3 mmol) with **20** (15 mmol) in ether was performed in the presence of TMEDA (3.6 mmol) or HMPA (30 mmol) at 20 °C for 5 h. By colum chromatography on silica gel, 1,1-diphenyl-3-(1-adamantyl)-1-propene (**22**) was isolated together with dimer **6f**. **22**: a solid; mp 102–104 °C (from hexane); *m/e* 328 (M^+); ^1H NMR δ 1.7 (m, 17 H), 6.12 (t, J = 8.1 Hz, 1 H), 7.2 (m, 10 H). Anal. Calcd for $C_{25}H_{28}$: C, 91.16; H, 8.81. Found: C, 91.60; H, 8.70.

The Competitive Reaction between Two Alkyl Bromides. The reaction of **1a** with a mixture of *tert*-butyl bromide (3 equiv) and 1-bromoadamantane (3 equiv) was undertaken in ether in the presence of TMEDA (1.2 equiv) at 20 °C for 1 h. By column chromatography on silica gel, a mixture of 40% **2a** and 60% **3a** was isolated in 45% yield, together with dimers **6a–8a** (8% yield). The reaction in the presence of HMPA (10 equiv) also gave only the two *tert*-butylation products **2a** and **3a** in 40% yield, the ratio being 74:26.

The reaction of **1a** with a mixture of *tert*-butyl bromide (3 equiv) and isopropyl bromide (3 equiv) was undertaken in ether in the presence of TMEDA (1.2 equiv) at 20 °C for 1 h. By column chromatography on silica gel, a mixture of 3-phenyl-4-methyl-1-pentene[8b] and 1-phenyl-4-methyl-1-pentene[8b] was obtained in 60% yield, the ratio being 96:4.

Acknowledgment. The donation of (*S*)-(+)-2-butyl alcohol by Daisel Chemical Industries Ltd. is greatly appreciated.

Conformational Cycloenantiomerism in 1,2-Bis(1-bromoethyl)-3,4,5,6-tetraisopropylbenzene

M. Dhaneshwar Singh,[1] Jay Siegel, Silvio E. Biali, and Kurt Mislow*

Contribution from the Department of Chemistry, Princeton University, Princeton, New Jersey 08544. *Received December 2, 1986*

Abstract: The concept of cycloenantiomerism is critically reexamined. It is shown that suitably substituted derivatives of hexaisopropylbenzene (**1**) illustrate a novel type of stereoisomerism, in which enantiomers are distinguished by the sense of conformational orientation of side chains for a given configurational distribution pattern of stereocenters. Such isomers, which may be described as conformational cycloenantiomers, have now been synthesized for the first time. Photobromination of 1,2-diethyl-3,4,5,6-tetraisopropylbenzene yields a mixture of the two diastereomeric 1,2-bis(1-bromoethyl)-3,4,5,6-tetraisopropylbenzenes (**2**), from which the (1′*RS*,2′*SR*) isomer (**2a**) is isolated by HPLC. This isomer is a racemic mixture of conformational cycloenantiomers. VT-NMR measurements yield a lower limit of $\Delta G^{\ddagger}$ = 24 kcal mol^{-1} for the enantiomerization of **2a**.

Recently it was shown that the tightly interlocking cyclic tongue-and-groove arrangement of isopropyl groups in hexaisopropylbenzene (**1**) leads to nonbonded interactions which effectively immobilize these groups on the laboratory time scale.[2] Arnett and Bollinger[3] had previously conjectured that such conformational rigidity might stabilize enantiomers of suitably derivatized hexaisopropylbenzenes.[4] We now show that certain substitution patterns do indeed give rise to a novel type of stereoisomerism,[5] and we report the synthesis of a derivative of **1** that fits this description.

Cyclostereoisomerism. This concept was introduced by Prelog and Gerlach[6] in 1964.[7] As described in their paper, cyclostereoisomers are composed of an equal number of enantiomeric building blocks ("Bauelemente"), possess the same arrangement of stereocenters, i.e., the same cyclic distribution pattern of configurational descriptors ("Verteilungsmuster"), and differ only in the sense of direction of the ring ("Ringrichtung").[8,11]

Cyclostereoisomerism in a broad sense deals with isomerisms that arise when cyclic arrangements of stereocenters are associated with ring systems. In the problems that we will be addressing, the stereocenters can be attached externally to the ring or incorporated as members of the ring, and the ring itself can be either directed or undirected. Ring directionality in the present context depends on the sequential order of bonded atoms, i.e., on the constitution of the ring, so that an undirected ring is characterized by a palindromic sequence of atoms, i.e., by a sequence with bilateral symmetry. There are thus four basic combinations of stereocenters with ring systems (Figure 1) which may be exemplified by *N,N′*-di-*sec*-butylpiperazine (type A), 2,5-diketo-*N,N′*-di-*sec*-butylpiperazine (type B), 2,5-diketo-3,6-dimethylpiperazine (type C), and inositol (type I).

(1) Government of India Scholar, on leave from Manipur University.
(2) Siegel, J.; Gutiérrez, A.; Schweizer, W. B.; Ermer, O.; Mislow, K. *J. Am. Chem. Soc.* **1986**, *108*, 1569.
(3) Arnett, E. M.; Bollinger, J. M. *J. Am. Chem. Soc.* **1964**, *86*, 4729.
(4) "A natural consequence of this [conformational rigidity] would be the existence of stable enantiomers related to hexaisopropylbenzene in which the symmetry, with respect to the ring, is destroyed, provided that the average time for rotation [of the isopropyl groups] is long enough to allow resolution."[3]
(5) Portions of this work were reported in preliminary communications: (a) Siegel, J.; Mislow, K. *J. Am. Chem. Soc.* **1983**, *105*, 7763. (b) Mislow, K. *Chimia* **1986**, *40*, 395.
(6) Prelog, V.; Gerlach, H. *Helv. Chim. Acta* **1964**, *47*, 2288. See also: Prelog, V. *Science* **1976**, *193*, 17.
(7) For an extensive discussion of cyclostereoisomerism see: Cruse, R. In Eliel, E. L. *Stereochemie der Kohlenstoffverbindungen*; Verlag Chemie: Weinheim, 1966; pp 215–225.
(8) Cruse's treatment of cycloenantiomerism[7] differs from that of Prelog and Gerlach in the implicit application of the Neumann–Curie principle,[9] and in the requirement for constitutional equivalence of the stereocenters. Cruse dissects Ringrichtung from Verteilungsmuster and abstracts each to its point group symmetry; from this he is able to demonstrate that the achiral symmetries of Ringrichtung (C_{2nh}) and Verteilungsmuster (C_{nv}) with a common C_n axis intersect in two enantiomorphous ways to yield two enantiomers, i.e., two cycloenantiomers. Cruse also notes that the absence of a C_2 axis perpendicular to the principal axis (i.e., the absence of dihedral ring symmetry) is a necessary condition for cycloenantiomerism. However, Cruse's insistence on the *constitutional* equivalence of stereocenters imposes an unnecessary limitation on his treatment: as has been shown in another connection, such a constraint is irrelevant in analyses of symmetry properties.[10]
(9) See: Shubnikov, A. V.; Koptsik, V. A. *Symmetry in Science and Art*; Plenum Press: New York, 1974; pp 328–336. Donaldson, J. D.; Ross, S. D. *Symmetry and Stereochemistry*; Halsted Press Div., Wiley: New York, 1972; p 132.
(10) Mislow, K.; Siegel, J. *J. Am. Chem. Soc.* **1984**, *106*, 3319.
(11) In speaking of the *sense of direction* in a ring, it is of course essential to specify the side or face from which the ring is being viewed.

0002-7863/87/1509-3397$01.50/0