particularly when combined with gas chromatographic considerations.

Conclusions

The chemical structures of specific brominated biphenyls were established from their ^{13}C NMR parameters. These compounds of known structure were then used to establish the occurrence of an ortho effect in the mass spectral fragmentation of brominated biphenyls having two or more ortho bromines on different rings. The ortho effect is seen as an increase in the abundance of the $[M - Br]^+$ fragment with respect to the $[M - 2Br]^{+\cdot}$ and $[M]^{+\cdot}$ ions. This effect allows one to establish the presence of 2,2′ substitution. It is analogous to that observed for three chlorines in the ortho chlorinated biphenyl series, yet persists for two, three, and to a lesser degree, for four ortho bromine substituents. Mass spectral differences brought about by the presence of 2,2′,3 substitution allow brominated biphenyls with this ring substitution to be distinguished from isomers without this substitution pattern.

Acknowledgment. We thank Steven A. Warner, Louis E. Feige, John T. Wilson, and Stephen B. Little for their help in obtaining the mass and NMR spectra, and David W. Hodgson for GC screening of the samples. We also thank Lynn A. Wright and Teena Cochran for several insightful suggestions.

Registry No. Biphenyl, 92-52-4; 2-bromobiphenyl, 2052-07-5; 3-bromobiphenyl, 2113-57-7; 4-bromobiphenyl, 92-66-0; 2,4-dibromobiphenyl, 53592-10-2; 2,5-dibromobiphenyl, 57422-77-2; 2,6-dibromobiphenyl, 59080-32-9; 2,2′-dibromobiphenyl, 13029-09-9; 4,4′-dibromobiphenyl, 92-86-4; 2,4,6-tribromobiphenyl, 59080-33-0; 2,2′,5-tribromobiphenyl, 59080-34-1; 2,3′,5-tribromobiphenyl, 59080-35-2; 2,4′,5-tribromobiphenyl, 59080-36-3; 2,2′,4′,5-tetrabromobiphenyl, 60044-24-8; 2,2′,5,5′-tetrabromobiphenyl, 59080-37-4; 2,2′,5,6′-tetrabromobiphenyl, 60044-25-9; 3,3′,5,5′-tetrabromobiphenyl, 16400-50-3; 2,2′,4,5′,6-pentabromobiphenyl, 59080-39-6; 2,2′,3,3′,4,4′-hexabromobiphenyl, 82865-89-2; 2,2′,4,4′,5,5′-hexabromobiphenyl, 59080-40-9; 3,3′,4,4′,5,5′-hexabromobiphenyl, 60044-26-0; 2,2′,4,4′,6,6′-hexabromobiphenyl, 59261-08-4; 2,2′,3,3′,4,4′,5,5′,6,6′-decabromobiphenyl, 13654-09-6; 2,2′,3,3′,4,4′,5,5′,6,6′-decabromodiphenyl ether, 1163-19-5; 2,2′,3,3′,4,4′,5,5′,6,6′-decachlorobiphenyl, 2051-24-3; 2,2′,3,3′,4,4′,5,5′,6,6′-decafluorobiphenyl, 434-90-2; 2,2′,3,3′,4,4′,5,5′,6,6′-decachlorodiphenyl ether, 31710-30-2; 2,2′,4,5,5′-pentabromobiphenyl, 67888-96-4; 2,3′,4,4′,5-pentabromobiphenyl, 67888-97-5; 2,2′,3,4′,5′,6-hexabromobiphenyl, 69278-59-7; 2,2′,3,3′,4,5′-hexabromobiphenyl, 82865-90-5; 2,2′,3,4,4′,5′-hexabromobiphenyl, 67888-98-6; 2,3,3′,4′,5′,6-hexabromobiphenyl, 82865-91-6; 2,3′,4,4′,5,5′-hexabromobiphenyl, 67888-99-7; 2,2′,3,3′,4,5,5′-heptabromobiphenyl, 82865-92-7; 2,2′,3,4,4′,5,5′-heptabromobiphenyl, 67733-52-2; 2,2′,3,3′,4,4′,5-heptabromobiphenyl, 69278-60-0; Firemaster BP-6, 59536-65-1.

Preparative Resolution of Racemates on a Chiral Liquid Chromatography Column

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A 2 in. × 30 in. liquid chromatography column packed with a chiral stationary phase derived from (*R*)-phenylglycine has been found capable of resolving gram or larger samples of a variety of racemates. Nine such resolutions are presented. The racemates resolved include alcohols, lactams, lactones, sulfoxides, bi-β-naphthols, and hydantoins. Use of the column in an automated preparative chromatography system is demonstrated.

Since Prelog's partial resolution of Troger's base on lactose in 1944,[1] a number of attempts have been made to resolve useful quantities of enantiomers by chromatographing racemates upon chiral adsorbents. Typically, readily available naturally occurring materials (cellulose, wool, sugars, starches) have been used, and, while there have been sporadic successes, the usual result is incomplete separation of enantiomers.[2] Synthetically prepared chiral stationary phases (CSPs) have a somewhat similar record, notable exceptions being the polyacrylamide CSP of Blaschke, upon which complete separation of enantiomers was achieved for 530 mg of racemic chlorthalidone,[3] and the proline CSP of Jozefonvicz, upon which complete resolution was achieved for 160 mg of racemic proline by ligand-exchange chromatography.[4]

For some time we have been interested in the development of chromatographic methods for separating enantiomers. We recently described a high-performance liquid chromatographic column packed with 5-μm spherical silica particles to which is bonded CSP 1 upon which one can separate the enantiomers of a wide array of solutes.[5-8] Such columns are primarily intended to serve as analytical tools for the determination of enantiomeric purity and absolute configuration, even though they can also be used to resolve milligram quantities of enantiomers.[9] We now describe the use of a preparative version of this type of column and report a number of examples where gram-sized or larger samples of racemates have been successfully resolved.[10] We also describe the automated resolution of an alcohol useful as a starting material for a different type of CSP.

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(1) Prelog, V.; Wieland, P. *Helv. Chim. Acta* **1944**, *27*, 1127.

(2) Many such instances are cited in the following reviews: Buss, D. R.; Vermeulen, T. *Ind. Eng. Chem.* **1968**, *60*, 12. Blaschke, G. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 13.

(3) Blaschke, G.; Markgraf, H. *Chem. Ber.* **1980**, *113*, 2031.

(4) Jozefonvicz, J.; Petit, M.; Szubarga, A. *J. Chromatogr.* **1978**, *147*, 177.

(5) Pirkle, W. H.; Finn, J. M.; Schreiner, J. L.; Hamper, B. C. *J. Am. Chem. Soc.* **1981**, *103*, 3964.

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(9) Chiral HPLC columns of this type are available from the Regis Chemical Co., Morton Grove, IL, and from the J. T. Baker Chemical Co., Phillipsburg, NJ.

(10) A portion of this work was presented at the 179th National Meeting of the Americal Chemical Society, Houston, TX, 1980.

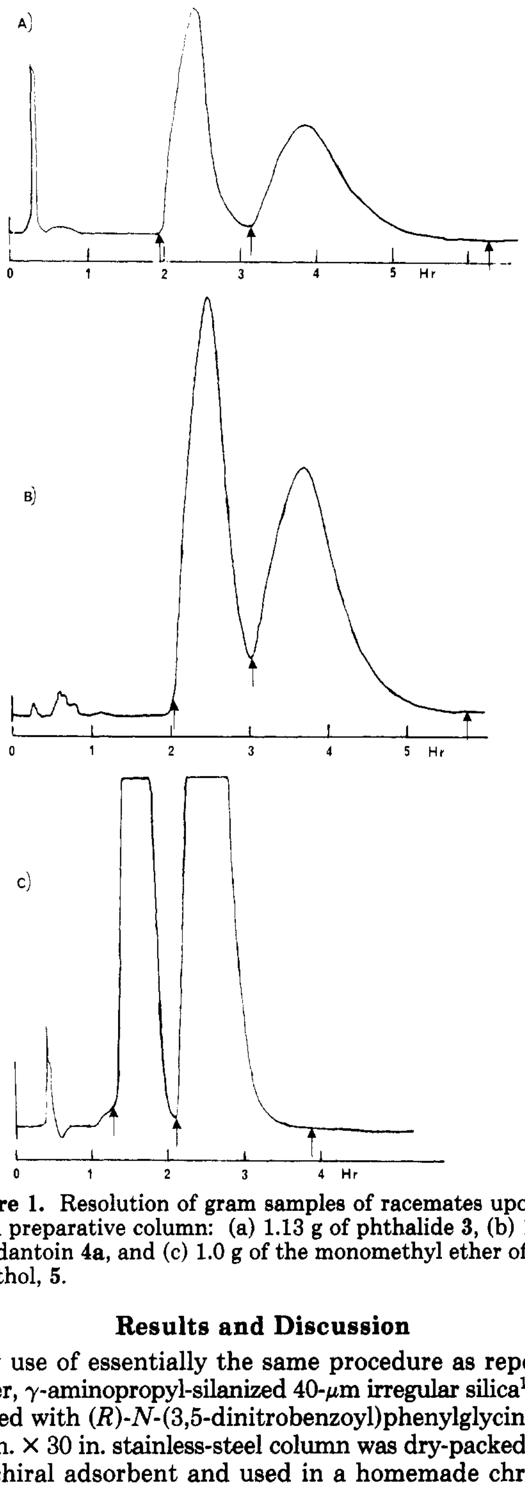

Figure 1. Resolution of gram samples of racemates upon the chiral preparative column: (a) 1.13 g of phthalide **3**, (b) 1.60 g of hydantoin **4a**, and (c) 1.0 g of the monomethyl ether of bi-β-naphthol, **5**.

Results and Discussion

By use of essentially the same procedure as reported earlier, γ-aminopropyl-silanized 40-μm irregular silica[11] was treated with (*R*)-*N*-(3,5-dinitrobenzoyl)phenylglycine (**2**). A 2 in. × 30 in. stainless-steel column was dry-packed with the chiral adsorbent and used in a homemade chromatography system, modified since its earlier description.[12] This automated system is capable of loading the column and collection of predesignated chromatographic bands into selected receivers from which the mobile phase is continuously distilled and returned to the pump reservoir. Automated repetition of the entire sequence is possible, although most of the presently reported resolutions were not so conducted.

Owing to the use of 40-μm irregular silica particles, the preparative column is of lower efficiency than the 5-μm-derived analytical column. However, the enantiomeric separability factor, α,[13] is somewhat greater.[14] In practice, the analytical column is used to quickly gauge the feasibility, conditions, and permissable scale of a preparative resolution. We have found that preparative resolution is routine in cases where the racemate is resolved upon a type-1 analytical column with an α value of 1.2 or greater. Figure 1 illustrates several representative preparative resolutions; Table I provides additional examples and pertinent data. Unless otherwise noted, each enantiomer was collected in a single fraction, the enantiomeric purity of that fraction being determined upon the analytical column. For the resolutions illustrated in Figure 1, each enantiomer was of >99% enantiomeric purity.

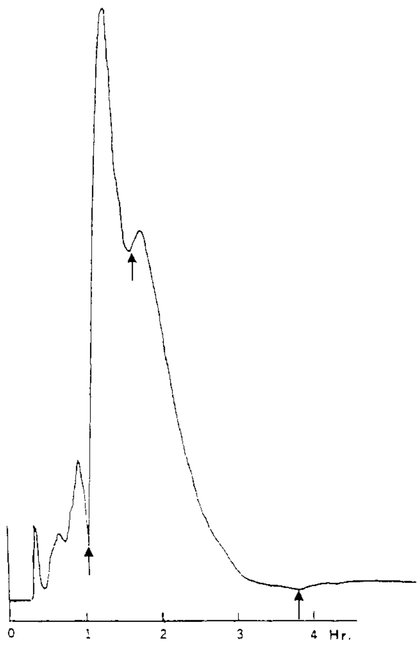

Figure 2. Resolution of 8 g of racemic alcohol **6** on the chiral preparative column. Owing to the distortion of band shapes, the fraction cutting occurred later than optimum.

The greater the magnitude of α, the greater the amount of racemate that can be resolved in a single pass. The α value noted for 2,2,2-trifluoro-1-(10-methylanthr-9-yl)-ethanol (**6**) is 1.45. Two grams of this alcohol can be resolved uneventfully although the enantiomeric purity of the second fraction is slightly reduced by tailing of the first band. Chromatography of an 8-g sample of this alcohol afforded reasonably good results (Figure 2) although band-shape distortion somewhat obscured the optimum point for fraction collecting. In the event of incomplete separation of the two enantiomers (small α' or sample overload), one might profitably collect more than two fractions or employ recycling techniques. For example, a 3.0-g sample of sulfoxide **7** (α = 1.24) was chromatographed, and each enantiomer was collected as early and late fractions. The outer fractions, comprising about 50% of the total, were of >99% enantiomeric purity. The middle fractions were rechromatographed.[15] Often, recrystallization of an incompletely resolved enantiomer will

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(11) This material is available from the J. T. Baker Chemical Co., Phillipsburg, NJ, as is the final chiral adsorbent.

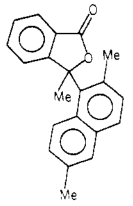
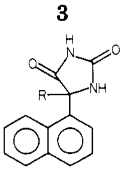
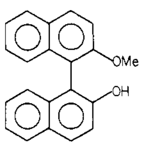
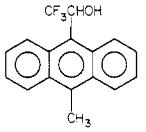
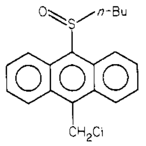
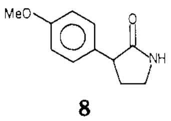
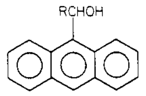
(12) Pirkle, W. H.; Anderson, R. W. *J. Org. Chem.* **1974**, *39*, 3901.

(13) The enantiomeric separability factor, α, is simply the ratio of the retention times of the enantiomers measured from the elution point of a nonretained substance. More directly, α is a ratio of the partition coefficients of the enantiomers between the stationary and mobile phases and is related to the stability difference of the diastereomeric interactions that occur during chromatography.

(14) The differences in α occur because of differences between the surfaces of the two types of silica, not because of differences in particle size.

(15) An alternate approach in such an instance would have involved recycling the largely resolved middle fractions back onto the column for a second pass.

Table I. Resolution of Racemates on a Preparative Liquid Chromatographic Column Packed with CSP 1

compd	g	α	% ee		% IPA in hexane
			first	second	
 3	1.13	1.68	>99	>99	10
 4a, R = $(CH_2)_3CH{=}CH_2$	1.60	1.55	>99	>99	10
b, R = CH_3	1.00	1.37	88	92	10
 5	1.00	1.86	>99	>99	5
 6	1.00	1.47	>99	>99	5
	2.00		>99	96	
	4.00		79	85	
	8.00		73	94	
 7	3.00	1.24	see text		5
 8	1.00	1.42	>99	92	10
 9a, R = CF_3	1.00	1.46	97	94	2
b, R = n-C_4H_9	1.00	1.63	97	99	5

afford enantiomerically pure material. In such instances, one might intentionally overload the column with the intention of quickly obtaining a quantity of substantially enriched material suitable for recrystallization.

Finally, as a demonstration the Maxwell's Demon-like character of the chiral column–automated chromatograph combination, 14 g of racemic alcohol 6 was resolved in 16 h in four portions. Once started, the system required no intervention by the operator. Figure 3 illustrates the repetitive nature of this resolution mode.

Experimental Section

General Procedures. Microanalyses were performed by J. Nemeth and Associates, University of Illinois. Solutes used herein were available from other studies; those not reported heretofore have been completely characterized and are unexceptional in their preparation. Analytical chromatography was performed with a Beckman 100A pump, a Model 152 dual-wavelength (254 and 280 nm) detector, and a Model 210 injector. Preparative chroma-

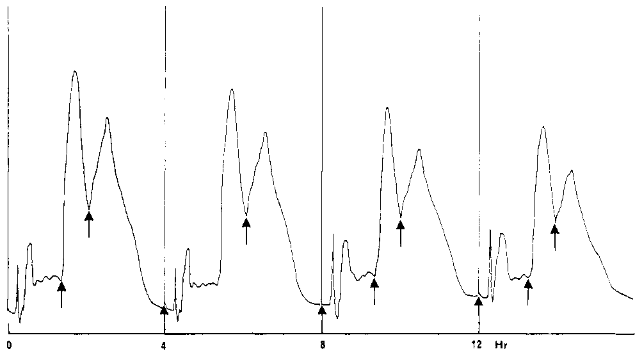


Figure 3. Automated repetitive chromatographic separation of the enantiomers of racemic alcohol 6 upon the chiral preparative column. Sample injections (lines) of ca. 3.5 g occur every 4 h. The volume of sample gravity-fed into the loop during a fixed interval progressively diminished as the sample reservoir emptied, owing to the diminishing hydrolic head. Automated fraction cuts occur at the arrows.

tography was conducted on the previously described system which now uses a Crane 202-C-50-43-5M ChemPump, a somewhat modified solvent-recovery system, and a sample injector comprised of a reservoir which gravity feeds sample into a loop through electrically operated solenoid valves.

Preparation of the Chiral Adsorbent 1. To a slurry of 900 g of γ-aminopropyl-silanized 40-μm irregular silica in 1 L of THF was added a THF solution of 250 g of (*R*)-*N*-(3,5-dinitrobenzoyl)phenylglycine (**2**) in 1 L of THF. After overnight stirring, the adsorbent was isolated by filtration and washed with THF and with CH_2Ch_2.

Anal. Found: C, 15.18; H, 1.97; N, 4.16; Si, 33.27. Calcd for 0.69 mol of chiral sites/g of support (based on C) and 0.70 mol of chiral sites/g of support (based on N).

Resolution of Racemates. The adsorbent was dry packed into a 2 in. × 30 in. stainless-steel column. Chromatographic resolutions were performed on an automated system by using hexane containing varying amounts of 2-propanol as a mobile phase. The racemic solutes were injected as CH_2Cl_2 solutions. Enantiomeric purity assays were performed directly on chromatographic fractions. The high-R_r and low-R_f enantiomers of several of the solutes were once recrystallized after resolution and found to have the following properties.

3-(2,6-Dimethylnaphth-1-yl)-3-methylphthalide (3). High-R_f enantiomer: mp 119–120 °C; $[\alpha]_D$ −474.9° (*c* 1.60, $CHCl_3$). Low-R_f enantiomer: mp 118–119 °C; $[\alpha]_D$ +460.0° (*c* 1.58, $CHCl_3$).

5-(1-Naphthyl)-5-(4-pentenyl)hydantoin (4a). High-R_f enantiomer: mp 199.5–200 °C; $[\alpha]_D$ −7.9° (*c* 1.45, EtOAc).

5-(1-Naphthyl)-5-methylhydantoin (4b). High-R_f enantiomer: mp 250 °C; $[\alpha]_D$ −84.2° (*c* 0.89, THF). Low-R_f enantiomer: mp 260 °C; $[\alpha]_D$ +83.9° (*c* 0.67, THF).

2′-Methoxy-2-hydroxy-1,1′-binaphthyl (5). High-R_f enantiomer: mp 107–110 °C; $[\alpha]_D$ −49.1° (*c* 1.54, $CHCl_3$). Low-R_f enantiomer: mp 108–112 °C; $[\alpha]_D$ +47.7° (*c* 0.94, $CHCl_3$).

2,2,2-Trifluoro-1-(10-methylanthr-9-yl)ethanol (6). High-R_f enantiomer: mp 138–139 °C; $[\alpha]_D$ −38.1 (*c* 1.81, EtOH). Low R_f enantiomer: mp 135–137 °C; $[\alpha]_D$ +32.5° (*c* 1.08, EtOH).

***n*-Butyl 10-(Chloromethyl)anthr-9-yl Sulfoxide (7).** High-R_f enantiomer: mp 108–111 °C; $[\alpha]_D$ −132.8° (*c* 2.14, $CHCl_3$). Low R_f enantiomer: mp 109–111 °C; $[\alpha]_D$ +127.0° (*c* 0.60, $CHCl_3$).

3-*p*-Anisyl-2-pyrrolidinone (8). High-R_f enantiomer: mp 82–83 °C; $[\alpha]_D$ −27.9° (*c* 1.89, $CHCl_3$). Low-R_f enantiomer: mp 82–83 °C; $[\alpha]_D$ +29.4° (*c* 3.08, $CHCl_3$).

2,2,2-Trifluoro-1-(9-anthryl)ethanol (9a). High-R_f enantiomer: mp 129–130 °C; $[\alpha]_D$ −30.1° (*c* 2.2, $CHCl_3$). Low-R_f enantiomer: mp 131–132 °C; $[\alpha]_D$ +30.0° (*c* 3.1, $CHCl_3$).

Acknowledgment. This work has been funded by the National Science Foundation. We are grateful to the J. T. Baker Chemical Co. for a gift of γ-aminopropyl-silanized silica and to the Kay-Fries Co. for gifts of (*R*)-phenylglycine and triethoxy(γ-aminopropyl)silane. Phthalide **3** and hydantoin **4a** were prepared by Thomas Sowin and Myung Ho Hyun, respectively.

Registry No. (*R*)-**2**, 74927-72-3; (±)-**3**, 82752-65-6; (+)-**3**, 82752-70-3; (−)-**3**, 82752-71-4; (±)-**4a**, 82752-66-7; (+)-**4a**, 82752-72-5; (−)-**4a**, 82752-73-6; (±)-**4b**, 82752-67-8; (+)-**4b**, 82752-74-7; (−)-**4b**, 82752-75-8; (±)-**5**, 35193-70-5; (+)-**5**, 79547-82-3; (−)-**5**, 35193-69-2; (±)-**6**, 74958-72-8; (+)-**6**, 63017-54-9; (1)-**6**, 53282-95-4; (±)-**7**, 82752-68-9; (+)-**7**, 82752-76-9; (−)-**7**, 82752-77-0; (*u*)-**8**, 82752-69-0; (+)-**8**, 82752-78-1; (−)-**8**, 82752-79-2; (±)-**9a**, 60686-64-8; (+)-**9a**, 60646-30-2; (−)-**9a**, 53531-34-3; (±)-**9b**, 77495-10-4; (+)-**9b**, 82752-80-5; (−)-**9b**, 82752-81-6.

α-Nitro Ketones and Esters from Acylimidazoles

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Received March 2, 1982

The anion of 2-(2-nitroethyl)-1,3-dioxolane (4), prepared from the corresponding 2-bromo compound (3), undergoes condensation with acylimidazoles to give the 3-nitro-4-oxobutanal acetals (9), which can serve as valuable polyfunctional intermediates. Condensation with 1-(methoxyoxalyl)imidazole gives the tetrafunctionalized methyl 4-(1,3-dioxolan-2-yl)-3-nitro-2-oxobutanoate (13), which, however, decomposed on attempted deprotection of the ester function. The syntheses in excellent yields of simple α-nitro ketones and α-nitro esters from acylimidazoles and nitroethane and 2-nitropropane are also described.

Aliphatic nitro compounds are valuable synthetic intermediates;[1] however, their full potential has not been realized because of the limited availability of satisfactory synthetic methods involving carbon–carbon bond-forming reactions of such nitro compounds. A major reason for this has been the propensity of aliphatic nitro compounds to undergo oxygen alkylation and acylation in preference to carbon alkylation[2] and acylation.[3,4] This has been overcome in an important way by the double deprotonated intermediates introduced by Seebach et al.,[5] but again this technique is not as widely applicable as one might wish. The mechanism of carbon alkylation of nitro compounds has been studied extensively.[3-9] The factors influencing the oxygen vs. carbon alkylation of ambident anions has been reviewed by le Noble.[10]

A significant improvement on the C-acylation of nitromethane anion was introduced by Baker and Putt,[4] by the use of highly reactive acylimidazoles as the acylating agents; however, this method was not extended to other aliphatic nitro compounds. We had made use of acylimidazoles in the synthesis of α-keto esters[11,12] and sought

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(1) D. Seebach, E. W. Calvin, F. Lehr, and T. Weller, *Chimia*, **33**, 1 (1979).

(2) L. Weiser and R. W. Helmkamp, *J. Am. Chem. Soc.*, **67**, 1167 (1945).

(3) G. B. Bachman and T. Hokama, *J. Am. Chem. Soc.*, **81**, 4882 (1959).

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(9) N. Kornblum, *Org. React.*, **12**, 101 (1962).

(10) W. J. le Noble, *Synthesis*, 1–6 (1970).

0022-3263/82/1947-4040$01.25/0