TABLE I
YIELD AND ANALYTICAL DATA ON PARA-SUBSTITUTED MANDELALDEHYDE DIMERS

Para substituent	Yield of 4, %	Yield of 6, %	Mp, °C	Formula	Calcd, % C	Calcd, % H	Calcd, % N or X	Found, % C	Found, % H	Found, % N or X
CH_3O	60	53	148–150	$C_9H_{10}O_3$	65.05	6.07		65.10	6.13	
CH_3	58	37	148–150	$C_9H_{10}O_2$	71.98	6.71		72.13	6.79	
Cl	52	61	160–161	$C_8H_7ClO_2$	56.33	4.14	20.78	56.24	4.12	20.56
F_3C	45	20	159–162	$C_9H_7F_3O_2$	52.95	3.46	27.92	*a*		
NO_2	27	40	163–167	$C_8H_7NO_4$	53.04	3.90	7.73	53.14	4.04	7.14

[a] Satisfactory analyses could not be obtained for the *p*-trifluoromethylmandelaldehyde dimer **6e**, the results being consistently low in carbon and fluorine. Nmr analysis, however, indicated that a trifluoromethyl, rather than a difluoromethyl, group was present.

100–101° (4.5 mm) [lit.[10] bp 133° (16 mm)]; ir (liquid) 1700 (C=O) and 1120 cm^{-1} (CH_3OC); nmr (CCl_4) δ 3.40 (s, 6, CH_3O), 5.03 (s, 1, CH), 7.18–7.53 (m, 3, Ar H), and 8.03–8.20 ppm (m, 2, Ar H). To a stirred suspension of 28.5 g (0.75 mol) of lithium aluminum hydride in 600 ml of tetrahydrofuran, a solution of 77 g (0.43 mol) of **3a** in 75 ml of tetrahydrofuran was added, dropwise, over a period of 1 hr. After refluxing for 12 hr the reaction mixture was cooled to 0°, treated with water, and worked up in the usual way to yield, after distillation of the crude product through a 75-cm spinning band column, 62 g (80%) of mandelaldehyde dimethyl acetal (**4a**) as a colorless liquid: bp 80–82° (0.5 mm); ir (liquid) 3550 (OH), 2990 (CH_3), and 1130 cm^{-1} (CH_3OC); nmr ($CDCl_3$) δ 3.08 (s, 3, CH_3O), 3.28 (s, 4, CH_3O plus OH), 4.11 (d, 1, J = 6.5 Hz, H at C-2), 4.49 (d, 1, J = 6.5 Hz, H at C-1), and 7.12–7.38 ppm (m, 5, Ar H). A-62 g (0.34 mol) sample of this material was added to 1500 ml of 0.5 *N* hydrochloric acid, and the mixture was stirred at room temperature for 5 days. The precipitated solid was collected by filtration and washed, consecutively, with water and reagent grade acetone to yield 36 g (75%) of mandelaldehyde dimer **6a** as a white powder, mp 149–152°. Further purification was effected by acetone extraction of this material for 5 days in a Soxhlet apparatus, the material remaining in the extraction thimble being obtained as a white powder: mp 164–165° (lit.[5] 134–137°); ir (KBr) 3550 (OH) and 1140 cm^{-1} (COC); uv (95% ethanol) 248 nm (ϵ 106), 252 (151), 258 (192), 264 (147), and 295 (6); nmr (degassed DMSO-d_6) δ 5.20 (d of d, 2, J = 5.0 and 2.0 Hz, CHCHOH), 5.37 (d, 2, J = 2.0 Hz, CHCHOH), 6.30 (d, 2, J = 5.0 Hz, CHCHOH), and 7.21–7.59 ppm (m, 10, Ar H).

Anal. Calcd for $C_8H_8O_2$: C, 70.57; H, 5.92. Found: C, 70.35; H, 6.02.

Deuteromandeladehyde Dimer 6g.—Substituting lithium aluminum deuteride for lithium aluminum hydride, a 90-g sample of **3a** was reduced in the fashion described above to yield, after distillation through a 75-cm spinning band column, 78 g (87%) of **4g** as a colorless oil: bp 88–90° (1 mm); ir (liquid) 3590 (OH), 3000 (CH_3), and 2180 cm^{-1} (CD); nmr (CCl_4) 3.08 (s, 3, CH_3O), 3.28 (s, 4, CH_3O plus OH), 4.12 (s, 1, CH), and 7.10–7.37 (m, 5, Ar H). This was hydrolyzed and the crude product purified as described above to yield **6g** as a colorless powder: mp 164–165°; ir (KBr) 3550 (OH), 2180 (C–D), and 1140 cm^{-1} (COC); nmr (degassed DMSO-d_6) δ 5.20 (d, 2, J = 5.0 Hz, CDCHOH), 6.30 (d, 2, J = 5.0 Hz, CDCHOH), and 7.21–7.59 ppm (m, 10, Ar H).

Para-Substituted Mandelaldehyde Dimers 6b–f.—*p*-Methoxy-, *p*-methyl-, *p*-chloro-, and *p*-trifluoromethylmandelaldehyde dimers were prepared in a fashion identical with that described above for mandelaldehyde dimer itself. In the preparation of *p*-nitromandelaldehyde dimer (**6f**) the reduction of the keto acetal **3f** was accomplished with sodium borohydride. The optimum yields in these syntheses were realized without isolation of intermediate reaction products until the substituted mandelaldehyde dimethyl acetals **4b–f** were reached, at which point purification was accomplished by distillation through a 75-cm spinning band column. The yields of the mandelaldehyde dimethyl acetal and the mandelaldehyde dimer, along with analytical data on the latter, are recorded in Table I.

Registry No.—**3a**, 6956-56-5; **4a**, 21504-23-4; **4g**, 29568-40-9; **6a**, 21504-13-2; **6b**, 29568-41-0; **6c**, 29568-42-1; **6d**, 29568-43-2; **6e**, 29568-44-3; **6f**, 29568-45-4; **6g**, 29568-46-5.

Acknowledgment.—This work was supported, in part, by Grant No. 5 RO1 AM 02398 from the National Institutes of Health and Grant No. GP-11087X from the National Science Foundation to whom the authors express their gratitude.

(10) W. Madelung and M. E. Oberwegner, *Chem. Ber.*, **65**, 931 (1932)

The Reduction of Some Halocyclopropanes with Sodium Naphthalenide

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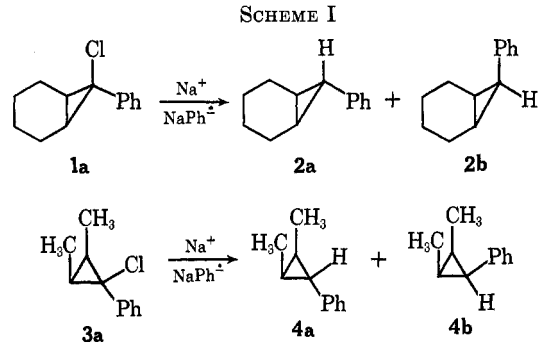
Herein we report some interesting solvent and temperature effects on the stereochemistry of the reduction of *anti*-7-phenyl-7-chloronorcarane (**1a**) and *anti*-1-phenyl-1-chloro-*cis*-2,3-dimethylcyclopropane (**3a**) with sodium naphthalenide (Scheme I).

SCHEME I



Compound **3a** was obtained in pure form by methods previously described.[2] Compound **1a** was synthesized by similar means (see Experimental Section) and has spectral and physical properties consistent with those reported by Schober.[3] The product ratios obtained in the reductions were determined by gas chromatography and are contained in Tables I and II.

We have defined as "dilute conditions" those reductions in which the reducing agent is added dropwise to a solution of the cyclopropyl halide, while "concen-

(1) Abstracted from the honors thesis of G. W. and the masters thesis of R. L. T., Middlebury College, 1970.
(2) D. B. Ledlie and S. MacLean, *J. Org. Chem.*, **34**, 1123 (1969).
(3) D. L. Schober, Ph.D. Thesis, University of Chicago, 1969.

TABLE I[a,b]
RELATIVE PERCENTAGES OF PRODUCTS OBTAINED IN THE REDUCTION OF 1a AND 3a WITH SODIUM NAPHTHALENIDE IN THF OR DME SOLVENT SYSTEMS

	Solvent (reagent solvent)	Room temp 2a	2b	4a	4b	−79° 2a	2b	4a	4b
	Dilute Conditions								
1	THF (THF)	64	36	86	14	83	17	92	8
2	DME (DME)	42	58	58	42				
	Concentrated Conditions								
3	THF (THF)	40	60	42	58	42	58	76	24
4	DME (DME)	40	60	58	42				

[a] Each entry is an average of at least two trials. In all cases data obtained in repeated runs differed by no more than 3%. [b] Absolute yields were between 80 and 100% for the reduction of 1a. Absolute yields were not determined for the reduction of 3a; however, in a similar study carried out in this laboratory which employed sodium biphenylide as the reducing agent yields averaged greater than 80%.

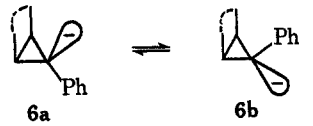
TABLE II[a]
RELATIVE PERCENTAGES OF PRODUCTS OBTAINED IN THE REDUCTION OF 1a AND 3a WITH SODIUM NAPHTHALENIDE IN DIETHYL ETHER SOLVENT SYSTEMS

	Solvent (reagent solvent)	Room temp 2a	2b	4a	4b	−79° 2a	2b	4a	4b
	Concentrated Conditions								
1	Et_2O (THF)	12	88	29	72	41	58	61	38
2	Et_2O (DME)	26	74	45	55				

[a] Each entry is an average of at least two trials. In all cases data obtained in repeated runs differed by no more than 3%.

trated conditions" are those in which the cyclopropyl halide is added to a solution of the reducing agent.[4]

As may be observed in Table I, the reductions carried out in tetrahydrofuran at −79° afforded a greater percentage of anti isomer than the corresponding reductions carried out at room temperature. In other words, as the temperature is lowered an increase in the thermodynamically more stable isomer results.[6] We feel that this occurs as a result of an increase in the concentration of the more stable cyclopropyl carbanion intermediate **6a** generated during the course of the reduction at this temperature. Several investigations which have



6a **6b**

= CH_3-, CH_3- or $-CH_2(CH_2)_2CH_2-$

a bearing on the mechanism of sodium naphthalenide and sodium biphenylide reductions of various organo halides have recently appeared.[5,7] From a perusal of these studies it seems quite clear that reductions of of alkyl bromides and chlorides with these reagents proceed *via* two, fast, one-electron transfers affording a carbanion which then abstracts a proton from solvent.

$$RX \xrightarrow{e} R\cdot + X^- \xrightarrow{e} R^- \xrightarrow{SH} RH$$

In addition, hydrogen abstraction from solvent by an intermediate radical does not seem to be a major competing reaction for the alkyl systems.[8] It is our contention that in the reduction of a system such as **1a** or **3a** a cyclopropyl radical is generated in which the barrier to inversion is quite low.[10,11] Thus, stereochemical integrity is quickly lost. A second electron is then rapidly added to generate the cyclopropyl carbanions **6a** and **6b** which because of the adjacent phenyl substituent are interconvertable. At the lower temperature there is a preponderance of **6a**, and as a result an increase in the percentage of the anti product is observed at this temperature.

If the reaction conditions are reversed (concentrated conditions, tetrahydrofuran), considerably more of the syn isomer is formed. It was observed that these reductions were much slower than for the corresponding dilute cases. Reactions carried out under the dilute conditions could be quenched immediately after the reducing agent had been added without effecting the yields of products. However, under the concentrated conditions the reaction mixture had to be stirred approximately 0.5 hr before starting material was completely consumed. This would imply that the halocyclopropanes are not soluble in the reducing medium, and perhaps the heterogeneous nature of the system and the more highly structured nature of the reducing medium as compared to the dilute cases places steric constraints upon the protonation process such that protonation from the less-hindered face of the carbanion is favored. This would result in more syn product.

In the dimethyoxyethane (DME) reductions, however, the product ratios are identical for both dilute and concentrated conditions. It might be argued that, due to the greater size of the DME molecule in comparison to that of THF, more of the syn product would be expected in the DME reductions and this is the overriding factor under both sets of reaction conditions. Further, one might expect to observe more of the syn product in reductions of **1a** than in the corresponding reductions of **3a** since the steric bulk of the methylene bridge in the carbanion derived from **1a** should tend to make protonation from the syn face of the molecule (resulting in anti product) less favorable than for the carbanion derived from **3a** which lacks a methylene bridge. In all cases tabulated in Table I this is observed.

Sodium naphthalenide has been shown to be unstable in diethyl ether; however, if enough THF and DME are present to adequately solvate the radical anion, solutions of the radical anion in THF–Et_2O or DME–Et_2O can be prepared.[12]

Several reductions were carried out employing solutions which were prepared by adding an excess of the reducing agent, dropwise, to 15 ml of anhydrous diethyl ether (see Table II). These solutions possessed the characteristic green color of the radical anion; however, their homogeneity is somewhat questionable since the

(4) The designation "dilute conditions" is not strictly correct since the reaction of the halide with the radical anion is very rapid and is probably over before the drop of reducing agent is completely dispersed.[5]

(5) S. J. Cristol and R. V. Barbour, *J. Amer. Chem. Soc.*, **90**, 2832 (1968).

(6) G. L. Gloss and R. A. Moss *ibid.*, **86**, 4042 (1969).

(7) (a) S. J. Cristol and R. W. Gleason, *J. Org. Chem.*, **34**, 1762 (1969); (b) J. F. Garst, P. W. Ayres, and R. C. Lamb, *J. Amer. Chem. Soc.*, **88**, 4260 (1966); (c) G. D. Sargent and M. W. Browne, *ibid.*, **89**, 2788 (1967); (d) G. D. Sargent, J. N. Cron, and S. Bank, *ibid.*, **88**, 5363 (1966); (e) J. Jacobs and D. Pensak, *Chem. Commun.*, 400 (1969).

(8) Walborsky and Chen have recently demonstrated in one case that a cyclopropyl radical is more reactive than an alkyl radical; thus, in our systems some hydrogen abstraction by an intermediate cyclopropyl radical may indeed be taking place.[9]

(9) H. M. Walborsky and J. Chen, *J. Amer. Chem. Soc.*, **92**, 7573 (1970).

(10) (a) R. W. Fessenden and R. H. Schuler, *J. Chem. Phys.*, **39**, 2147 (1963); (b) M. J. S. Dewar and M. Shanshall, *J. Amer. Chem. Soc.*, **91**, 3654 (1969).

(11) A planar species cannot be ruled out in this instance.

(12) N. D. Scott, J. F. Walker, and V. C. Hansley, *ibid.*, **58**, 2442 (1936).

concentration of THF or DME is initially too low to stabilize the radical anion and thus sodium and naphthalene are probably formed to some extent. Of particular interest in Table II is the Et_2O (THF) system at room temperature which afforded considerably more of the syn product than did the THF (THF) system under comparable conditions (Table I). Again, one can envoke steric arguments in explaining these results; however, the probably nonhomogeneous nature of these solutions precludes a detailed picture of the protonation process.

It is evident from the data presented in Tables I and II that the stereochemistry of reduction for this type of system can be controlled by appropriate choice of reaction conditions. The problem of removing naphthalene and other aromatic by-products from the reaction mixture after a reduction has been carried out makes the synthetic worth of this technique somewhat questionable. In the systems here studied this was indeed a problem. However, one can envision phenylcyclopropane systems which are amenable to separation, and for these cases the technique has merit. Yields are usually high and cyclopropane cleavage products are not obtained. This is a serious drawback in the sodium–liquid ammonia reduction of cyclopropyl halides possessing a phenyl substitutent.

Experimental Section[13]

7-Phenyl-7-chloronorcarane (1a and 1b).—The compound was prepared in a 34% yield according to the method of Closs and Coyle.[14]

***anti*-7-Phenyl-7-chloronorcarane (1a).**—A mixture of the epimers **1a** and **1b** (27.3 g, 0.132 mol; 2/1 = **1a**/**1b**) and silver nitrate (8.99 g, 0.053 mol) in 50 ml of methanol was stirred for 24 hr. The reaction mixture was filtered, water and ether were added to the resulting solution, and the organic layer was separated. The reaction mixture was then worked up in the usual manner. Compound **1a** was separated from 7-phenyl-7-methoxynorcarane and 2-phenyl-3-methoxycycloheptene by column chromatography on silica gel and elution with ligroin. After five recrystallizations from pentane, 6.96 g of a white solid (mp 36–37°) was obtained. Spectral data and melting point were in complete agreement with those previously reported.[3]

***anti*-1-Phenyl-1-chloro-*cis*-2,3-dimethylcyclopropane (3a).**—The compound was prepared as previously described.[2]

Sodium Naphthalenide.—Sodium naphthalenide was prepared in both DME and THF according to the method of Scott.[12]

Sodium Naphthalenide Reductions.[15] **Dilute Conditions.**—To a solution of compound **1a** or **3a** (50 mg) in 15 ml of freshly dried DME or THF or ether was added dropwise with stirring approximately a twofold excess of sodium naphthalenide reagent (1.0 *M*). The reaction mixture was stirred for 5 min and quenched with water. An internal standard was added and the resulting mixture was analyzed by vpc (column a for the reduction of **1a** and column b for the reduction of **3b**).

Concentrated Conditions.—To a solution of 2 ml of reagent (1.0 *M*) in 15 ml of freshly dried DMF, THF, or ether was added with stirring neat or in solution approximately 50 mg of **1a** or **3b**. The reaction mixture was then stirred for 30 min. It was worked up and analyzed as described above.

Registry No.—**1a**, 6434-79-3; **3a**, 13154-00-2; sodium naphthalenide, 12521-84-5.

Acknowledgment.—Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of this research.

(13) Infrared spectra were determined with a Perkin-Elmer Model 137 or Model 457 recording spectrophotometer. All spectra were measured in carbon tetrachloride unless otherwise stated. The nmr spectra were measured at 60 Hz with an Hitachi Perkin-Elmer R20 spectrometer using tetramethylsilane as the internal reference. Columns used for gas chromatography (vpc) were (a) 10% Carbowax 20M 8 ft × 0.25 in. and (b) 20% DCQF1 12 ft × 1/8 in. All yields were determined by vpc. Unless otherwise stated, magnesium sulfate was employed as the drying agent. All reactions involving air or moisture sensitive compounds were carried out under a nitrogen atmosphere.

(14) G. L. Closs and J. J. Coyle, *J. Org. Chem.*, **31**, 2759 (1966).

(15) The reduction products were characterized by vpc retention times and comparison of infrared spectra with authentic samples. We thank Professor G. L. Closs for supplying us with the infrared spectra of compounds **2a** and **2b**.

Synthesis and Nuclear Magnetic Resonance Investigation of Some Fluorothiophenes

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Some years ago, we reported[1] the general synthesis of fluorine-containing thiophenes *via* the reaction of thienyllithiums with perchloryl fluoride. Recently renewed interest[2,3] in this reaction prompts us to report further work in this area. Fluorine derivatives of five-membered heterocycles have been only slightly investigated.[4] Recent evidence has indicated[5] that fluorine in the 2 position of thiophene has a stronger electron-withdrawing effect than in fluorobenzene. For these reasons, it became of interest to us to determine the position of electrophilic substitution and lithiation of 2-fluorothiophene.

Acylation of 2-fluorothiophene (**1**) with acetyl chloride and stannic chloride gave 5-fluoro-2-acetylthiophene (**2**). This ketone gave 5-fluoro-2-thenoic acid (**3**) upon treatment with sodium hypochlorite and base. Iodination of **1** by the iodine–mercuric oxide method and nitration, using nitric acid in acetic anhydride, also gave the corresponding 5-substituted products **4** and **5**. In all three of these examples, the products were 98% isomerically pure on the basis of nmr examination of the reaction mixture work-up. The assignment of substitution position was based on a comparison with recently observed coupling constants[2] for 2-fluorothiophene. In all cases, typical $J_{F\text{-}H_3}$ values of 1.4–2.1 Hz and $J_{H_3\text{-}H_4}$ values of 4.0–4.6 Hz were recorded (Table I).

Lithiation of 2-fluorothiophene with *n*-butyllithium followed by treatment with dimethylformamide gave 5-fluoro-2-thenaldehyde (**6**). The aldehyde was readily oxidized to **3** by silver oxide in base. The formation of **3** by this route as well as the observed nmr parameters for **6** (Table I) confirm the structure of the aldehyde.

(1) R. D. Schuetz, D. D. Taft, J. P. O'Brien, J. L. Shea, and H. M. Mork, *J. Org. Chem.*, **28**, 1420 (1963).

(2) S. Rodmar, B. Rodmar, M. K. Sharma, S. Gronowitz, H. Christiansen, and U. Rosen, *Acta Chem. Scand.*, **22**, 907 (1968).

(3) H. Christiansen, S. Gronowitz, B. Rodmar, S. Rodmar, J. Rosen, and M. K. Sharma, *Ark. Kemi.*, **30**, 561 (1969).

(4) Tetrafluorofuran is known but rapidly polymerizes at room temperature: J. Burdon, J. C. Tatlow, and D. F. Thomas, *Chem. Commun.*, 48 (1966). Tetrafluorothiophene is known and stable: J. Burdon, J. G. Campbell, I. W. Parsons, and J. C. Tatlow, *ibid.*, 27 (1969).

(5) Based on the difference in p*K* between 2-thenoic and 5-fluoro-2-thenoic acid: G. P. Nilles and R. D. Schuetz, *J. Org. Chem.*, in press.