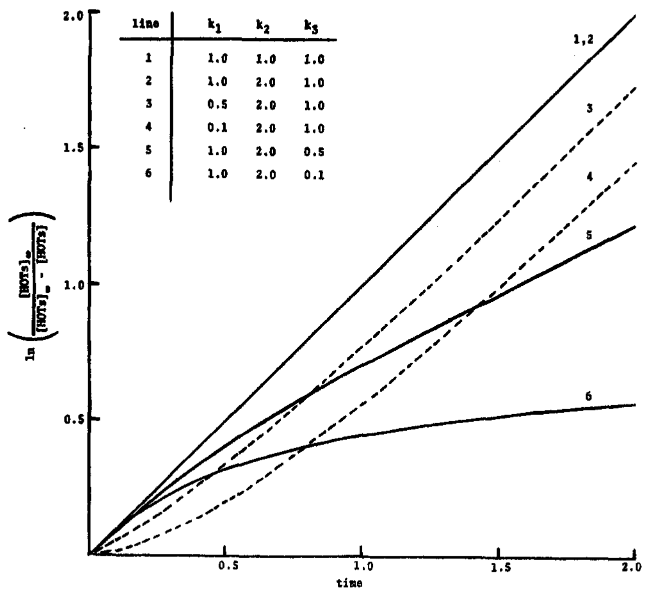

Figure 1.—Plots of $\ln \{ [\text{HOTs}]_\infty/([\text{HOTs}]_\infty - [\text{HOTs}]_t)\}$ *vs.* time for various values of k_1, k_2, and k_3 (eq 8).

where $K_1 = k_i k_r[\text{ROTs}]_0/(k_s + k_r)$ and $K_2 = k_i'k_s/(k_s + k_r)$. Solution of eq 10 as for eq 5 leads to

$$[\text{R'OTs}]_t = \frac{k_i k_r[\text{ROTs}]_0}{k_i'k_s - k_i k_s - k_i k_r}\left[e^{-k_i t} - e^{-\left(\frac{k_i'k_s}{k_s+k_r}\right)t}\right] \quad (11)$$

Applying the mass-balance relationship (eq 7), eq 11 gives

$$[\text{HOTs}]_t =$$
$$[\text{ROTs}]_0\left[1 - \frac{k_s(k_i - k_i')e^{-k_i t} + k_i k_r e^{-\left(\frac{k_i'k_s}{k_s+k_r}\right)t}}{k_i k_s + k_i k_r - k_i'k_s}\right] \quad (12)$$

One may consider the following special cases of eq 12.

(a) $k_r = 0$:

$$[\text{R'OTs}]_t = 0 \text{ and } [\text{HOTs}]_t = [\text{ROTs}]_0(1 - e^{-k_i t}) \quad (12a)$$

(b) $k_i' = 0$:

$$[\text{HOTs}]_t = \frac{k_s[\text{ROTs}]_0}{k_s + k_r}(1 - e^{-k_i t}) \quad (12b)$$

(c) $k_i = k_i'$:

$$[\text{HOTs}]_t = [\text{ROTs}]_0\left[1 - e^{-\left(\frac{k_i'k_s}{k_s+k_r}\right)t}\right] \quad (12c)$$

In both eq 12a and 12b it can be seen that k_t (eq 1) is to be identified with k_i, while in the case of eq 12c k_t will equal k_i $(=k_i')$ only if $k_r \ll k_s$, but above all it can be seen that

$$k_1 = \frac{k_i k_s}{k_s + k_r} \qquad k_2 = \frac{k_i k_r}{k_s + k_r} \qquad k_3 = \frac{k_i'k_s}{k_s + k_r}$$

and if $k_i \gg k_i'$

$$k_t = k_1 + k_2 = \frac{k_i k_s + k_i k_r}{k_s + k_r} = k_i$$

Thus the mechanism shown in eq 2 *is* an adequate representation of the "true" mechanism given in eq 9.

It is usually stated[1-5] that negative curvature in first-order plots of eq 1 indicates that $k_1 > k_3$ (or $k_i > k_i'$) and that positive curvature implies the converse. From eq 8 we see[9]

$$\frac{d}{dt}\ln\left(\frac{[\text{HOTs}]_\infty}{[\text{HOTs}]_\infty - [\text{HOTs}]_t}\right) =$$
$$\frac{d}{dt}\ln\left[\frac{k_1 + k_2 - k_3}{k_2 e^{-k_3 t} + (k_1 - k_3)e^{-(k_1+k_2)t}}\right] \quad (13)$$

Negative curvature will appear only if $k_3 < k_1$ *and* $k_1 \lesssim k_2$. Similarly positive curvature requires that $k_3 > k_1$ *and* $k_2 \gtrsim k_1$. Thus for there to be any deviation from linearity k_2 must be at least comparable in magnitude to k_1. Sample plots with various relative values of k_1, k_2, and k_3 are shown in Figure 1.[12] As may be obvious from eq 13, lines 3 and 4 (positive curvature) as well as lines 5 and 6 (negative curvature) all approach having slopes equal to k_3 as $t \rightarrow \infty$.

Acknowledgments.—We wish to thank Professor Paul von R. Schleyer for a stimulating discussion. Acknowledgment is made to the donors of the Petroleum Research Fund of the American Chemical Society for support of this work.

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[12] A FORTRAN IV program has been written which permits best values for k_1, k_2, and k_3 (eq 2) to be calculated. The program is of the interactive on-line variety, making use of a remote console. Initial estimates of the rate constants are progressively refined until the deviation between calculated and experimental values of $\ln \{[\text{HOTs}]_\infty/([\text{HOTs}]_\infty - [\text{HOTs}]_t)\}$ reaches an acceptable value. A listing of the program will be supplied upon request.

Synthesis of Mandelaldehyde Dimers

David W. Griffiths[1] and C. David Gutsche*

Department of Chemistry, Washington University,
St. Louis, Missouri 63130

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As a model system for gaining information concerning the interconversion between glyceraldehyde and dihydroxyacetone, the isomerization of mandelaldehyde to 2-hydroxyacetophenone has been studied.[2] For this purpose it was necessary to secure mandelaldehyde itself, 1-deuteriomandelaldehyde, and several para-substituted mandelaldehydes; this paper describes the syntheses of these substances.

In an early attempt to prepare mandelaldehyde (**5a**) by the acid-catalyzed hydrolysis of mandelaldehyde acetate, Nef obtained only 2-hydroxyacetophenone as the product.[3] More recently, successful syntheses have been effected by oxidative hydrolysis of the dimethyl thioacetal by means of bromine[4] and iodine,[5] the product in both cases being identified on the basis of the infrared spectrum as the dimer of mandelaldehyde (**6a**). In the present scheme, simple acid-catalyzed hydrolysis of mandelaldehyde dimethyl acetal proved to be effective. The dimethyl acetal **4a** was synthesized by lithium aluminum hydride reduction of the dimethyl acetal of phenylglyoxal **3a** which, in turn, was prepared by the action of trimethyl orthoformate and methanol on phenylglyoxal **2a**.

The amorphous white powder obtained from the hydrolysis of **4a** had an elemental analysis compatible with a $(C_8H_8O_2)_n$ compound, showed a strong ir band at 1140 cm^{-1} characteristic of a C–O–C linkage, and was trans-

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[1] National Aeronautics and Space Administration Predoctoral Trainee, 1966–1969; National Science Foundation Predoctoral Trainee, 1969–1970.

[2] D. W. Griffiths and C. D. Gutsche, *J. Amer. Chem. Soc.*, in press.

[3] J. U. Nef, *Justus Liebigs Ann. Chem.*, **335**, 247 (1904).

[4] F. Weygand, H. J. Bestmann, H. Ziemann, and E. Klieger, *Chem. Ber.*, **91**, 1043 (1958).

[5] G. A. Russell and L. A. Ochrymowycz, *J. Org. Chem.*, **34**, 3618 (1969).

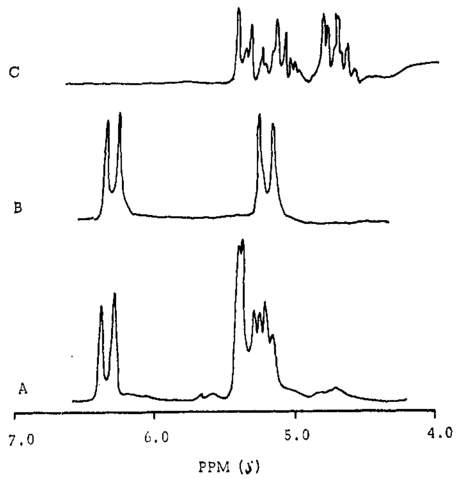
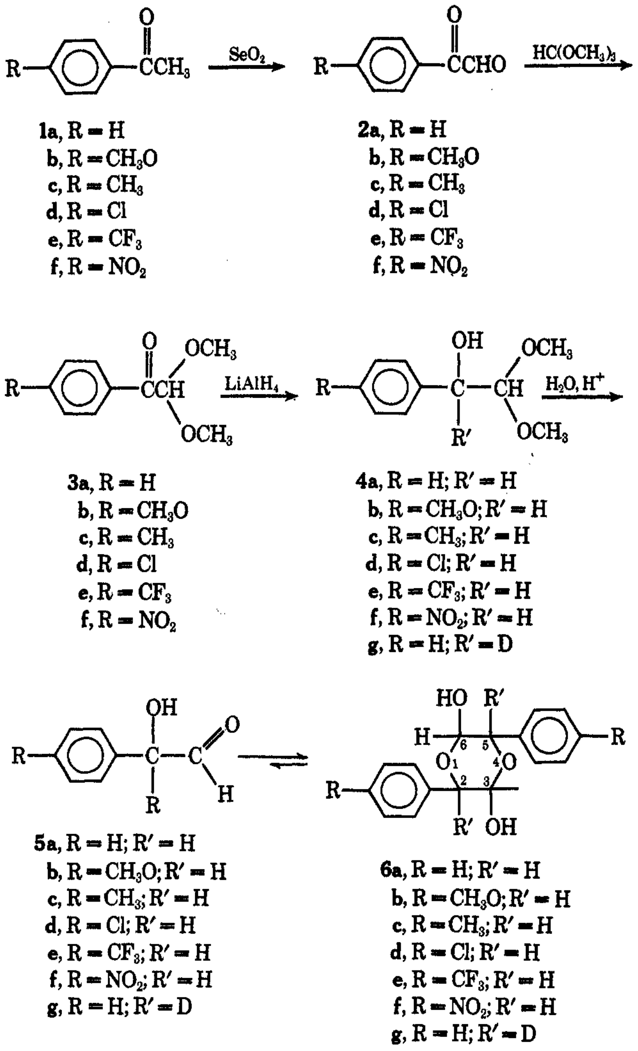


Figure 1.—Nmr spectra of mandelaldehyde dimers in DMSO-d_6: (A) freshly prepared dimer **6a**; (B) freshly prepared deuterated dimer **6g**; (C) aged dimer **6a**.

parent in the ir in the carbonyl region, in accord with the dimer structure **6a**. The nmr (see Figure 1) of freshly prepared samples of the dimer in dimethyl sulfoxide (DMSO-d_6) was rather simple, having a 10-proton multiplet for the aromatic protons, a 2-proton doublet for the protons at C-3 and C-6, a 2-proton doublet of doublets for the protons at C-2 and C-5, and a 2-proton doublet for the hydroxyl protons. Support for this interpretation was provided by the nmr spectrum (see Figure 1) of the C-3,C-6 dideuterio dimer **6g** (prepared by reducing **3a** with lithium aluminum deuteride), which displayed, in addition to the resonances arising from the aromatic ring, a pair of doublets with identical coupling constants. If, on the other hand, the sample of the dimer **6a** in DMSO-d_6 was allowed to stand at room temperature for several hours before spectral analysis, the spectrum was considerably more complex (see Figure 1), indicative of a mixture of isomers. In this spectrum, the resonance from the hydroxyl protons had become very broad.[6]

Para-substituted mandelaldehydes were prepared by the scheme outlined above for the parent compound. Only in the para nitro derivative case was the scheme modified with the substitution of sodium borohydride for lithium aluminum hydride in the reduction step.



In all cases, the products were assigned the dimeric structure on the basis of the ir spectra.

Experimental Section[7]

Mandelaldehyde Dimer 6a.[8]—Following a published procedure,[9] acetophenone (**1a**) was converted in 80% yield to phenylglyoxal **2a**. A 112-g (0.84 mol) sample of this material was treated with a cooled solution of 300 ml of trimethyl orthoformate and 300 ml of methanol containing 5.6 g of ammonium chloride. After being stirred at room temperature for 24 hr the solution was cooled, diluted with 500 ml of 0.2 *N* ammonium hydroxide solution, and extracted four times with ether. The combined ether extract was processed in the usual fashion to yield, after distillation of the residue through a 75-cm spinning band column, 110 g (73%) of the dimethyl acetal **3a** as a pale yellow liquid: bp

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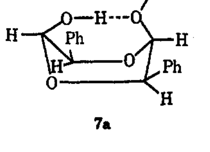
[6] To account for these observations, it is conjectured that the dimer, in the solid state, exists in a boat conformation stabilized by transannular hydrogen bonds (**7**). In this conformation the magnetic environments of the ring protons are essentially insensitive to the configuration at C-3 and C-6, thus producing equivalent sets of hydrogens in the three diastereomers for which transannular hydrogen bonding is possible. If, then, this conformation is retained in freshly prepared solutions, the less complex spectrum is observed. In solution, however, the transannular hydrogen bond structure can eventually equilibrate with other conformations which may, in turn, interconvert to other configurations at C-2 and C-5 through ring-opened intermediates to produce a mixture of diastereomers in which the equivalence of the ring protons as well as the hydroxyl protons is lost. In this case, the more complex spectrum is observed.



7a

[7] All melting points and boiling points are uncorrected. Infrared spectra were recorded on a Perkin-Elmer Model 137 Infracord spectrometer; uv spectra were recorded on a Cary Model 14 spectrometer; nmr spectra were recorded on a Varian Model A-60A spectrometer, and chemical shifts are reported in parts per million downfield shift from tetramethylsilane, used as an internal standard. The nmr spectrum of mandelaldehyde was obtained in degassed anhydrous hexadeuteriodimethyl sulfoxide solutions. The samples were prepared by placing a weighed amount of dry mandelaldehyde in an nmr tube fitted with a 10/30 standard taper joint. The tube was attached to a vacuum manifold, and after evacuation approximately 0.4 g of DMSO-d_6, previously degassed by at least three freeze–thaw cycles, was distilled into the sample tube through the all-glass system. The sample tube was then sealed off at 10^{-3} mm. Microanalyses were performed by Micro-Tech Laboratories, Skokie, Ill., and by Mikroanalytisches Laboratorium, Vienna, Austria.

[8] We are indebted to Dr. D. W. Holty for carrying out exploratory experiments in this series.

[9] H. A. Riley and A. R. Gray, "Organic Syntheses," Collect. Vol. II, Wiley, New York, N. Y., 1943, p 509.

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.

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

The Reduction of Some Halocyclopropanes with Sodium Naphthalenide

DAVID B. LEDLIE,* ROBERT L. THORNE,[1]
GEOFFREY WEISS[1]

Department of Chemistry, Middlebury College,
Middlebury, Vermont 05753

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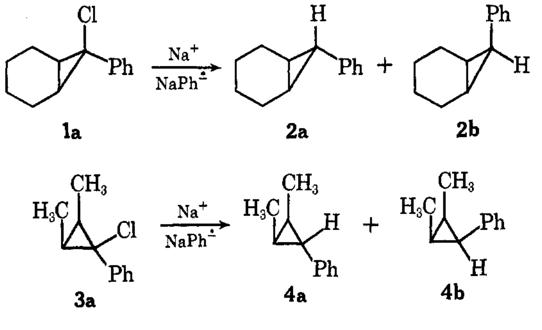
Herein we report some interesting solvent and temperature effects on the stereochemistry of the reduction of *anti*-7-phenyl-7-chloronorcarane (**1a**) and *anti*-1-phenyl-1-chloro-*cis*-2,3-dimethylcyclopropane (**3a**) with sodium naphthalenide (Scheme I).

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-

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[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.