Quantitative Studies in Stereochemistry by Isotope Dilution. Series B. Photochemistry. The Ratio of Diastereoisomeric Glycols Formed in the Ultraviolet-Promoted Bimolecular Reduction of Acetophenone-7-C^{14}

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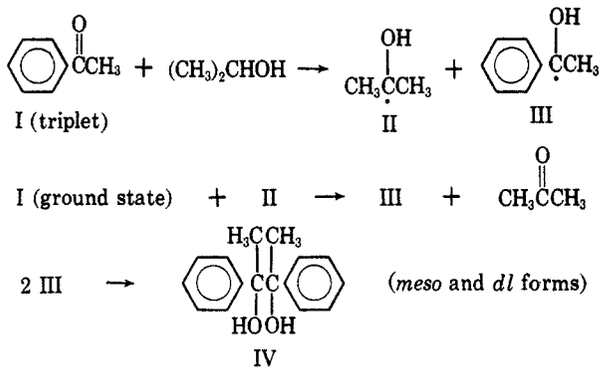
Irradiation of acetophenone in 2-propanol with ultraviolet light of wavelengths greater than 3000 A gave a quantitative yield of acetophenone pinacol with the *dl* form predominating over the *meso* in an 11:10 ratio. This ratio was independent of time, concentration of ketone, intensity of radiation, substitution of cyclohexane for 2-propanol, and degassing, although these factors varied the yield from 5 to 100%. No interconversion of diastereoisomers was observed. With light of shorter wavelength, a second process, not affected by the presence of oxygen, involving the preferential decay of the *meso* form was found. Under these latter conditions, interconversion of diastereoisomeric forms was observed.

The bimolecular reduction of ketones to pinacols in the presence of a suitable hydrogen donor under the influence of ultraviolet radiation has been known and studied extensively for over 60 years.[1] Two diastereoisomeric forms of the glycol, a *meso* and a *dl* form, are possible when unsymmetrical ketones are employed. While two pinacolic products have been isolated in some cases,[2] the statement does not appear to have been made that the reaction is stereoselective. A careful examination of the experimental sections of some studies in this area indicates that single pinacolic products of a narrow melting point range were isolated in greater than 50% yield;[3] by implication the reaction must have been at least stereoselective. Further, the predominant product does not appear to have been assigned a diastereoisomeric identity in any of these cases;[4] additionally, no reliable quantitative data are available. The present paper, to be the first of several, offers quantitative information about the stereochemical course of such a photochemical reaction. It is hoped that the study, when complete, will permit prediction and, possibly, control of the pertinent stereochemistry.

The choice of acetophenone as the pinacol precursor was attractive for the following reasons. It is commercially available in labeled form; synthetic routes to the pure diastereoisomeric glycols have been reported;[5] and the stereochemical identity of the individual diastereoisomers has been unequivocally demonstrated.[6]

The generally accepted mechanism of photopinacolization involves the ketone in an excited state having an n,π^* configuration and triplet multiplicity interacting with donor-solvent alcohol as follows.[7]



The present study is concerned with the stereochemistry of the last step above. The ratio of the diastereoisomeric glycols formed in this step has been investigated employing a number of variations in experimental procedure, including wavelength and intensity of radiation, concentration of ketone, degassing *vs.* no degassing, and reaction time. Product stability under reaction conditions has also been examined.

The spectra exhibited by the several ultraviolet sources are given in Figure 1. The results of the studies are tabulated in Table I and II.

Experimental Section

Spectrophotometric quality 2-propanol and cyclohexane were used as recived. Aceophenone-7-C^{14} was purchased from Nuclear Research Chemicals, Orlando, Fla., and diluted with Eastman white-label material to suitable levels of activity. *meso*-2,3-Diphenyl-2,3-butanediol (mp 120–121°) was prepared by the stereoselective addition of methyllithium to benzil; the *dl* form (mp 125–126°) was similarly prepared by the addition of phenyllithium to freshly distilled biacetyl. C^{14}-labeled *meso*-pinacol was prepared correspondingly from labeled benzil; the labeled *d* form was recovered from the photochemical studies. Radioactivity was measured on a Tri-Carb scintillation counter (Packard Instrument Co., Inc.). Melting points were determined on a Kofler hotstage and are uncorrected.

A prototype Griffin–Srinivasan photoreactor, employing a vertically mounted circle of 12 lamps was used in most runs. In any run the lamps were exclusively either Sylvania G8T5 (Germicidal) or F8T5 (BLB). The spectrum emitted by a representative lamp of each of these types, as obtained on an Aminco Bowman spectrophotofluorometer, is shown in Figure 1. Pyrex glassware was employed with the F8T5 lamps; quartz was used in all other runs excepting 18. Use of the Hanovia high-pressure lamps (100 w, No. 608A36, or 450 w, No. 679A36) involved irradiation from a center, air-cooled, quartz well of a solution contained in an outer, concentric tube, or, alternately, from an externally placed lamp. The construction of the Hanovia lamps prevented effective irradiation of the relatively small volumes of solution from an inner well without more elaborate

(1) Of the many possible references, the following were found to be among the most useful: (a) A. Schönberg, "Preparative Organische Photochemie," Springer-Verlag, Berlin, 1958, pp 109 ff; (b) J. G. Calvert and J. N. Pitts, Jr., "Photochemistry," John Wiley and Sons, Inc., New York, N. Y., 1966, pp 528 ff; and (c) N. D. Heindel, Ph.D. Thesis, University of Delaware, 1963.

(2) For examples, see (a) C. Weizmann, E. Bergmann, and Y. Hirshley, *J. Am. Chem. Soc.*, **60**, 1530 (1938); (b) S. G. Cohen, D. A. Laufer, and W. V. Sherman, *ibid.*, **86**, 3060 (1964); (c) W. L. Bencze, C. A. Burckhardt, and W. L. Yost, *J. Org. Chem.*, **27**, 2865 (1962).

(3) (a) S. G. Cohen and M. N. Seddique, *J. Am. Chem. Soc.*, **86**, 5047 (1964); (b) W. L. Bencze and M. J. Allen, *ibid.*, **81**, 4015 (1959); (c) F. Bergmann and Y. Hirshberg, *ibid.*, **65**, 1429 (1943); these authors report an isolated 80% of an α-pinacol with no trace of β form found.

(4) Unpublished work by Dr. N. D. Heindel of Lehigh University, Bethlehem, Pa., involving the same system reported here (acetophenone–isopropyl alcohol), has led him independently to observe the predominant production of racemic pinacol. The authors are happy to acknowledge a most fruitful correspondence with Dr. Heindel.

(5) J. H. Stocker, P. Sidisunthorn, B. M. Benjamin and C. J. Collins, *J. Am. Chem. Soc.*, **82**, 3913 (1960).

(6) D. J. Cram and K. R. Kopecky, *ibid.*, **81**, 2748 (1959).

(7) J. N. Pitts, Jr., R. L. Letsinger, R. P. Taylor, J. M. Patterson, G. Rectenwald, and R. B. Martin, *ibid.*, **81**, 1068 (1959).

TABLE I

IRRADIATION OF C^{14}-LABELED ACETOPHENONE IN 2-PROPANOL

Run[b]	Time	Products[a] % *dl*	% *meso*	Ratio *dl*:*meso*	Modifications[c]
		3500-A Radiation (F8T5/BLB)			
1	18 hr	52.2	48.1	1.09	
2	18 hr	50.3	44.7	1.13	Ketone (0.70 g) in 0.80 ml of 2-PrOH (50%)
3	18 hr	45.1	42.5	1.06	Ketone (0.81 g) in 400 ml of 2-PrOH (0.3%)
4	23 min	2.7	2.6	1.04	
5	52 min	6.8	6.1	1.11	
6	75 min	10.3	9.4	1.10	
7	120 min	19.2	17.2	1.12	
8	240 min	38.2	33.4	1.14	
9	490 min	52.7	46.7	1.13	
10	18 hr	52.1	48.0	1.09	Reaction mixture saturated with dry O_2 prior to irradiation
11	72 hr	<0.3	<0.3	...	Continuous stream of dry O_2 passed through reaction mixture during irradiation period
12	18 hr	51.9	48.4	1.07	Continuous stream of dry N_2 passed through reaction mixture during irradiation period
13	18 hr	5.5	4.9	1.12	Irradiation with one lamp instead of 12
14	18 hr	4.4	4.2	1.05	Cyclohexane solvent
		2537-A Radiation (G8T5)			
15	18 hr	48.3	41.4	1.17	
16	18 hr	47.7	42.2	1.13	Duplicate run
17	18 hr	6.0	5.2	1.15	Irradiation with one lamp instead of 12
18	18 hr	11.1	9.5	1.17	Pyrex apparatus used
		Hanovia Broad Spectrum Radiation			
19[d]	72 hr	10.0	5.8	1.72	100-w internal source, not degassed
20[d]	72 hr	25.9	17.7	1.46	100-w internal source, not degassed, 2 g of ketone–20 ml of 2-PrOH, continuous stirring
21[d]	72 hr	3.5	1.5	2.33	100-w internal source, not degassed
22[d]	72 hr	9.6	4.7	2.04	450-w internal source, not degassed
23	72 hr	37.9	32.3	1.17	100-w external source
24	24 hr	24.1	20.8	1.16	100-w external source
25	18 hr	15.9	14.0	1.14	450-w external source
26	72 hr	15.9	13.1	1.21	100-w internal source
27	72 hr	0.7	0.5	...	See run 11

[a] For sample sizes in the 10–25-mg range, permitting counts of the order of 5–10,000 dpm (counted in excess of 100,000 counts), the percentage yields may be considered reproducible to at least 0.3%. Run 1 would calculate, accordingly, to a ratio of 1.085 ± 0.013. Smaller total yields would give rise to somewhat less accurate ratios. [b] Designation of run number does not represent chronological order of experiment. [c] Variations in the General Procedure as reported in Experimental Section. [d] Runs 19–22 were open to the atmosphere and thus there was no control over the amount of oxygen present in the system.

apparatus and external use was found to give higher yields. This mechanical problem accounts for the apparent variations in intensity observed in the Hanovia runs.

General Procedure.—A solution of approximately 1.000 g of acetophenone-7-C^{14} (0.4020 mc/m) in 10 ml of 2-propanol to which 1 drop of glacial acetic acid was added was placed in a 15 × 100 mm straight test tube (1-mm wall thickness). The test tube was sealed with a rubber septum and the solution degassed *via* hypodermic needles with a fine stream of pure, dry nitrogen for 30 min. Following irradiation for 18 hr, the reaction mixture was transferred quantitatively and diluted to 100 ml with absolute methanol. A 50-ml aliquot was added to each of two flasks containing, respectively, 1 g of pure *meso*- and 1 g of pure *dl*-2,3-diphenyl-2,3-butanediol. The two solutions were evaporated almost to dryness, the residues taken up in hot hexane, and recrystallized from hexane to constant melting point. This experimental workup represents an adaptation of the technique employed in an earlier investigation involving organometallic reagents.[5] The results, after radioassay, including occasional modifications in general procedure, are tabulated in Table I.

Those runs involving pure diastereoisomers were carried out in analogous fashion and are tabulated in Table II. The *meso* form employed had an activity of 0.2886 mc/m, the *dl* form, 0.1227 mc/m.

TABLE II

IRRADIATION OF C^{14}-LABELED ACETOPHENONE PINACOLS IN 2-PROPANOL

Run	Soln irradiated[a]	Ultraviolet source, A	Time, hr	% *dl*	% *meso*
28	0.5 g of *dl*-C^{14}, 0.6 g of acetophenone	2537	72	Appreciable labeled *dl* form lost, labeled *meso* found[b]	
29	0.903 g of *meso*-C^{14}	3500	72	<0.2	96.5
30	0.911 g of *meso*-C^{14}, 3 ml of acetone, 7 ml of 2-PrOH	3500	72	<0.4	94.3
31	1.009 g of *dl*-C^{14}	Hanovia 100 w	72	71.0	8.0
32	0.907 g of *meso*-C^{14}	Hanovia 100 w	72	10.2	60.8
33[c]	1.008 g of *meso*-C^{14}	Hanovia 100 w	72	7.1	59.6

[a] 2-Propanol (10 ml) containing 1 drop of glacial acetic acid was used in all runs unless otherwise specified. All reactions degassed by flushing with dry nitrogen for 30 min prior to irradiation. [b] If it is assumed that the acetophenone originally present reacted quantitatively to yield the corresponding *dl*- and *meso*-glycols in a ratio of 1.15, values of 53.2% *dl* form recovered and 7.0% converted to the *meso* form may be calculated. [c] Continuous stream of dry O_2 passed through reaction mixture during irradiation period.

Results and Discussion

Certain general conclusions can be drawn from the data tabulated in Tables I and II.

(a) Utilizing 3500-A radiation, the stereochemistry of radical combination is independent of time (runs 4–9), concentration (runs 1–3), intensity (runs 1 and 13), degassing, *i.e.*, presence of oxygen (run 10), removal of acetone product (run 12), and substitution of nonpolar solvent-donor cyclohexane for 2-propanol.

(b) Similar results were observed when the radiation was changed to predominantly 2537 A (runs 15–18).

From these data, it may be inferred that the ketyl dimeration step has a low stereoselectivity, producing *dl*-pinacol preferentially to *meso* in an 11:10 ratio. It is essentially independent of all the variables involved, is kinetically controlled, and is probably dependent on small variations in preferred steric approach.

Use of the Hanovia high-pressure lamps, notable for their broad spectrum emission, gave rise to data that can only be interpreted as due to a second reaction, following pinacolization, and involving the pinacols themselves. The following points must be considered: this new reaction is insensitive to oxygen (runs 32 and 33), is relatively slow compared to photopinacolization,

is probably due to shorter wavelengths (runs 29 and 32), and effectively (if not selectively) destroys the *meso* form more rapidly than the *dl*.

Possibly the simplest rationale, based on the limited data available, would be the formation of an excited pinacol molecule that had either not fully separated into two free radicals or had done so in a sufficiently "protected" (solvent cage) environment so as to be inaccessible to any oxygen present. This specie would then be capable of "recombining" and/or being removed from the pinacolization picture to a product or products unknown. This "unknown" cannot be acetophenone or III. Either the excitation, or the "recombining," or both steps, must be stereoselective. This competitive process suggests that caution should be exercised in the use of broad spectrum irradiation, particularly for long periods of time in photopinacolization employed for synthetic purposes.[8]

The data in Table I from 72-hr Hanovia source irradiation, with and without degassing, derive from a resultant of these two distinct reactions (pinacolization and decay). Either a slow pinacolization reaction (oxygen present) or a low *pinacolization* intensity (relative to the "*decay*" intensity), for a given period of time, will give rise to a poorer yield and a higher *dl* to *meso* ratio.

Examination of the pertinent stereochemistry required, of necessity, certain variations in procedure that also gave rise to useful nonstereochemical data. While much of this has been previously investigated, it may be of some interest to note it here.

(a) The reaction is zero order. A graph of the yield of glycol *vs.* time (runs 4–8) produces a straight line.

(b) The reverse reaction, *i.e.*, photooxidation, is a neglible process in the acetophenone pinacol–2-propanol system (runs 12 and 30).

(c) The presence of oxygen in the reaction mixture does not appreciably reduce the yield of pinacol if a continuous supply is not provided and sufficient reaction time is allowed (runs 10 and 11).[9]

(8) This novel reaction clearly merits further study. Since it is probable that other systems presently under study (propiophenone, benzaldehyde, 2-acetopyridine, among others) will display similar behavior, possibly to a greater degree, investigation of the route of excitation and decomposition of the pinacols, as well as the identity of the decomposition products, has been deferred against the selection of optimal circumstances.

(9) The oxygen may be expected to unite with all radicals present, subsequently producing hydrogen peroxide and regenerating, in the case of III, acetophenone. Accordingly, the reaction is slowed rather than stopped. See ref 7, p 1077.

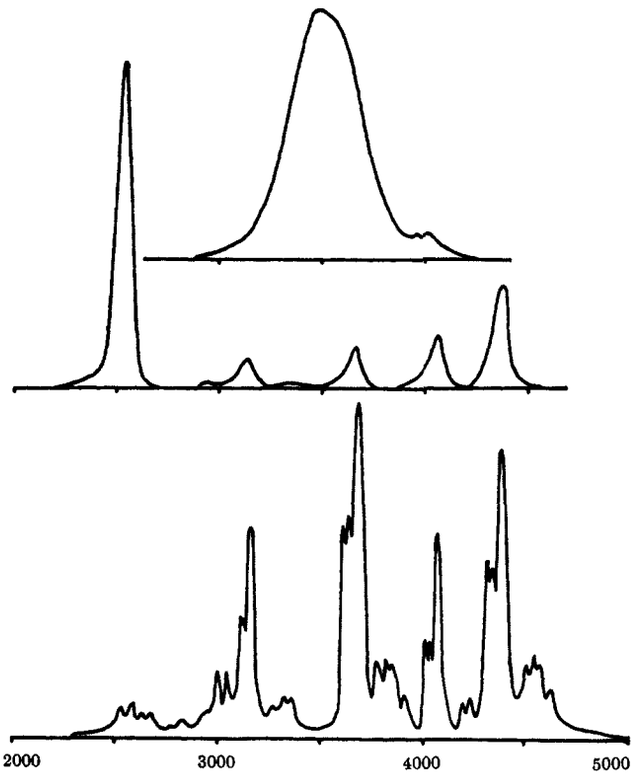


Figure 1.—Spectra of ultraviolet sources. Upper, Sylvania F8T5/BLB; middle, Sylvania G8T5; lower, Hanovia 608A36.

(d) Cyclohexane is a considerably poorer hydrogen donor than 2-propanol. (run 14).[10]

(e) $\pi \rightarrow \pi^*$ excitation may manifest itself as n,π^* reactivity (run 15 *vs.* 18).[11]

Preliminary data from other systems presently under study suggest that higher stereoselectivities will be found in these systems. Accordingly it seems advisable to defer further predictive speculation until additional firm data are available.

Acknowledgment.—This research was conducted under A. E. C. Contract No. AT-(40-1)-2833.

(10) C. Walling and M. J. Gibian [*J. Am. Chem. Soc.*, **87**, 3361 (1965)] have reported that 2-propanol displays approximately 4.5 times the reactivity of cyclohexane *in re:* hydrogen abstraction by the benzophenone triplet.

(11) Reference 16, p 530. These authors describe similar behavior in benzophenone pinacolizations.