experience with the ylids **4** and **5**, the least nucleophilic ylid (**2c**) would be expected to afford the smallest k_4/k_1 value, contributing to a higher *cis/trans* ratio. The betaine decomposition step should be fastest with **2c** and least so with **2e** owing to the increased positive character of the phosphorus atom in the former facilitating oxyanion attack. In other words, **2c** should afford the smallest k_6/k_3 ratio, also contributing to the largest *cis/trans* ratio. Therefore, both the betaine formation and decomposition steps favor the highest *cis/trans* ratio for the tri(*p*-chlorophenyl) ylid (**2c**). This combination of effects led to the unusually high *cis/trans* ratio when the phosphorus atom carried electron-withdrawing groups.

The fact that in the methoxybenzylidenephosphorane series the *cis/trans* ratio increased by a factor of 5.2 when the triphenylphosphonium group was replaced by the tri(*p*-chlorophenyl)phosphonium group, but in the nitrobenzylidenephosphorane series the ratio increased by a factor of only 3.1, probably indicates that the k_6/k_3 ratio was small for both tri(*p*-chlorophenyl)phosphonium ylids. The difference in the two factors may indicate that the k_4/k_1 ratio was closer to unity for the methoxy series than for the nitro series, the latter being the least nucleophilic and therefore most discriminating. The *cis/trans* ratios must be determined by a delicate balance of the rate constant ratios k_4/k_1 and k_6/k_3.

Wittig reactions normally involve the use of triphenylphosphonium ylids, presumably because of the availability of triphenylphosphine. From this work it appears that formation of *trans* olefins can be strongly favored by use of phosphonium ylids carrying electron-donating phosphorus substituents (*e.g.*, tri-*n*-butylphosphonium ylids) while formation of *cis* olefins can be favored by use of ylids carrying electron-withdrawing phosphorus substituents [*e.g.*, tri(*p*-chlorophenyl)phosphonium ylids]. Tri-*n*-butylphosphine required for the former is a commercial product and tri(*p*-chlorophenyl)phosphine is readily prepared.[12]

Experimental Section[13]

Phosphines.—Triphenylphosphine and tri-*n*-butylphosphine were used directly as received from commercial sources. Tri-(*p*-chlorophenyl)phosphine was prepared as described by Mann and Chaplin,[12] m.p. 102–103°.

Phosphonium Salts.—The phosphonium salts were prepared by heating 40 mmoles of *p*-methoxybenzyl bromide or *p*-nitrobenzyl bromide with 40 mmoles of phosphine in 100 ml. of benzene for about 12 hr. The precipitated salts were removed by filtration and recrystallized from benzene–chloroform. The following were prepared: *p*-methoxybenzyltriphenylphosphonium bromide, m.p. 236–238°; *p*-nitrobenzyltriphenylphosphonium bromide, m.p. 269–270°; *p*-methoxybenzyltri(*p*-chloro phenyl)phosphonium bromide, m.p. 269–271°; *p*-nitrobenzyltri(*p*-chlorophenyl)phosphonium bromide, m.p. 260–261°; *p*-methoxybenzyltri(*p*-methoxyphenyl)phosphonium bromide, m.p. 254–256°; *p*-nitrobenzyltri(*p*-methoxyphenyl)phosphonium bromide, m.p. 222–223°; *p*-methoxybenzyltri-*n*-butylphosphonium tetraphenylborate, m.p. 184–186°; and *p*-nitrobenzyltri-*n*-butylphosphonium bromide, m.p. 165–166°.

Wittig Reactions.—To 2.5 mmoles of phosphonium salt slurried in 80 ml. of benzene flushed with nitrogen was added 2.5 mmoles of *n*-butyllithium in hexane. The colored solution was stirred at room temperature for 1 hr. after which time 2.5 mmoles of the appropriate substituted benzaldehyde was added. After stirring overnight (at room temperature for the methoxybenzylides but with gentle warming to 40° for the nitrobenzylides), the reaction was hydrolyzed with 20 ml. of 40% sodium bisulfite. Water was added, the organic components were extracted with ether, and the organic layer was dried over magnesium sulfate. The solvents were removed *in vacuo* at or below room temperature, leaving an oily crude residue containing *cis*- and *trans*-4-nitro-4′-methoxystilbenes, phosphine oxide, and unreacted starting materials.

For purposes of quantitative analysis a portion of the crude residue was taken up in hexadeuterioacetone and its n.m.r. spectrum was recorded. The *cis/trans* ratios obtained are recorded in Table I.

For isolation purposes the crude residue was chromatographed on Merck 71707 alumina. Elution with 1:1 benzene–hexane afforded *cis*-4-nitro-4′-methoxystilbene, m.p. 65–67° (lit.[6] m.p. 69–70). Elution with 9:1 benzene–chloroform afforded *trans*-4-nitro-4′-methoxystilbene, m.p. 132–133° (lit.[6] m.p. 131–132°). Attempts to recrystallize the *cis* isomer invariably led to very low recovery of *cis* olefin and the isolation of considerable amounts of the *trans* isomer. The total yield of both isomers from reaction between **2a** and **3a** (reaction 1) was 0.52 g. (78%).

Placing 0.12 g. of *cis* olefin on an alumina column and eluting with 1:1 benzene–hexane led to the recovery of only 0.09 g. of the *cis* isomer, the remainder being the *trans* isomer. The same procedure with a 55.8/44.2 mixture of *trans* and *cis* olefins afforded a 69.6/30.4 mixture of *trans* and *cis* isomers.

N.m.r. Analyses.—The n.m.r. spectra of the crude Wittig reaction products were recorded in hexadeuterioacetone at ambient temperatures. The methoxyl protons were at 228.0 c.p.s. for the *cis* isomer and at 230.5 c.p.s. for the *trans* isomer. *p*-Anisaldehyde did not interfere (232 c.p.s.) but tri(*p*-methoxyphenyl)phosphine oxide did (231 c.p.s.). The peaks were integrated using a sweep width of 100 c.p.s. The ratio of the integrated peaks heights was taken as directly proportional to the ratio of the two isomers present in the solution.

Known ratios of *cis*- and *trans*-4-nitro-4′-methoxystilbenes were weighed out and their spectra were recorded in hexadeuterioacetone. The theoretical *cis/trans* ratios compared with the observed ratios as follows: calcd. 31.6/68.4, found 28.6/71.4; calcd. 46.4/53.6, found 44.0/56.0; calcd. 59.9/40.1, found 57.5/42.5; calcd. 73.5/26.5; found 71.4/28.6. The maximum deviation from the theoretical values was 3%. The observed values for the *cis/trans* ratios always were low, a direction consistent with the known facile *cis*-to-*trans* isomerization of the stilbenes.

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[12] F. G. Mann and E. J. Chaplin, *J. Chem. Soc.*, 527 (1937). This compound was prepared by R. Swor whose assistance we acknowledge.

[13] Melting points are uncorrected. N.m.r. spectra were recorded on a Varian A-60 n.m.r. spectrometer, the purchase of which was aided by a grant from the National Science Foundation.

Cycloadditions. VI. Photosensitized Dimerization of α-Phellandrene[1]

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Received August 17, 1965

Photosensitized dimerizations of conjugated dienes are believed to take place by a mechanism involving transfer of excitation from a triplet sensitizer to the diene; the resulting excited triplet diene combines with an unactivated diene giving a biradical intermediate, which collapses to products through spin inversion and cyclization.[3,4] Modes of cycloaddition

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[1] Paper V: J. E. Baldwin and R. A. Smith, *J. Am. Chem. Soc.*, **87**, 4819 (1965).

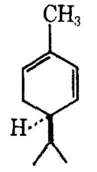
[2] National Science Foundation Undergraduate Research Participant, summer 1965.

[3] D. Valentine, N. J. Turro, Jr., and G. S. Hammond, *J. Am. Chem. Soc.*, **86**, 5202 (1964), and earlier papers cited therein.

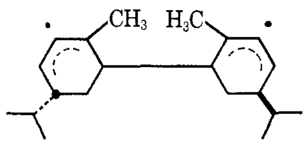
[4] D. J. Trecker, R. L. Brandon, and J. P. Henry, *Chem. Ind.* (London), 652 (1963).

producing more stable biradical intermediates are favored over those involving relatively unstable ones. Correlations between intermediate biradical stabilities and cycloaddition product distributions have been recognized and exploited in related processes.[5–7]

We have investigated the photosensitized dimerization of (−)-α-phellandrene (**1**). The most stable biradicals obtained by linking two molecules of **1** would be anticipated to be stereoisomers of **2**, for both allylic methyl groups in **2** may help stabilize the intermediate. The photosensitized dimerization, then, should give products derived from **2**.

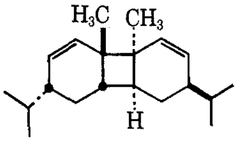


1

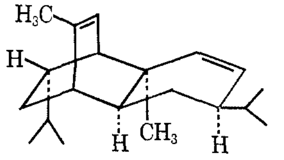


2

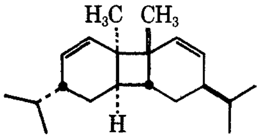
The naphthalene-photosensitized dimerization of α-phellandrene gave in a 4.5:1:1 ratio three major $C_{20}H_{32}$ products; the first two photodimers could be assigned structures **3a** and **4a** or **3b** and **4b**. The third dimer is probably **5** or an isomer (**3b** or **3a**) of the major photoproduct (**3a** or **3b**). The major photoproduct was isolated by preparative g.l.p.c. on an XF 1150 column; its origin, molecular ion peak at m/e 272, and n.m.r. spectrum having vinyl hydrogens at τ 4.4 (4H) but no vinyl methyl absorptions near τ 8.2 are consistent with its formulation as a dimer of type **6**. The photodimer was thermally unstable: at 173° its first-order disappearance occurred with $k_1 = 3.7 \times 10^{-5}$ sec.$^{-1}$. This facile rearrangement may be taken as sufficient evidence for a 1,2-divinylcyclobutane moiety in the product; hence, the major dimer is **3a**, **3b**, or **5**.



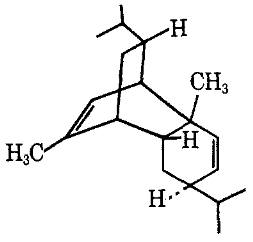
3a



4a



3b



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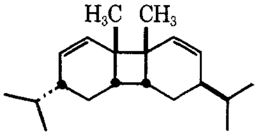

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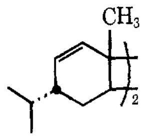
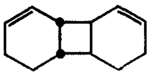


6

The rate of decomposition of the dimer (3.7×10^{-5} sec.$^{-1}$ at 173°) may be compared with the rates of rearrangement for **7** and **8** estimated for this temperature from the data of Valentine, Turro, and Hammond[3]: 0.4×10^{-5} and 12×10^{-5} sec.$^{-1}$, respectively.



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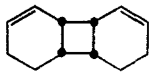


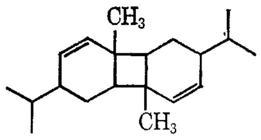
8

Methyl substituents on the cyclobutane ring in the photodimer should speed its decomposition[8] relative to the unsubstituted analogs **7** and **8**. The observed rate of rearrangement of the photodimer falls between the rates for **7** and **8**; thus, structure **3** for the major photodimer is in better accord with expectations than structure **5**. Dimer **3** gives α-phellandrene, the second photodimer (**4**), and other products on thermal rearrangement; this behavior reinforces the structural assignment of **3** rather than **5** (*cf.* the product ratios reported by Hammond and DeBoer[8]).

Formulation of the second dimer as **4** is based on its production both from the photosensitized dimerization of **1** and from thermal rearrangement of **3**; direct analogy is available from work on the dimers of 1,3-cyclohexadiene.[3]

Thus, the mechanistic insights derived from investigations of other dienes have proved sufficient to predict the basic course of the photosensitized dimerization of α-phellandrene. The methyl substituent on the diene system contributes importantly to the stability of the biradical intermediates **2** involved: all three major products may be formed directly from the stereoisomers of biradical **2**.

The report[9] that the duroquinone-photosensitized dimerization of α-phellandrene gives the dimer **9** remains anomalous.



9

Experimental Section[10]

Photosensitized Dimerization of α-Phellandrene.—A solution of 0.5 g. of naphthalene in 25 g. of (−)-α-phellandrene was irradiated under nitrogen through Pyrex with a 450-w. Hanovia high-pressure mercury lamp for 24 hr. Distillation of the reaction mixture gave 3.0 g. of material having b.p. 100–117° (0.2 mm.). Analysis of the crude product mixture by g.l.p.c. on a 1 × 300 cm. 10% XF 1150 on Chromosorb W column at 200° showed three major components of relative retention times 1.00:1.12:1.25 in a 4.5:1:1 ratio. Samples of the three components were collected by preparative g.l.p.c.

The major photodimer showed a molecular ion peak in its mass spectrum at m/e 272, and an n.m.r. spectrum with absorptions at τ 4.4 (4H) and 7.6–9.4 (complex); the region near τ 8.2 showed no signal which could be attributed to a vinyl methyl group.

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(5) J. D. Roberts and C. M. Sharts, *Org. Reactions*, **12**, 1 (1962).

(6) P. D. Bartlett, L. K. Montgomery, and B. Seidel, *J. Am. Chem. Soc.*, **86**, 616 (1964), and following papers.

(7) N. J. Turro and P. D. Bartlett, *J. Org. Chem.*, **30**, 1849 (1965).

(8) G. S. Hammond and C. D. DeBoer, *J. Am. Chem. Soc.*, **86**, 899 (1964).

(9) G. O. Schenck and R. Wolgast, unpublished, 1962; quoted by G. O. Schenck and R. Steinmetz, *Bull. soc. chim. Belges*, **71**, 781 (1962), and by K. Schaffner, *Fortschr. Chem. Org. Naturstoffe*, **22**, 1 (1964).

(10) Perkin-Elmer Model 521, Varian A-60, and Atlas CH-4 spectrometers were used for determining infrared, n.m.r., and mass spectra. A Wilkins Model A-90-P instrument was used for chromatographic estimation and isolation of hydrocarbons.

The first and third photodimer had strong absorption in the infrared spectrum at 745 cm.$^{-1}$ (*cis*-disubstituted double bond[11]), while the second dimer (**4**) had bands of approximately equal intensity at 745 and at 845 and 805 cm.$^{-1}$ (trisubstituted double bond[11]).

Thermal Rearrangement of Dimer 3.—Aliquots of a solution of the major photodimer from α-phellandrene (29 mg., purified by preparative g.l.p.c.) and an internal standard (*cis*-1,9-octadecadiene, 7 μl.) in chloroform (45 μl.) were sealed in melting point capillaries and heated in an oil bath at 173 ± 3°. Samples were withdrawn and analyzed by g.l.p.c. on an XF 1150 column; the data for the disappearance of dimer **3** (six points) followed good first-order kinetics through two half-lives with $k_1 = 3.7 \times 10^{-5}$ sec.$^{-1}$. The thermal rearrangement of dimer **3** led to the second photodimer **4**, α-phellandrene, and other products having retention times appropriate for dimeric hydrocarbons.

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[11] K. Nakanishi, "Infrared Absorption Spectroscopy," Holden-Day, Inc., San Francisco, Calif., 1962, p. 24.

Deuterated Amino Acids. I. The Synthesis of Glycine-d_5 and Related Derivatives[1a]

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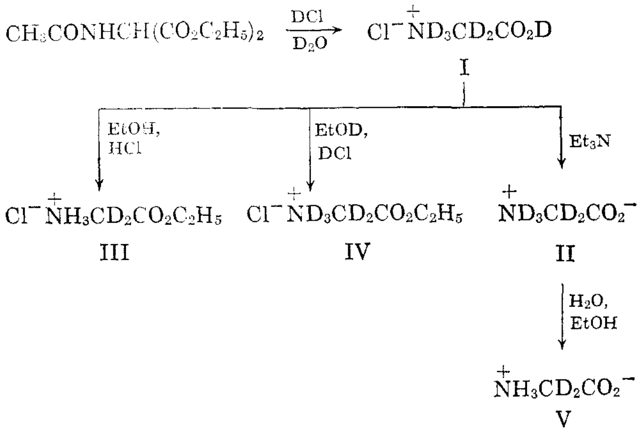
Received August 31, 1965

As part of a general research program concerned with the synthesis of deuterated amino acids and derived peptides, an inexpensive and efficient method for the preparation, in quantity, of glycine-d_5 and its ethyl ester hydrochloride was required. Examination of the literature revealed that the best preparations of glycine-d_5 were those which involved a standard exchange technique.[2] Since a thorough deuterium substitution of the nonlabile protons is both costly and time consuming owing to the necessity of performing several exchanges, the following synthetic scheme was devised.



When diethyl acetamidomalonate is refluxed in a DCl–D_2O solution, prepared by the reaction of thionyl chloride with D_2O, glycine-d_5 deuteriochloride (I) is produced in 97% yield. The deuteriochloride salt I is quantitatively converted to glycine-d_5 (II) (97.1% isotopic purity) by treatment with triethylamine. Recrystallization of the amino acid II from water produced glycine-d_2 (V) which possesses >99% deuteration on the *α-carbon atom.* Glycine-2-d_2 ethyl ester hydrochloride (III), and the d_5 derivative IV are prepared in high yields from the salt I by Fischer esterification. A high degree of deuterium substitution on the α-carbon atom of salts I, III, and IV was indicated by n.m.r. (>95%) and substantiated by deuterium analysis[3] of V (99.7 atom % D). Deuterium analysis of salts I, III, and IV gave somewhat lower results (89–96 atom % D) than for compounds II and V owing to the hygroscopic nature[4] of the former substances.

Experimental Section[5]

Glycine-d_5 Deuteriochloride (I).—Diethyl acetamidomalonate (21.7 g., 0.1 mole) was hydrolyzed[6] by refluxng overnight in an acidic solution prepared by carefully adding 30 ml. (0.413 mole) of redistilled thionyl chloride to 126 g. of 99.7% D_2O at 0° in a dry atmosphere. The reaction mixture was concentrated to a semisolid at reduced pressure, and 400 ml. of tetrahydrofuran was added to precipitate the product. The mixture was chilled, filtered, and washed with absolute ether to give 11.42 g. (97%) of compound I as crystalline white needles. The product is slightly hygroscopic and should be protected from moisture at all times. Infrared analysis showed $\lambda_{\max}^{\mathrm{KBr}}$ 3.35, 4.18–4.62, 5.83, and 7.34 μ. Analysis by n.m.r. (D_2O) revealed no signal for the compound. The amino acid gave a single spot on paper chromatography, R_f 0.63.

Anal. Calcd. for $C_2D_6ClNO_2$: C, 20.43; H, 5.72; Cl, 30.16; N, 11.91. Found: C, 20.79; H, 5.44; Cl, 30.13; N, 12.15.

The hydrogen analysis was based on 10.28% deuterium such that the calculated percentage of hydrogen obtained by routine analysis is 5.72%.

Anal. Calcd. for $C_2D_6ClNO_2$: D, 100 atom %. Found: D, 88.5 atom %.

Glycine-d_5 (II).—The conversion of the salt I to the amino acid II was carried out in a nitrogen atmosphere (glove bag) in the following manner. The deuteriochloride I (2.00 g., 0.017 mole) was dissolved in 2 ml. of 99.7% D_2O, treated with 2.7 ml. (0.0193 mole) of freshly distilled triethylamine, and stirred magnetically for 10 min. Dry acetone (25 ml.) was added and the mixture was stirred an additional 10 min. The slurry of compound I and triethylamine deuteriochloride was filtered and washed with 10 ml. of acetone, three 10-ml. portions of chloroform, and finally with anhydrous ether to give 1.36 g. (100%) of compound II. Recrystallization from deuterium oxide afforded an analytical sample: $\lambda_{\max}^{\mathrm{KBr}}$ 4.16–4.78, 6.26, 7.10, 8.50, and 11.43 μ. Analysis by n.m.r. (DCl, D_2O) showed no absorption bands. Paper chromatography indicated a single spot, R_f 0.64.

Anal. Calcd. for $C_2D_5NO_2$: C, 29.99; H, 7.00; N, 17.49. Found: C, 30.21; H, 6.74; N, 17.14.

The deuterium analysis accounts for 12.58% deuterium such that the calculated percentage of hydrogen as obtained by a routine analysis is 7.00%.

Anal. Calcd. for $C_2D_5NO_2$: D, 100 atom %. Found: D, 97.1 atom %.

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[1] (a) This study was supported in part by the National Science Foundation, Grant No. G-18902; (b) Esso Education Foundation Fellow, 1964–1965; (c) National Institutes of Health Molecular Biology Training Grant Postdoctoral Fellow, 1965.

[2] (a) A. Murray, III, and D. L. Williams, "Organic Syntheses with Isotopes," Interscience Publishers, Inc., New York, N. Y., 1958; (b) S. Suzulci, T. Shimanovchi, and M. Tsuboi, *Spectrochim. Acta,* **19**, 1195 (1963); (c) P. Neelakantan, R. S. Krishnan, and Y. Iitaka, *Proc. Indian Acad. Sci.*, **58**, 275 (1963).

[3] Unless otherwise stated, all deuterium analyses were performed by the falling-drop technique.

[4] The true degree of deuteration of these salts is difficult to ascertain, since they are unavoidably exposed to the atmosphere just prior to analysis.

[5] Melting points were taken on a Fisher-Johns apparatus and are uncorrected. Microanalyses were performed by Micro-Tech Laboratories, Skokie, Ill. Deuterium analyses were carried out by Josef Nemeth, Urbana, Ill. Infrared spectra were recorded on a Perkin-Elmer Infracord spectrophotometer, proton magnetic resonance spectra on a Varian Associates 60-Mc., Model A-60 instrument. Paper chromatography was performed by the ascending technique on Whatman No. 1 paper employing the solvent system ethanol-water (1:1) and ninhydrin as developer. Diethyl acetamidomalonate was obtained from the Aldrich Chemical Co., Inc., and recrystallized from absolute ethanol before use.

[6] For a related synthesis of tritiated glycine, see H. R. V. Arnstein and J. C. Crawhill, *Biochem. J.*, **67**, 180 (1957).