

manner described for the preparation of VIIa. White crystals separated from ethanol, mp 187–189°.

Anal. Calcd for $C_{16}H_{17}NO$: C, 80.30; H, 7.16; N, 5.85. Found: C, 79.64; H, 7.05; N, 5.87.

Although the carbon value is low, the nmr spectrum is consistent with the expected structure.

1-(4-Pyridylmethyl)-5-indanol (VIIIb).—Demethylation of IIIc in the manner described above provided a 58% yield of VIIIb as fine, white crystals from benzene–ethanol, mp 223–226°.

Anal. Calcd for $C_{15}H_{15}NO$: C, 79.97; H, 6.71; N, 6.22. Found: C, 79.68; H, 6.77; N, 6.26.

5-(4-Piperidylmethyl)-5,6,7,8-tetrahydro-2-naphthol (IXa).—Demethylation of IVa in the manner described above provided a 24% yield of IXa as fine, white crystals from ethanol–hexane, mp 184–186°.

Anal. Calcd for $C_{16}H_{23}NO$: C, 78.32; H, 9.45; N, 5.71. Found: C, 78.07; H, 9.51; N, 5.80.

5-(1-Acetyl-4-piperidylmethyl)-5,6,7,8-tetrahydro-2-naphthol (IXb).—To a 1.5-g sample of IXa suspended in 50 ml of dry ether

was added 1.7 ml of triethylamine followed by 0.87 ml of acetyl chloride in 10 ml of dry ether. This mixture was stirred for 50 min at room temperature, treated with ice–water, and extracted with chloroform. The chloroform layer was extracted with Claisen's alkali, and the basic extract was acidified with 6 *N* hydrochloric acid. Crystallization of the solid so obtained from ethanol gave 1.12 g (64%) of IXb as white crystals: mp 173–176°; ν_{\max} 3598, 3250 (broad), and 1615 cm^{-1} .

Anal. Calcd for $C_{18}H_{25}NO_2$: C, 75.22; H, 8.77; N, 4.87. Found: C, 75.03; H, 8.76; N, 4.93.

1-Acetyl-4-methylpiperidine.—This amide was prepared by acetylating 4-methylpiperidine according to the procedure described for the preparation of Vb. The colorless oil had bp 91.5–93.0° (5.9 mm), ν_{\max} 1623 cm^{-1} .

Anal. Calcd for $C_8H_{15}NO$: C, 68.06; H, 10.71; N, 9.92. Found: C, 67.84; H, 10.91; N, 10.04.

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Preparation and Geometric Isomerism of Dipiperonylidenesuccinic Acid and Anhydride

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Yellow *trans,trans*- α,α' -dipiperonylidenesuccinic anhydride was transformed by light into reddish orange *cis,trans*- α,α' -dipiperonylidenesuccinic anhydride. The configurational assignments are supported by spectral data and several chemical transformations.

The "fulgenic acids" are a large group of colored, crystalline arylmethylenesuccinic acids generally prepared by a Stobbe condensation of an aromatic aldehyde or ketone with a monoalkylidenesuccinate ester or diethyl succinate.^{1–5} They are convertible into more deeply colored anhydrides, called "fulgides,"⁶ which exhibit a structural change, sometimes reversible, by the action of iodine, heat, or light, and generally in acetone or benzene solution.^{7–10} An interpretation of this last phenomenon is complicated by the ready oxidative cyclization of the fulgides under related conditions to afford naphthalene derivatives.^{11–13}

It is probable that previous workers on the fulgide isomerization puzzle considered the color changes to be a consequence of double-bond isomerization; however, no definite configurational assignments appear to have been made for any particular set of fulgenic acid to fulgide interconversions, although discrete free-radical intermediates¹⁴ and mesomeric forms¹⁵ have

been offered as suggestions to explain the behavior of these compounds. In connection with two recent studies,^{16,17} there simultaneously arose the opportunity of solving one phase of this problem, and our joint results are reported at this time.

Piperonal reacted with diethyl succinate in ether using either sodium methoxide^{18–22} at -10° or potassium *t*-butoxide in *t*-butyl alcohol¹² at reflux as the catalyst to give *trans,trans*- α,α' -dipiperonylidenesuccinic acid (Ia).²³ The addition of diazomethane to the diacid Ia afforded the corresponding dimethyl ester (Ib),^{22,24,25} which was desired for further comparison work. Treatment of the diacid Ia with either acetyl chloride or acetic anhydride produced yellow *trans,trans*-dipiperonylidenesuccinic anhydride (Ic).^{18,21,25} The *trans,trans* configurations for Ia and Ic are strongly supported by their symmetrical nmr spectra, particularly in the case of the anhydride. The simple vinyl and aromatic patterns as well as the single methylenedioxy peak seen for these two compounds imply that

(1) Many of these substances are described in an extensive work by Stobbe, *et al.*, *Ann.*, **380**, 1 (1911).

(2) H. Stobbe, G. Ljungren, and J. Freyberg, *Ber.*, **59**, 265 (1926).

(3) F. G. Baddar, L. S. El-Assal, and M. Gindy, *J. Chem. Soc.*, 1270 (1948).

(4) L. Hänel, *Naturwissenschaften*, **37**, 91 (1950).

(5) R. Cluzel and P. Cordier, *Compt. Rend.*, **235**, 622 (1952).

(6) H. Stobbe and P. Naoum, *Ber.*, **37**, 2240 (1904).

(7) H. Stobbe, *ibid.*, **37**, 2465 (1904).

(8) H. Stobbe, *ibid.*, **37**, 2656 (1904).

(9) H. Stobbe and K. Leuner, *ibid.*, **38**, 3897 (1905).

(10) H. Stobbe, *Z. Elektrochem.*, **14**, 473 (1908).

(11) H. Stobbe, *Ber.*, **40**, 3372 (1907).

(12) L. S. El-Assal and A. H. Shehab, *J. Chem. Soc.*, 2983 (1963).

(13) D. C. Ayres, B. G. Carpenter, and R. C. Denney, *ibid.*, 3578 (1965).

(14) A. Schonberg, *Trans. Faraday Soc.*, **32**, 514 (1936).

(15) C. V. Gheorghiu, *Bull. Ecole Polytech. Jassy*, **2**, 141 (1947); *Chem. Abstr.*, **42**, 1514c (1948).

(16) D. Brown and R. Stevenson, *J. Org. Chem.*, **30**, 1759 (1965).

(17) G. A. Swoboda, K.-T. Wang, and B. Weinstein, *J. Chem. Soc.*, in press.

(18) H. Stobbe, W. Viewig, R. Eckert, and G. Reddelien, *Ann.*, **380**, 78 (1911).

(19) R. Dietzel and J. Naton, *Ber.*, **58**, 1314 (1925).

(20) S. Keimatsu, T. Ishiguro, and Y. Nakamura, *J. Pharm. Soc. Japan*, **55**, 775 (1935).

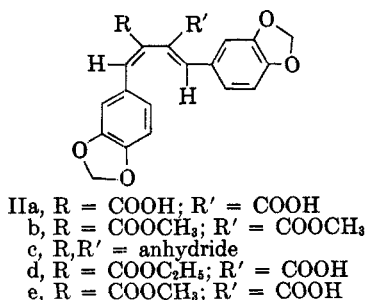
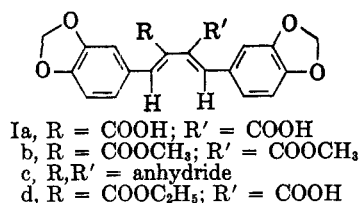
(21) R. D. Haworth and D. Woodcock, *J. Chem. Soc.*, 1985 (1938).

(22) K. Freudenberg and T. Kempermann, *Ann.*, **602**, 184 (1957).

(23) For the purpose of definition, the stereochemistry as shown in the first set of drawings is called *trans,trans*, in the sense that the phenyl substituents are located *trans* to the central carbon–carbon bridge of the butadiene system. The second set of drawings is utilized for the *cis,trans* series.

(24) B. H. Alexander and W. F. Barthel, *J. Org. Chem.*, **23**, 381 (1958).

(25) L. S. El-Assal and S. A. M. El-Wahhab, *J. Chem. Soc.*, 849 (1960).

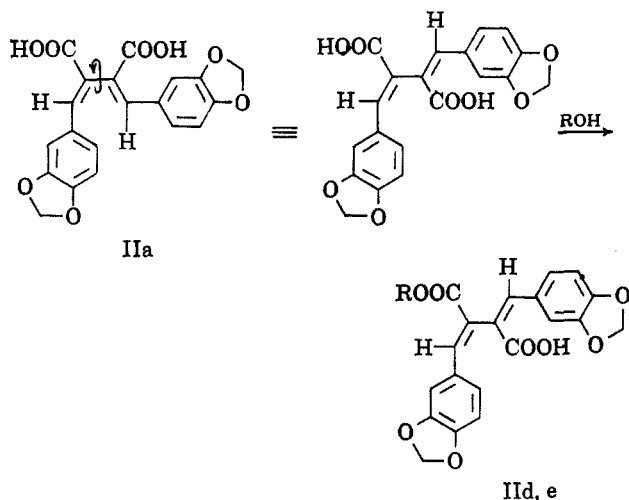


the aromatic rings are in the same magnetic environment. Further evidence for the symmetrical *trans,trans* structures in this series was the fact that only a single, stable monoethyl ester (Id) was obtained by heating the anhydride Ic with excess ethanol. The corresponding *cis,trans* isomers (II) would be expected to display more complex and unsymmetrical patterns, owing to a deshielding effect on one of the aromatic rings. The strong steric interactions in the *cis,cis* form, the remaining possibility, whose existence is rendered highly improbable under the conditions of formation here, provide a sufficient reason to exclude this series from further discussion. It is recognized that the diacid Ia and the diester Ib can exist in the *trans*-butadiene conformation rather than the *cis*-butadiene structure, as represented in I. In fact, a recent study employing molecular models reached the conclusion that the *trans*-butadiene arrangement represents the most stable configuration for both the fulgenic acid and ester isomers.²²

Attention is drawn at this point to the interesting historical observations in which dicumylfulgide,²⁶ dianisylfulgide,²⁷ and piperonylidenephenylfulgide²⁸ were converted by heat or light into isomeric, more deeply colored compounds. This behavior was described as "strange," and was "to be reported later;" however, no further details seem to have been published on these products.²⁶ On this basis, it seemed probable that one could change dipiperonylidene fulgide into an isofulgide by a repetition of these older experiments. A solution of the yellow anhydride Ic was exposed to sunlight²⁹ or ultraviolet radiation to produce a reddish orange photoisomer that is assigned the structure *cis,trans*- α,α' -dipiperonylidene succinic anhydride (IIc).³⁰ As expected, the new compound exhibited in the nmr spectrum both a vinyl proton and an aromatic ring shifted considerably downfield owing to deshielding.³¹ The ultraviolet maximum in chloroform solution of the 318-m μ band of the reddish orange anhydride IIc is of

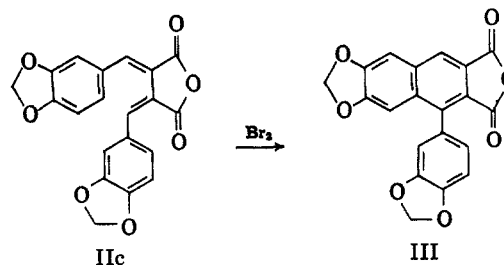
half the intensity of the yellow anhydride Ic, as expected for a partial *cis*-cinnamoyl chromophore.³² The change in the visual color of the compound is probably due to the strong absorption at about 440 m μ , which tails into the orange region.

The *cis,trans*-anhydride IIc on hydrolysis produced the *cis,trans*- α,α' -dipiperonylidene succinic acid (IIa), which on heating easily reverted to the original reddish orange anhydride. Treatment of the *cis,trans*-diacid IIa with diazomethane gave the *cis,trans*-dimethyl ester (IIb), while Fischer-Speier esterification with either ethanol or methanol formed the *cis,trans*-monoethyl ester (IId), and the *cis,trans*-monomethyl ester (IIe), respectively. The diacid IIa, the dimethyl ester IIb, and the monoethyl ester IId possess completely different physical properties from the equivalent compounds Ia, Ib, and Id. As an example, it may be noted that the *cis,trans*-anhydride and diester melt higher than the related *trans,trans* analogs.



The formation of the *cis,trans*-monoalkyl esters may be explained by the existence of the *cis,trans*-diacid IIa in the predominant, most stable *trans*-soidiene conformation (see above), in which considerable hindrance exists in the neighborhood of one of the carboxyl groups. In contrast, both the *cis,trans*-diacid IIa and the corresponding monomethyl ester IIe react with diazomethane to give the same dimethyl ester IIb.

Finally, treatment of either the *cis,trans*-anhydride IIc or the *trans,trans*-anhydride Ic with bromine at room temperature causes cyclization to 6,7-methylenedioxy-1-(3',4'-methylenedioxyphenyl)naphthalene-2,3-dicarboxylic acid anhydride (III).^{16,33} This same compound can be formed by thermal closure from the *cis,trans*-anhydride IIc.



(26) H. Stobbe and R. Härtel, *Ann.*, **380**, 59 (1911).

(27) H. Stobbe and E. Benary, *ibid.*, **380**, 71 (1911).

(28) H. Stobbe, *ibid.*, **380**, 83 (1911).

(29) The reaction was dependent upon the intensity of outdoor light (5 hr., California; 10 days, Massachusetts).

(30) The "red" form was not mentioned by Haworth³¹ (cloudy England), but was apparently obtained by El-Assal²² (cloudless Egypt), who made no comment on the color difference, as well as the higher melting point.

(31) D. N. Kevill, E. D. Weiler, and N. H. Cromwell, *J. Org. Chem.*, **29**, 1276 (1964).

(32) A. I. Scott, "Interpretation of the Ultraviolet Spectra of Natural Products," The Macmillan Company, New York, N. Y., 1964, pp 115, 119, 122.

(33) R. D. Haworth and W. Kelly, *J. Chem. Soc.*, 745 (1936).

All of the above data support the assumption that the yellow α,α' -dipiperonylidene fulgide is geometrically *trans,trans* and that the related reddish orange isomer is in the *cis,trans* series. It is felt that a similar explanation can be used to rationalize various other fulgide color changes noted in the literature.

Experimental Section³⁴

trans,trans- α,α' -Dipiperonylidene succinic Acid (Ia). **A. Low-Temperature Condensation.**—Freshly distilled piperonal (51.0 g, 0.34 mole) and diethyl succinate (30.0 g, 0.173 mole) in ether (250 ml) were added to a suspension of sodium methoxide (18.8 g, 0.348 mole) in ether (250 ml) and kept at -10° . After 1 week the reaction was quenched with water, the aqueous phase was separated, washed with ether, and acidified with dilute hydrochloric acid to give a yellow solid, which was crystallized from acetic acid, mp 210–215° [lit.^{12,18,20,21} mp 210° dec, 208°, 212° (from acetic acid)]. Recrystallization from acetone–benzene gave yellow *trans,trans*- α,α' -dipiperonylidene succinic acid (25.6 g, 45%): mp 220–223° dec [lit.^{21,22} mp 228°, 223–225° (from acetone–benzene)]; neut equiv 192; ν_{\max} 2933 (OH), 1665 (C=O), 1240 (CO), 920 (OCH₂O), and 805 (Ph) cm⁻¹; $\lambda_{\max}^{\text{ethanol}}$ 230 sh m μ (ϵ 25,000), 287 (19,500), and 327 (24,700); δ 7.72 (vinyl CH, singlet, two protons), 7.11, 7.08, and 7.07 (aromatic CH, multiplet, six protons), and 6.03 (methylenedioxy CH₂, singlet, four protons).

Anal. Calcd for C₂₀H₁₄O₈: C, 62.83; H, 3.69. Found: C, 62.98; H, 3.91.

B. High-Temperature Condensation.—Piperonal (19.2 g, 0.128 mole) and diethyl succinate (11.6 g, 0.073 mole) in *t*-butyl alcohol were added to a solution of potassium *t*-butoxide (prepared from 11.5 g of potassium) in *t*-butyl alcohol (250 ml), and the resulting solution was refluxed for 1.5 hr under a nitrogen atmosphere. The cooled mixture was acidified with concentrated hydrochloric acid (15 ml) in ice (45 g), the solvents were removed under reduced pressure, and the solid residue was dissolved in ether. The ethereal extract was shaken with saturated sodium bicarbonate solution and the alkaline layer was acidified with hydrochloric acid to precipitate a yellow solid (12.9 g). Recrystallization from acetone–benzene and aqueous dimethylformamide gave yellow prisms of the product (4.2 g), mp 222–225°. The solid residue from the ether extraction was dissolved in saturated sodium bicarbonate solution, which in turn was extracted several times with ether. Acidification of the alkaline extract yielded a yellow solid (15.0 g) that was recrystallized to give a further quantity of acid, mp 223–225°.

trans,trans- α,α' -Dipiperonylidene succinic Acid Dimethyl Ester (Ib).—A solution of diazomethane in ether was added to *trans,trans*- α,α' -dipiperonylidene succinic acid in methanol, the mixture was allowed to stand at 0° for 18 hr, the solvent was removed, and the product was crystallized from methanol as prisms: mp 184–185° [lit.^{22,24,25} mp 184°, 181°, 185°]; $\nu_{\max}^{\text{chloroform}}$ 1712 (C=O) cm⁻¹; $\lambda_{\max}^{\text{dioxane}}$ 235 m μ (ϵ 24,500), 291 (21,800), and 328 (28,500) [lit.²² $\lambda_{\max}^{\text{dioxane}}$ 235 m μ (ϵ 22,400), 293 (20,000), and 330 (26,900)].

Anal. Calcd for C₂₂H₁₈O₈: C, 64.39; H, 4.42. Found: C, 64.5; H, 4.3.

trans,trans- α,α' -Dipiperonylidene succinic Anhydride (Ic). **A. Acetyl Chloride Condensation.**—A mixture of *trans,trans*- α,α' -dipiperonylidene succinic acid (4.50 g, 0.0118 mole), benzene (40.0 ml), and acetyl chloride (40.0 ml) was refluxed for 3 days. After evaporation to dryness, the residue was crystallized from benzene to yield yellow anhydride (2.30 g, 80%): mp 210–213° [lit.^{18,21,25} mp 210°, 213°, 231° (red rosettes in the latter case)]; neut equiv 183; ν_{\max} 1803 and 1755 (O=COC=O), 1230 (CO), 912 (OCH₂O), and 807 (Ph) cm⁻¹; $\lambda_{\max}^{\text{chloroform}}$ 318 m μ (ϵ 17,100) and 428 m μ (ϵ 13,400); $\lambda_{\max}^{\text{dioxane}}$ 264 m μ (ϵ 13,300), 309 (14,000), and 425 (15,000); δ 7.72 (vinyl CH, singlet, two protons), 6.65 (aromatic CH, singlet, four protons), 6.30 (aromatic CH, singlet,

two protons), and 5.94 (methylenedioxy CH₂, singlet, four protons).

Anal. Calcd for C₂₀H₁₂O₇: C, 65.94; H, 3.32. Found: C, 65.90; H, 3.56.

B. Acetic Anhydride Condensation.—A mixture of the *trans,trans*-diacid (1.0 g) and acetic anhydride (5.0 ml) was heated under reflux for 1 hr, the solvent was removed under reduced pressure, and the residue was crystallized from methylene chloride–isopropyl ether to give yellow prisms (0.628 g), mp 212–215°. The analytical sample was recrystallized from the same solvent pair, mp 217–219°. The compound can be conveniently purified also by chromatography on silica gel, with elution by chloroform–benzene (1:1).

trans,trans- α,α' -Dipiperonylidene succinic Acid Monoethyl Ester (Id).—A mixture of *trans,trans*- α,α' -dipiperonylidene succinic anhydride (0.38 g), ethanol (10.0 ml), and sulfuric acid (1 drop) was refluxed for 20 hr. The alcoholic solution was diluted with ether (50.0 ml), washed with water, and extracted with dilute sodium bicarbonate. Acidification of the base extract gave the crude product, which was crystallized from ether–petroleum ether (bp 40–60°) to yield the half acid ester (0.24 g): mp 163–165°; neut equiv 412; ν_{\max} 3400 (OH), 1690 (C=O), 1240 (CO), 913 (OCH₂O), and 805 (Ph) cm⁻¹; $\lambda_{\max}^{\text{ethanol}}$ 218 m μ (ϵ 22,800), 230 sh (19,800), 290 (18,500), and 328 (24,200); δ 7.78 (vinyl CH, singlet, two protons), 7.13, 6.93, 6.85 (aromatic CH, multiplet, six protons), 6.14 (methylenedioxy CH₂, singlet, four protons), 4.12 (CH₂, quartet, two protons), and 1.12 (CH₃, triplet, three protons).

Anal. Calcd for C₂₂H₁₈O₈: C, 64.39; H, 4.42. Found: C, 64.17; H, 4.59.

cis,trans- α,α' -Dipiperonylidene succinic Anhydride (IIc). **A. Sunlight.**—A solution of *trans,trans*- α,α' -dipiperonylidene succinic anhydride (0.830 g, 0.00211 mole) in acetone (40.0 ml) was exposed to outdoor sunlight (July, 1965, Stanford campus) for 5 hr. The reddish orange needles were collected (0.407 g) and crystallized from benzene to give *cis,trans*- α,α' -dipiperonylidene succinic anhydride (0.358 g), mp 231–233°. Alternatively, a solution of yellow anhydride (0.300 g) in benzene (125.0 ml) was allowed to stand in daylight (April, 1963, Brandeis campus) for 10 days (about 3 days of appreciable sunlight). The resulting precipitate (0.096 g) was crystallized from acetone–benzene to afford the product: mp 235–237°; neut equiv 189; ν_{\max} 1795 and 1745 (O=COC=O), 917 (OCH₂O) and 810 (Ph) cm⁻¹; $\lambda_{\max}^{\text{chloroform}}$ 318 m μ (ϵ 8600), 358 sh (11,700), and 440, (28,200); $\lambda_{\max}^{\text{dioxane}}$ 262 m μ (ϵ 9600), 310 sh (7400), 355 (10,200), and 432 (25,600); δ 7.95 (aromatic CH, doublet, two protons), 7.77 (vinyl CH, singlet, two protons), 7.58 (aromatic CH, quartet, two protons), 7.08 (aromatic CH, doublet, two protons), and 6.16 (methylenedioxy CH₂, partially split singlet, four protons).

Anal. Calcd for C₂₀H₁₂O₇: C, 65.94; H, 3.32; O, 30.74. Found: C, 65.91; H, 3.53; O, 30.25.

B. Ultraviolet Light.—A solution of *trans,trans*-anhydride (0.300 g) in benzene was irradiated for 2 hr in a quartz apparatus using a Hanovia 608A-36 high-pressure mercury vapor light source with water cooling. A green fluorescent solution was immediately produced, followed by precipitation of orange crystals (0.186 g), mp 238–240°. Crystallization from acetone–benzene gave the *cis,trans*-anhydride as bright, reddish orange needles, mp 239–240°.

cis,trans- α,α' -Dipiperonylidene succinic Acid (IIa).—A solution of potassium hydroxide (0.800 g) in methanol (10.0 ml) was added to a suspension of the *cis,trans*- α,α' -dipiperonylidene succinic anhydride (0.100 g) in dioxane (5.0 ml). After the mixture had been refluxed for 1 hr, it was cooled, diluted with water, and acidified with concentrated hydrochloric acid to precipitate a pale yellow solid, which was collected by ether extraction, and the extract was washed with water and dried over sodium sulphate. Removal of the ether gave a yellow, crystalline solid (0.115 g), mp 230–235° (turns orange at 120°). Successive recrystallization from acetone–isopropyl ether caused lowering and erratic behavior of the melting point, which was also affected, by the heating rate: ν_{\max} 2976 (OH), 1727 and 1689 (C=O) 937 (OCH₂O), and 818 (Ph) cm⁻¹; δ 6.92 (aromatic CH, multiplet), 6.68 and 6.65 (aromatic CH, singlets), and 6.09 (methylenedioxy CH₂, singlet).

Anal. Calcd for C₂₀H₁₄O₈: C, 62.83; H, 3.69. Found: C, 62.9; H, 3.5.

The *cis,trans*-diacid (0.028 g) was heated at 150° in an open tube for 30 min, during which the color changed from yellow to orange. Crystallization of the product from acetone–benzene

(34) All melting points are uncorrected. Microanalyses were provided by Alfred Bernhardt, Mülheim, West Germany; Carol K. Fitz, Needham Heights, Mass.; and Erich H. Meier and J. Consul, Stanford University. Some of the infrared and ultraviolet spectra were obtained by Mrs. Linda D. Carroll, while the integrated nmr spectra were furnished by Dr. Lois J. Durham, both of Stanford University. Unless otherwise stated, infrared spectra were recorded in potassium bromide wafers, and nmr spectra were determined in deuteriodimethyl sulfoxide at 60 Mc/sec.

gave the *cis,trans*-anhydride, mp 233–235°, identical with an authentic specimen.

***cis,trans*- α,α' -Dipiperonylidenesuccinic Acid Dimethyl Ester (Iib).**—A solution of diazomethane in ether was added to a suspension of *cis,trans*- α,α' -dipiperonylidenesuccinic acid (0.047 g) in ether (10.0 ml), the mixture was stored at 0° overnight, a few drops of acetic acid was added to destroy excess reagent, and the solvents were removed under reduced pressure. Crystallization of the pale yellow residue (0.046 g) from chloroform-methanol gave pale yellow needles of *cis,trans*- α,α' -dipiperonylidenesuccinic acid dimethyl ester: mp 205–207°; ν_{\max} 1727 (C=O), 1230 (CO), 907 (OCH₃O), and 817 (Ph) cm⁻¹; $\lambda_{\max}^{\text{dioxane}}$ 350 m μ (ϵ 29,200); δ 6.90 and 6.76 (aromatic CH, singlets) and 6.09 (methylenedioxy CH₂, singlet).

Anal. Calcd for C₂₂H₁₈O₈: C, 64.39; H, 4.42. Found: C, 64.53; H, 4.20.

***cis,trans*- α,α' -Dipiperonylidenesuccinic Acid Monoethyl Ester (Iid).**—A suspension of *cis,trans*- α,α' -dipiperonylidenesuccinic anhydride (0.107 g) in ethanol (20.0 ml)–benzene (20.0 ml) containing 1 drop of concentrated sulfuric acid was refluxed for 4 days. The solution was decanted from some unchanged *cis,trans*-anhydride (0.022 g), and worked up as described for the *trans,trans*-monoethyl ester to afford crude, light yellow product (0.054 g), mp 220–225° (prior melting at 155°). Crystallization from benzene gave pale yellow needles of *cis,trans* half acid ethyl ester: mp 224–227°; neut equiv 422; ν_{\max} 3500 (OH), 1710 (C=O), 1250 (CO), 913 (OCH₂O), and 801 (Ph) cm⁻¹; $\lambda_{\max}^{\text{ethanol}}$ 346 m μ (ϵ 26,900).

Anal. Calcd for C₂₂H₁₈O₈: C, 64.39; H, 4.42. Found: C, 64.67; H, 4.57.

The *cis,trans* half acid ethyl ester was heated at 150° in an open tube for 30 min, during which the color changed from yellow to red. Crystallization of the product from benzene gave the *cis,trans*-anhydride, mp 231–232°, identical with an authentic specimen.

***cis,trans*- α,α' -Dipiperonylidenesuccinic Acid Monomethyl Ester (Iie).**—A few drops of concentrated sulfuric acid was added to a suspension of *cis,trans*- α,α' -dipiperonylidenesuccinic anhydride (0.100 g) in methanol (100 ml) and the mixture was refluxed for 24 hr. Concentration of the solution caused separation of a small quantity of unchanged *cis,trans*-anhydride (mp 229–230°), which was removed by filtration. The filtrate was diluted with water and extracted with ether, and the dried (sodium sulfate) extract was evaporated to give a semicrystalline, yellow solid (0.061 g), mp 216–221° (turns orange at 120°). Crystallization from chloroform-methanol gave yellow prisms of

cis,trans- α,α' -dipiperonylidenesuccinic acid monomethyl ester: mp 218–223° (with prior color change); δ 6.85 (aromatic CH, multiplet), 6.62 and 6.50 (aromatic CH, singlets), 6.07 (methylenedioxy CH₂, singlet), 3.79 (ester CH₃, singlet), and 3.27 (solvate CH₃, singlet).

Anal. Calcd for C₂₁H₁₆O₈·CH₃OH: C, 61.68; H, 4.71. Found: C, 61.96; H, 4.47.

Treatment of the above *cis,trans*-monoethyl ester (0.034 g) with an ethereal solution of diazomethane gave the *cis,trans*-dimethyl ester, mp 202–204°, identical with an authentic specimen.

6,7-Methylenedioxy-1-(3',4'-methylenedioxyphenyl)naphthalene-2,3-dicarboxylic Acid Anhydride (III). A. Bromine Cyclization of *cis,trans*- α,α' -Dipiperonylidenesuccinic Anhydride.

—A solution of bromine (0.104 g) in dioxane (2.0 ml) was added to a solution of *cis,trans*- α,α' -dipiperonylidenesuccinic anhydride (0.053 g) in dioxane (10.0 ml), the mixture was allowed to stand overnight at room temperature, water was added, and the product was extracted with ether. Removal of the ether from the washed and dried extract gave a semicrystalline solid, which on two recrystallizations from chloroform-methanol yielded yellow crystals of 6,7-methylenedioxy-1-(3',4'-methylenedioxyphenyl)naphthalene-2,3-dicarboxylic acid anhydride, mp 220–226°, identical with an authentic specimen (lit.^{16,33} mp 226°, 246°).

B. Thermal Cyclization.—Solid *cis,trans*- α,α' -dipiperonylidenesuccinic anhydride (4.0 g) was heated at about 270° (refluxing ethyl cinnamate) for 1.5 hr, then triturated with ether to form a dark product (3.0 g), mp 210–215°. This material was dissolved in chloroform-benzene and chromatographed on silica gel (50.0 g). Elution with the same solvent mixture gave pale yellow crystals (1.0 g), mp 224–226°, which were recrystallized from chloroform to yield the naphthalenic anhydride, mp 230–231°.

C. Bromine Cyclization of *trans,trans*- α,α' -Dipiperonylidenesuccinic Anhydride.³⁶—A solution of the yellow *trans,trans* anhydride (0.05 g) in dioxane (10.0 ml) was treated with bromine as in A above. Crystallization of the product from chloroform-methanol gave yellow crystals of the naphthalenic anhydride (0.019 g), mp 229–231°.

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Nuclear Magnetic Resonance Studies of Spiro[tetralin-1,4'-piperidine] Compounds

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The nmr spectra of unreported 7-methoxy-1'-methyl-2-oxospiro[tetralin-1,4'-piperidine] (I), its salts, and the corresponding alcohol (III) have been measured in a variety of solvents, and the results have been analyzed using a provisional first-order approach. Model compounds have been used to assist in the analysis, as well as temperature, decoupling, and deuteration experiments. Unusual chemical shift data have been used to study conformational equilibria in this series of molecules. The nmr spectrum of compound I hydrochloride, measured in deuteriochloroform, showed an aromatic proton selectively deshielded 24 cps compared with the aromatic protons of the free base I. In compound I hydrochloride measured in aprotic solvents the 3',5'-equatorial protons of the piperidine ring appeared at higher field than the corresponding axial ones.

The unreported 1'-alkyl-2-oxospiro[tetralin-1,4'-piperidine] ring system (*e.g.*, compound I) was synthesized,² and several salts and derivatives were prepared

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(2) Some of the spiro compounds of this series were synthesized for their evaluation as analgesics. Compound V was found to be inactive at 100 mg/kg in the preliminary tail burn analgesic test when administered by intraperitoneal injection to rats. This inactivity compared with the open-chain piperidine analog 4-(3-hydroxyphenyl)-1-methyl-4-propionylpiperidine (see C. M. Suter in "Medicinal Chemistry," Vol. II, F. F. Blicke and C. M. Suter, Ed., John Wiley and Sons, Inc., New York, N. Y., 1958, p 227) is ascribed to the rigidity of the spiro structure in compound V.

for a nuclear magnetic resonance (nmr) study that is the subject of this paper.

Compound I was prepared in a straightforward though rather specific fashion from 7-methoxy-2-tetralone, bis(2-chloroethyl)methylamine, and potassium tertiary butoxide in dimethyl sulfoxide under nitrogen (eq 1). 2-Tetralone behaved similarly forming 1'-methyl-2-oxospiro[tetralin-1,4'-piperidine] (II). Ketone I was reduced with sodium borohydride to the corresponding alcohol (III) which was converted to its acetyl derivative (IV). Hydrolysis of compound I