Diphenyl-9-*n*-butyl-3,7-diazaadamantan-9-ol, 1 g. (0.0033 mole), was heated on a steam bath for 5 min. with 5 ml. of acetic anhydride. The reaction mixture was allowed to stand for 1 night at room temperature; then 10 ml. of benzene and 20 ml. of ether were added, and the mixture was placed in the deep freeze overnight. The white crystalline material obtained was filtered and recrystallized from ethanol, m.p. 189–90° (1 g., 80% yield).

Anal. Calcd. for $C_{27}H_{34}N_2O_3$: C, 74.62; H, 7.89; N, 6.45. Found: C, 74.45; H, 7.87; N, 6.36.

1,5-Diphenyl-9-butylidene-3,7-diacetylbispidine (V). 1,5-Diphenyl-9-*n*-butyl-3,7-diazaadamantan-9-ol, 3 g. (0.01 mole), was heated on a steam bath for 3 hr. with 15 ml. of acetic anhydride. The acetic anhydride was removed on the water bath under vacuum, leaving a white solid, m.p. 197–198° (3 g., 85% yield). The product was recrystallized twice from ethanol, m.p. 198–199°.

Anal. Calcd. for $C_{27}H_{32}N_2O_2$: C, 77.85; H, 7.74; N, 6.73. Found: C, 77.70; H, 7.79; N, 6.89.

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[CONTRIBUTION FROM MCNEIL LABORATORIES, INC.]

Bicyclic Bases. III. Isomeric 2-Amino-3-phenylnorbornanes[1]

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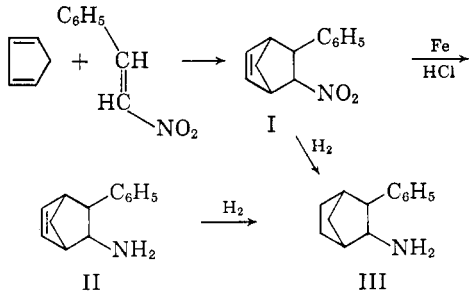
Proof of the stereochemistry of the known *trans*-2-amino-3-phenylnorbornane is given. Synthesis and structure proof of the other *trans* isomer as well as the *endo-cis* isomer are also accomplished. Attempts are described to obtain the fourth possible isomer with the *exo-cis* configuration.

In connection with our interest in correlating stereochemistry with pharmacological activity, we have investigated several of the isomeric 2-amino-3-phenylnorbornanes.

Our work started with a repetition of the synthesis of 2-amino-3-phenylnorbornene (II) and-norbornane (III) reported by Parham, Hunter, and Hanson[2] from the adduct I[3] of cyclopentadiene and

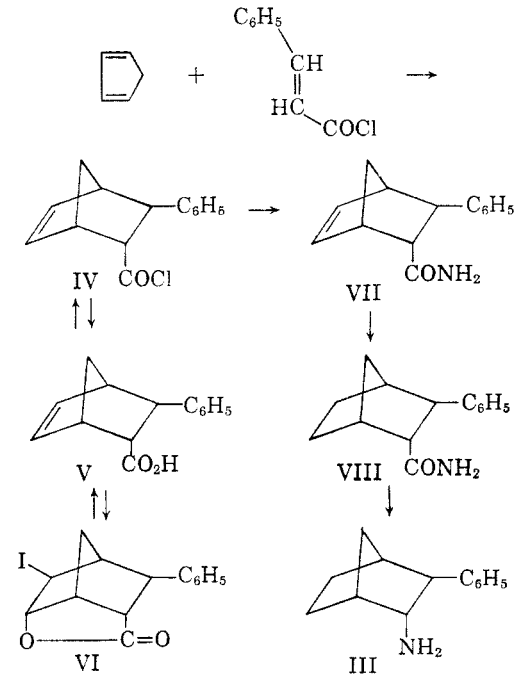


trans-β-nitrostyrene. These workers had reduced I to the unsaturated amino compound II in about 50% yield with iron and hydrochloric acid. Both I and II were reduced catalytically to the saturated amine III. The amines II and III were characterized by Parham and co-workers as crystalline benzenesulfonamides. However, yields of the benzenesulfonamides were not reported, and no stereochemistry was assigned. We repeated the iron–hydrochloric acid reduction of nitro compound I and obtained unsaturated amine II in 50% yield. The latter was converted in good yield to a single benzenesulfonamide which agreed reasonably well in melting point with that reported.[2] After repeating this portion of the reported work without difficulty, we then set about to (a) prove the stereochemistry of amines II and III; and (b) investigate more critically the nature of the cyclopentadiene-*trans*-β-nitrostyrene adduct I since apparently the work with these compounds had been a side issue with Parham, Hunter, and Hanson.

Reasoning from the "maximum accumulation of unsaturation" of "Alder rule II"[4] in the orientation of *trans*-β-nitrostyrene and cyclopentadiene during their condensation, one would expect adduct I to contain only *trans* adducts and to be predominantly the *endo*-nitro-*exo*-phenyl isomer IX and hence the amines II and III to be the *trans-endo*-amino compounds. An unequivocal synthesis of the saturated amine III proved this to be the case. The cyclopentadiene-*trans*-cinnamoyl chloride adduct IV, known to have the *endo*-acid chloride function and *exo*-phenyl group by interconversion to the acid V and iodolactone VI,[5] was aminated to the unsaturated amide VII. The latter, upon hydrogenation to the saturated amide VIII, gave amine III by Hofmann reaction.

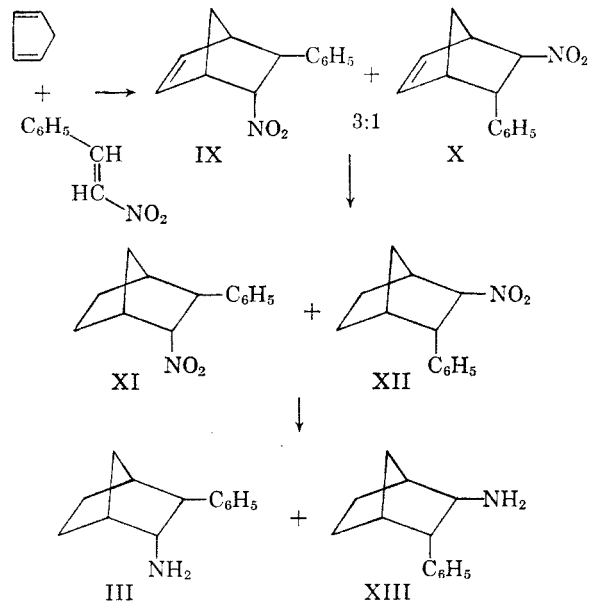
Since the completion of this phase of our work, several reports have appeared on efforts directed towards the proof of the stereochemistry of the amine obtained by reduction of the cyclopentadiene-

(1) Paper II in this series; *J. Org. Chem.*, **26**, 2576 (1961).
(2) W. E. Parham, W. T. Hunter, and R. Hanson, *J. Am. Chem. Soc.*, **73**, 5068 (1951).
(3) C. F. H. Allen, A. Bell, and J. W. Gates, *J. Org. Chem.*, **8**, 373 (1943).
(4) K. Alder and G. Stein, *Angew. Chem.*, **50**, 514 (1937).
(5) C. S. Rondestvedt and C. D. Ver Nooy, *J. Am. Chem. Soc.*, **77**, 4878 (1955).



trans-β-nitrostyrene adduct. Trivette[6] converted amine III *via* nitrous acid deamination, oxidation, and Wolff-Kishner reduction to *exo*-2-phenylnorbornane and then prepared this compound for comparison by Hunsdiecker reaction and reductive debromination of the saturated acid derived from compound V by hydrogenation. Weinstock and Flores[7] have described a proof of structure very similar to ours in which the saturated acid corresponding to V was converted to amine III *via* the acyl azide, rearrangement to the isocyanate and hydrolysis to the amine.

We have investigated the cyclopentadiene-*trans*-β-nitrostyrene adduct I in some detail. As obtained by the reported method,[2,3,6,7] this product contains about 5% of unchanged *trans*-β-nitrostyrene which can be detected by its strong ultraviolet absorption at 300 mμ (ε 16,600). Careful fractionation removes styrene in the head fractions; the pure adduct has no selective absorption at 300 mμ. Adduct I was shown to be a 3:1 mixture of the two *trans* isomers IX and X by hydrogenation of the double bond over platinum catalyst[6,8] and analysis of the resulting mixture of saturated nitro compounds XI and XII by vapor phase chromatography.[9] That saturated



endo-nitro compounds IX and XI were major components was shown by further hydrogenation of the nitro group over palladium catalyst to the mixture of amines III and XIII (again shown to be a 3:1 mixture by vapor phase chromatography) and conversion to their benzenesulfonamides which were separated by adsorption chromatography over alumina. The pure benzenesulfonamide of III was obtained in 35% yield while that of XIII was obtained in 7% yield. Although these two derivatives have almost the same melting points, the two compounds were shown to be different by infrared spectra and mixed melting point. The 3:1 ratio of isomeric adducts IX and X was obtained from several runs of the diene condensation although temperatures and times of heating were varied.

In order to prepare sufficient quantities of the *trans*-2-amino-3-phenylnorbornane XIII for pharmacological testing, an alternate method of synthesis was used. Cyclopentadiene and phenylpropiolyl chloride condense exothermically to give the liquid, doubly unsaturated acid chloride XIV which was used without distillation. With aqueous ammonia, XIV gave the crystalline amide XVI along with a small amount of the phenylnorbornadiene carboxylic acid XV as by-product.

After we had completed this work, Cristol and La Londe[10] reported the preparation of acid XV by saponification of either acid chloride XIV or the corresponding methyl ester which they obtained by condensation of cyclopentadiene with the corresponding phenylpropiolic acid derivative. In subsequent work where we had need of acid XV for synthesis, it was prepared *via* phenylpropiolic ester because of the excellent yields obtained by this route.[10]

Phenylnorbornadiene carboxamide (XVI) on

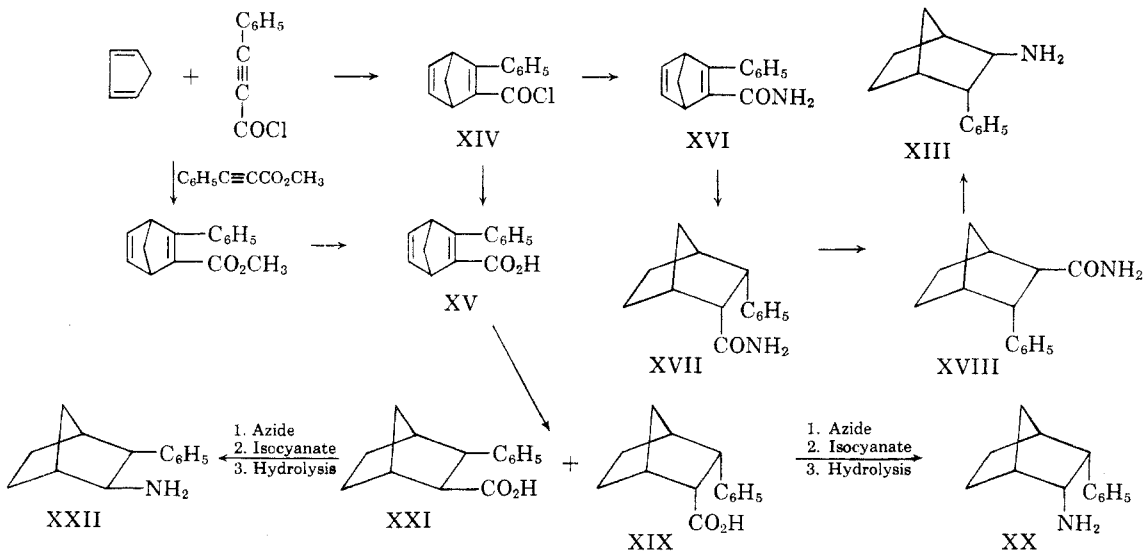
(6) C. D. Trivette, Jr., Ph.D. thesis, Duke University (1959).

(7) J. Weinstock and M. C. Flores, Abstracts of Papers, Third Delaware Valley Regional Meeting, Philadelphia, Pa., February 25, 1960, p. 46.

(8) W. C. Wildman and C. H. Hemminger, *J. Org. Chem.*, **17**, 1641 (1952).

(9) Vapor phase chromatography of the unsaturated nitro compounds was not attempted due to the anticipated reversal of the diene condensation at the high temperatures necessary. We are indebted to Dr. W. C. Wildman for his invaluable assistance and advice with the vapor phase chromatography.

(10) S. J. Cristol and R. T. La Londe, *J. Am. Chem. Soc.*, **81**, 5417 (1959).



catalytic reduction over platinum gave a 75% yield of a single crystalline saturated amide. Structure XVII was assigned due to the expected *cis-exo* addition of hydrogen. Proof for this assignment is as follows. This amide was different from the saturated amide VIII obtained from *trans*-cinnamoyl chloride. On treatment with base, XVII was readily isomerized in high yield to a third isomeric amide which was assigned the *trans* structure with the *endo*-phenyl and *exo*-carboxamide orientation (XVIII). This was confirmed by Hofmann reaction of amide XVIII which gave amine XIII. Identity with the minor product obtained previously from *trans*-β-nitrostyrene was shown by a comparison of benzenesulfonamides.

For the preparation of the *cis*-2-amino-3-phenylnorbornanes, we turned to the catalytic hydrogenation of doubly unsaturated acid XV. This compound readily absorbed two moles of hydrogen to give a good yield of *cis-endo* acid XIX. Using the mixed anhydride technique, acid XIX was converted to the acyl azide which was then rearranged to the isocyanate, and the product was hydrolyzed to give the *cis-endo* amine XX in an over-all yield of about 50%.[7] Amine XX was shown to be different from isomers III and XIII by a comparison of hydrochlorides and benzenesulfonamides.

Apparently a small amount of the *cis-exo* acid XXI was formed in the catalytic hydrogenation of unsaturated acid XV. An acid mixture enriched in XXI from the crystallization mother liquors of XIX was converted to amine *via* the azide and isocyanate sequence. From this amine a benzenesulfonamide was prepared. Fractional crystallization served to separate 1% (over-all from XV) of a sharply melting derivative, most likely the benzenesulfonamide of XXII. Although its melting point (132°) and infrared spectrum were different from those of the benzenesulfonamides of III, XIII, and XX, its melting point was not lowered on admixture with the benzenesulfonamide of XX (mp. 126°). Unfortunately this is not a practical sequence for obtaining the pure *cis-exo* amine in sufficient quantity for pharmacological testing.

Recently a report appeared[11] describing the high temperature condensation of cyclopentadiene with *cis*-cinnamic acid to give the *cis-endo* acid as the major product. A small quantity of the *cis-exo* acid was also obtained from this reaction, but the low yield (3%) again makes it impractical as a source of the fourth isomeric aminophenylnorbornane.

A possible approach to obtaining the *cis-exo* amine in quantity would be the isomerization of *exo*-phenyl-*trans*-nitro compounds IX or XI to the *cis-exo* form followed by reduction. Zimmerman and Nevins[12] have shown that *trans*- 1-nitro-2-phenylcyclohexane can be isomerized in good yield to the corresponding *cis* isomer by acidification of an alcoholic potassium hydroxide solution of the *aci*-nitro conjugate base with alcoholic sulfuric acid.

Although we did not have a pure *trans*-nitro compound in hand, both the unsaturated mixture I and saturated mixture (XI and XIII) of bicyclic nitro compounds were subjected to the isomerization conditions of Zimmerman and Nevins.[12] In both cases, the major product was the unchanged *trans*-nitrophenyl compound (IX and XI, respectively). These experiments were repeated a number of times under varying conditions, but no isomerization to the *cis* isomers could be detected. Nef hydrolysis to the phenylnorcamphors was found to be a noticeable side reaction, particularly in isomerization attempts with the saturated *trans*-nitro compound mixture (see Experimental section).

Results of pharmacological testing.[13] When tested intravenously in the morphine-chloralose anesthetized dog, the *endo*-amino-*exo*-phenyl compounds

(11) K. Alder and W. Günzl, *Ber.*, **93**, 809 (1960).

(12) H. E. Zimmerman and T. E. Nevins, *J. Am. Chem. Soc.*, **79**, 6559 (1957).

(13) We are indebted to our Department of Biological Research for these results.

II and III showed a biphasic effect on blood pressure at doses below 0.5 mg./kg. The other *trans* isomer XIII and the *cis-endo* isomer XX were qualitatively similar but considerably less potent being one-eighth and one-twentieth of II and III, respectively.

EXPERIMENTAL[14]

trans-2-Nitro-3-phenyl-5-norbornene (I). Cyclopentadiene (75 g., 1.13 moles) and β-nitrostyrene (100 g., 0.67 mole) were combined essentially as described in the literature.[3] Distillation of the product gave 131.0 g. (91%), b.p. 114°/0.10 mm., n_D^{26} 1.5633, λ_{max} 3.27, 3.36, 3.48, 6.12, 6.23, 6.48, 6.65, 6.87, 7.25–7.28, 7.47 μ (lit. b.p. 136–138°/1–2 mm., n_D^{20} 1.5641), $\lambda_{max}^{CH_3OH}$ 300 mμ ($\Sigma_{1\ cm.}^{1\%}$ 64). The ultraviolet absorption is equivalent to 5.8% β-nitrostyrene. Two distillations of the adduct through a vacuum-jacketed Vigreux column gave a β-nitrostyrene-free sample, b.p. 121–122°/0.03 mm., n_D^{24} 1.5660, as judged by the lack of ultraviolet absorption at 300 mμ.

2-Amino-3-phenyl-5-norbornene hydrochloride (II).[2] A mixture of 35 g. of iron filings, 75 ml. of water, 35 g. of nitro adduct I, and 10 ml. of concd. hydrochloric acid was heated on the steam bath with rapid stirring for 6.5 hr. The alkaline mixture was acidified with hydrochloric acid and filtered. The filtrate was extracted with methylene chloride and then with *n*-butyl alcohol. The methylene chloride extract containing neutral material was discarded. The butanol extract was washed with water, dried over anhydrous magnesium sulfate, and concentrated nearly to dryness. The resulting crystals were slurried with ether, collected on a filter, washed with ether, and dried; 18.5 g. (51%), melting at 240–250° dec. Recrystallization from methanol-ether gave 13.5 g., m.p. 248–252° dec.

Anal. Calcd. for $C_{13}H_{16}ClN$: N, 6.32. Found: N, 6 25

The benzenesulfonamide prepared from 0.50 g. of the hydrochloride amounted to 0.72 g. (98%) melting at 160–168°. Recrystallization from methanol and ethanol gave 0.42 g., m.p. (165°) 170–172°, λ_{max}^{KBr} 2.92, 3.08, 3.27, 3.31, 3.36, 3.43, 5.76 vw, 6.24 w, 6.31 vw, 6.68, 6.89, 6.99 μ (lit.[2] m.p. 165–166°).

exo-3-Phenyl-5-norbornene-endo-2-carboxylic acid (V) *via endo-6-hydroxy-exo-5-iodo-exo-3-phenylnorbornane endo-2-carboxylic acid lactone* (VI). A procedure similar to that described[5] was used. Cyclopentadiene (30 ml.), cinnamoyl chloride (25 g.), and a few crystals of picric acid were warmed together without solvent under gentle reflux for 1 hr. Volatile material was removed under vacuum, and the residual crude acid chloride was saponified by addition to cold 10% sodium hydroxide containing a small amount of detergent. After warming to 50°, the basic mixture was cooled, diluted with 250 ml. of water, filtered, and acidified. The product was extracted into ether and the ether solution was washed, dried, and concentrated to dryness. Two recrystallizations of the residue from heptane provided 23.6 g. (74%) of 3-phenyl-5-norbornene-2-carboxylic acid, m.p. 89–105°. With iodine (49 g.)–potassium iodide (95 g.) solution (285 ml.), 20 g. of this acid in 570 ml. of 0.5*N* sodium bicarbonate gave 25 g. (80%) of crude iodolactone VI. Recrystallization from benzene-ether gave the pure lactone VI, m.p. 118.5–120° (lit.[5] m.p. 118–119° and 126.0–126.5°).

Anal. Calcd. for $C_{14}H_{13}IO_2$: C, 49.43; H, 3.84. Found: C, 49.43; H, 3.91.

Reduction of 17.5 g. of VI in 100 ml. of 90% acetic acid with 40 g. of zinc dust (4 hr. of reflux) gave 8.3 g. (75%) of pure acid V, m.p. 108–110°, after recrystallization from heptane. The analytical sample showed the same melting point (lit.[5] m.p. 107–108°); λ_{max}^{Nujol} 3.27, br. 3.6–3.9, 5.88 μ.

exo-3-Phenyl-5-norbornene-endo-2-carboxamide (VII). Although Rondestvedt and Ver Nooy apparently made this compound (ref. 5, Table I), no properties or procedure were reported. We prepared VII by two methods.

A. *From crude* IV. A benzene solution of the crude cyclopentadiene-cinnamoyl chloride adduct (from 50 g. of acid chloride; see preparation of V and VI above) was added to 200 ml. of ice-cold concentrated aqueous ammonia. The precipitated solid was collected by filtration, washed, and thoroughly dried to give 55 g. (88%) m.p. 93–135°. After recrystallization from benzene and chloroform–petroleum ether (b.p. 30–60°), there was obtained 26 g. (42%), m.p. 143–146°; λ_{max}^{Nujol} 2.88, 3.14, 3.26, 6.02, 6.15, 6.19 μ. The ultraviolet spectrum showed only benzene ring absorption.

Anal. Calcd. for $C_{14}H_{15}NO$: N, 6.57. Found: N, 6.47.

B. *From pure V.* A solution of 0.5 g. of *exo*-3-phenyl-5-norbornene-*endo*-2-carboxylic acid (V, m.p. 107–110°) in 10 ml. of anhydrous benzene was treated with 0.5 ml. of oxalyl chloride at room temperature with stirring. After 2 hr. at room temperature, the reaction solution was concentrated to dryness under vacuum, and the residual oil was treated at ice temperature with 10 ml. of cold concd. aqueous ammonia solution. The resulting white solid was stirred for 2 hr., collected on a filter, washed with water and dried to give 0.47 g., m.p. 143–146°. Recrystallization from chloroform–petroleum ether (b.p. 30–60°) provided 0.43 g. (87%) of pure amide VII melting at 147–148°. This sample was the same by mixed melting point and spectra with the analytical sample described in section A above.

exo-3-Phenyl-endo-2-norbornanecarboxamide (VIII). A 5.0-g. sample of VII was dissolved in methyl alcohol and hydrogenated using platinum dioxide catalyst. The calculated amount of hydrogen was taken up in 1 min. and no more hydrogen was absorbed for 1 hr. The solution was then filtered and evaporated, and the residue was recrystallized from chloroform–petroleum ether. The crystalline product weighed 4.0 g. and melted at 138–140°. When admixed with a sample of VII, the mixture melted at 125–135°; λ_{max}^{Nujol} 2.94, 3.12, 6.06 μ.

Anal. Calcd. for $C_{14}H_{17}NO$: N, 6.51. Found: N, 6.53.

endo-2-Amino-exo-3-phenylnorbornane (III) *hydrochloride.* A solution of 2.4 g. of sodium hydroxide in 20 ml. of water was cooled to 0°, stirred, and treated with 0.8 ml. of bromine. To the yellow solution was added 2.16 g. of VIII. The mixture was stirred at 0° for 1 hr. and then heated to 60° for 10 min. The oily layer which formed was collected by ether extraction. The ether solution was extracted with two 25-ml. portions of 6*N* hydrochloric acid. The acid solution was cooled, made basic with sodium hydroxide, and extracted with ether. The ether solution was dried over sodium sulfate, filtered, treated with anhydrous hydrogen chloride gas, and evaporated. The residue was recrystallized from isopropyl alcohol–heptane and from chloroform–petroleum ether to give III hydrochloride, melting at 204–206°; λ_{max}^{Nujol} 3.83, 5.00, 6.23, 6.56, 6.64 μ.

Anal. Calcd. for $C_{13}H_{18}ClN$: N, 6.26. Found: N, 6.26, 6.41.

From the amine hydrochloride (0.651 g., 0.00291 mole), benzenesulfonyl chloride (1.4 ml., 1.0 g., 0.0057 mole), and 10% sodium hydroxide (5 ml.), there was obtained 0.870 g. (96.4%) of the benzenesulfonamide, m.p. 133–140°. Recrystallization from absolute ethanol gave the constant melting derivative, m.p. 142–143° (lit.[2] m.p. 136–137.5°); $\lambda_{max}^{CHCl_3}$ 2.97, 3.08, 6.25, 6.76, 6.90 μ.

Anal. Calcd. for $C_{19}H_{21}NO_2S$: C, 69.69; H, 6.47; N, 4.28. Found: C, 69.71; H, 6.41; N, 4.22.

endo-2-Nitro-exo-3-phenylnorbornane (XI) *and exo-2-nitro-endo-3-phenylnorbornane* (XII). A mixture of 21.5 g. (0.1 mole) of the nitro adduct I (actually a mixture of the

(14) Melting points are corrected. Infrared spectra were determined with a Perkin-Elmer Model 21 spectrometer and ultraviolet spectra were obtained with a Cary Model 14 spectrometer. A Perkin-Elmer Model 154C Vapor Fractometer was used for vapor phase chromatography analysis.

stereoisomers IX and X), 150 ml. of absolute methanol, and 0.1 g. of platinum dioxide was shaken with hydrogen at an initial pressure of 40 p.s.i. After 5 min., 0.1 mole had been consumed and the absorption of hydrogen stopped. The catalyst was removed, and the solvent was evaporated under reduced pressure. The product, after one distillation, was obtained as a colorless liquid in 85% yield (18.4 g.), b.p. 106–112°/0.1 mm., n_D^{29} 1.5491–1.5502; λ_{max}^{Neat} 6.22, shl. 6.47, 6.65, 6 74, 6.85, shl. 7.27, 7.54, 7.65 μ.

Anal. Calcd. for $C_{13}H_{15}NO_2$: C, 71.86; H, 6 96; N, 6.45. Found: C, 71.91; H, 6.96; N, 6.43.

Vapor phase chromatography was carried out using a 2 meter × 5 mm. column packed with 14.8% polyethylene glycol succinate on 80–100 mesh acid-washed Chromasorb W and a thermistor detector at 223° and a helium flow rate of 3 ml./min.; 5–10-μl. samples were separated into two distinct bands in a ratio of 3:1. Retention times were 19.4 and 20.8 min., respectively for XI and XII.

endo-2-Amino-exo-3-phenylnorbornane (III) *and exo-2-amino-endo-3-phenylnorbornane* (XIII). The adduct mixture I (*i.e.* IX and X) (13.5 g., 0.0629 mole), 12 g. of 10% palladium-on-carbon and 125 ml. of absolute ethanol were shaken with hydrogen at an initial pressure of 59 p.s.i. After 20 min. the calculated amount of hydrogen was absorbed. The catalyst was removed by filtration and washed thoroughly with ethanol, and the filtrate was concentrated at reduced pressure to give 11.2 g. (95.6%) of a semisolid residue, $\lambda_{max}^{CCl_4}$ 3.28, 3.33, 3.45, 6.23, 6.66, 6.76, 6.87 μ.

A mixture of the crude reduction product (1 04 g., 0.00558 mole), freshly distilled benzenesulfonyl chloride (1.0 ml., 1.38 g., 0.00785 mole), and 5 ml. of 10% sodium hydroxide was shaken for 1 hr. and allowed to stand overnight. The precipitate was collected on a filter, washed with water, and air dried, yielding 1.82 g. (100%), m.p. 98–125°. Five recrystallizations from absolute ethanol gave 0.37 g. (20.7%) of the benzenesulfonamide of III, m.p. 141–142°; the sample did not depress the melting point of III-benzenesulfonamide but did depress the melting point of XIII-benzenesulfonamide.

The combined mother liquors were concentrated, and a 1.19-g. portion of the residual oil was dissolved in benzene and chromatographed on 30 g. of neutral Woelm alumina. From the fractions eluted with benzene and benzene-ether, there was obtained an additional 0 29 g. of the benzenesulfonamide of III, m.p. 141–142° (total yield 36%). Further elution with ether and ether-chloroform gave mixtures. Elution with methanol gave 0.15 g. of the benzenesulfonamide of XIII which after washing with ether amounted to 0.13 g. (6.9%), m.p. 140–142°. The characterization of this compound is given in a following section. When mixed with the benzenesulfonamide of III, the mixture melted at 117–131°.

Phenylpropiolyl chloride.[15] Sodium phenylpropiolate was prepared by dissolving 14.6 g. (0.1 mole) of phenylpropiolic acid in 40 ml. of water and neutralizing with 10% sodium hydroxide solution (39 ml. required). The resulting solution was concentrated to dryness under vacuum (first under aspirator vacuum and finally with warming under high vacuum). The lumps of salt were crushed to a fine powder, suspended in benzene, and the mixture evaporated to dryness with final prolonged warming at 0.01 mm. pressure. This product is a very fine powder and appears to be essentially devoid of moisture.

The salt was then suspended in 100 ml. of dry benzene and, with stirring and ice-cooling, treated rapidly dropwise with 10 ml. (0.117 mole) of oxalyl chloride. After gas evolution had subsided, the mixture was allowed to stir at room temperature for 2 hr. and then filtered. The filtrate was concentrated under vacuum and the residual oil was distilled. There was obtained 14.08 g. (85%) of pale yellow distillate, b.p. 53–65°/0.1–1.0 mm. (lit.[15] b.p. 119°/12 mm.).

3-Phenyl-2,5-norbornadiene-2-carboxylic acid (XV) *and 3-phenyl-2,5-norbornadiene-2-carboxamide* (XVI). To 14.0 g. (0.085 mole) of phenylpropiolyl chloride were added 20 ml. (0.3 mole) of freshly prepared cyclopentadiene and a few crystals of picric acid. The resulting solution warmed spontaneously after 10 min. finally reaching a temperature of 60–70° after 30 min. After 1 hr., an additional 10 ml. of cyclopentadiene was added and the solution heated under reflux for 1 hr. Volatile components were removed under vacuum with final warming at 100° and 0.1 mm. The residue (24 g. of brown gum) was dissolved in 150 ml. of benzene and added slowly to cold concentrated ammonia solution. After standing at room temperature overnight, the mixture was concentrated *in vacuo* until all of the benzene was gone The gummy product was extracted with methylene chloride. Acidification of the aqueous part followed by extraction with methylene chloride gave 1.6 g. of crystalline acid XV, m.p. 120–125°. The sample was recrystallized twice from ether–petroleum ether and melted at 135–136° (lit.[10] m.p. 135–136°); λ_{max}^{Nujol} 3.67, w, 3.8–3.9, 6.05, 6.28, 6.40, 6.67 μ; $\lambda_{max}^{CH_3OH}$ 292 mμ (ϵ 6060); $\lambda_{shl}^{CH_3OH}$ 224 mμ (ϵ 9480).

Anal. Calcd. for $C_{14}H_{12}O_2$: C, 79.22; H, 5.70. Found: C, 79.34; H, 5.86.

The methylene chloride solution of neutral product was concentrated to dryness and crystallized with ether to afford 17 g. (90%) of crude amide, m.p. 90–102°. Recrystallization from acetone–petroleum ether (b.p. 30–60°) gave 10.8 g. of a first crop, m.p. 102–103.5°, and 3.8 g. of a second crop, m.p. 101.5–103°. The combined yield of XVI was 14.6 g. (78%) from phenylpropiolyl chloride. An analytical specimen was recrystallized from ether and showed m.p. 101–103°; λ_{max}^{Nujol} 2.88, 2.94, 3.23, 6.11, 6.19, 6.26, 6.32, 6.42 μ; $\lambda_{max}^{CH_3OH}$ 288, 222.5 mμ (ϵ 6040, 14,600).

Anal. Calcd. for $C_{14}H_{13}NO$: C, 79.59; H, 6.20; N, 6.63. Found: C, 79.77; H, 6.23; N, 6.56.

endo-3-Phenyl-endo-2-norbornanecarboxamide (XVII). A solution of 5.25 g. (0.0249 mole) of XVI in 100 ml. of methanol was hydrogenated using 0.5 g. of platinum oxide catalyst. The theoretical 0.05 mole of hydrogen was absorbed in less than 10 min. After removal of the catalyst by filtration and concentration of the filtrate to dryness, there was obtained a solid residue which was recrystallized twice from chloroform–petroleum ether to yield 4.35 g. (82%) m.p. 132–135°; λ_{max}^{nujol} 2.87, 2.94, 3.02, 3.15, shl. 5.98, 6.03, 6.10, 6.21, 6.67 μ.

Anal. Calcd. for $C_{14}H_{17}NO$, N, 6.51. Found: N, 6.50.

endo-3-Phenyl-exo-2-norbornanecarboxamide (XVIII). A solution of 10 g. of the *cis* amide XVII in 100 ml. of methanol was treated with 50 ml. of 10% sodium hydroxide and concentrated at atmospheric pressure until most of the methanol was removed. The mixture was diluted with water, and the crystalline product was collected, washed, and dried, giving 9.0 g., m.p. 152–153°. Recrystallization of a sample from benzene-ether afforded pure XVIII, m.p. 153–154°; λ_{max}^{nujol} 2.95, 3.12, 5.87 w, 6.05, 6.17, 6.66, 6.85 μ.

Anal. Calcd. for $C_{14}H_{17}NO$: N, 6.51. Found: N, 6.46.

exo-2-Amino-endo-3-phenylnorbornane (XIII). A solution of 2.4 g. of sodium hydroxide in 20 ml. of water was stirred, cooled to 0°, and treated with 0.8 ml. of bromine. To the cold solution was added 2.16 g. (0.01 mole) of XVIII. The mixture was stirred at 0° for 1 hr. and then heated to 60° for 15 min. After cooling it was extracted with ether. The ether layer was extracted with three 35-ml. portions of 6*N* hydrochloric acid. The acid solution was cooled, made basic with sodium hydroxide, and extracted with ether. The ether extract was dried over sodium sulfate, filtered, treated with hydrogen chloride gas, and evaporated. The oily residue was crystallized from chloroform–petroleum ether, affording the

(15) Watson, *J. Chem. Soc.*, **85**, 1324 (1904), reports the preparation from phenylpropiolic acid with thionyl chloride. In our hands, this method gave up to 35% of 1-phenyl-2,3-naphthalene dicarboxylic acid anhydride as by-product as did oxalyl chloride on the acid. Using sodium phenylpropiolate and oxalyl chloride, it is essential that the sodium salt be anhydrous to obtain good yields of phenylpropiolyl chloride.

crystalline hydrochloride of XIII, m.p. 213–217°; λ_{max}^{Nujol} 3.70, 3.83, 4.87, 6.22, 6.63, shl. 6.73 μ.

Anal. Calcd. for $C_{13}H_{17}N \cdot HCl$: N, 6.26. Found: N, 6.18.

A mixture of 0.153 g. (0.00685 mole) of XIII hydrochloride, 1.0 ml. (0.0041 mole) of benzenesulfonyl chloride, and 5 ml. of 10% sodium hydroxide was shaken for 4 hr. The product was collected on a filter and washed thoroughly with water and dried, affording 0.181 g. (81%) m.p. 131–140°. Repeated recrystallizations from absolute ethanol gave 0.151 g. of the pure benzenesulfonamide of XIII, m.p. 141–143°; $\lambda_{max}^{CHCl_3}$ 2.94, 3.03, 6.23, 6.75, 6.86 μ.

Anal. Calcd. for $C_{19}H_{21}NO_2S$: C, 69.69; H, 6.47; N, 4.28. Found: C, 69.88; H, 6.60; N, 4.47.

This product was identical by mixed melting point and infrared spectrum with the benzenesulfonamide of the minor product obtained by reduction of the cyclopentadiene-*trans*-β-nitrostyrene adduct I.

3-Phenyl-2,5-norbornadiene-2-carboxylic acid (XV).[10] Methyl 3-phenyl-2,5-norbornadiene-2-carboxylate was prepared by the method of Cristol and La Londe.[10] From 12.0 g. of freshly distilled cyclopentadiene (0.187 mole), 25 g. of methyl phenylpropiolate (0.156 mole), and 250 ml. of dry benzene, there was obtained 24.1 g. (68.5%) of the ester of XV, b.p. 111–114°/0.5 mm.; $\lambda_{max}^{CHCl_3}$ shl. 5.84, 5.91, 6.18, 6.23, 6.66, 6.94 μ; $\lambda_{max}^{CH_3OH}$ 296 mμ (ϵ 5860) (lit.[10] b.p. 111–116°/0.6 mm.).

Hydrolysis of 20 g. (0.0885 mole) of the above ester with 400 ml. of 20% sodium hydroxide solution gave 12.0 g. (63.9%) of the acid XV, m.p. 139–140° (lit.[10] m.p. 135–136°); identical with the sample described in a previous section.

endo-3-Phenylnorbornane-endo-2-carboxylic acid (XIX). A mixture of 3-phenyl-2,5-norbornadiene-2-carboxylic acid (XV, 7.00 g.), 10% palladium-on-carbon (0.8 g.) and absolute ethanol (80 ml.) was shaken at room temperature under 2 atm. of hydrogen. The calculated amount of hydrogen for two double bonds was absorbed in 20 min., and there was no further uptake for 1 hr. The catalyst was collected on a filter and washed throughly with absolute ethanol. Evaporation of the filtrate at reduced pressure gave 7.12 g. (100%) of a crystalline solid, m.p. 145–161°; ultraviolet: only end-absorption. Recrystallization of a 6.10-g. sample of the crude hydrogenation product from ethyl acetate gave 3.60 g. (50.6%) of XIX, m.p. 155–157° (sealed tube) (lit.[11] m.p. 157–158°); $\lambda_{max}^{CHCl_3}$ 2.84, 3–4 br., 5.87, 6.20, 6.66, 6.73, 6.86 μ. For analysis, a sample was repeatedly recrystallized from benzene followed by ethyl acetate; m.p. 157–158° (sealed tube).

Anal. Calcd. for $C_{14}H_{16}O_2$: C, 77.75; H, 7.46. Found: C, 77.85; H, 7.37

Evaporation of the combined mother liquors from the preceding recrystallizations gave a mixture of the *cis* acids, XIX and XXI, m.p. 143–158°.

endo-2-Amino-endo-3-phenylnorbornane (XX). To a slurry of acid XX (2.00 g., 0.00926 mole), water (3 ml.), and acetone (20 ml.), cooled to 0° in an ice-bath, a solution of triethylamine (3.0 ml., 0.022 mole) and acetone (30 ml.) was added in one portion with stirring. The reaction mixture was stirred until the temperature remained constant at 0°, and a solution of ethyl chloroformate (2.0 ml., 0.021 mole) and acetone (10 ml.) was added dropwise at a rate such that the reaction temperature did not exceed 5°. The resulting solution was stirred at 0° for 1 hr., and a solution of sodium azide (1.50 g., 0.0104 mole) and water (5 ml.) was added dropwise with stirring at a rate such that the reaction temperature did not exceed 5°. After stirring at 0° for 1 hr., the reaction mixture was poured onto ice and extracted with ether. The combined ether extracts were washed with saturated sodium chloride solution, dried over anhydrous magnesium sulfate, filtered, and evaporated at reduced pressure and room temperature. The colorless residual oil (2.20 g.) was dissolved in dry toluene (15 ml.), and the resulting solution was heated on the steam bath for 1 hr. during which time there was a smooth evolution of nitrogen. Evaporation of the solvent at 60° under aspirator vacuum gave 2.10 g. of a colorless oil which showed an intense band at 4.38 μ (isocyanate) in the infrared.

A suspension of the above oil and 20% hydrochloric acid (40 ml.) was heated under reflux for 4 hr. and allowed to cool. The precipitate was collected on a filter and washed with water and ether; yield 1.05 g. of a tan solid, m.p. *ca.* 200° dec.; λ_{max}^{KBr} 2.85 br., 3.19 3.27, 3.43, 3.5–4 br., 5.05, 6.22, 6.35, 6.61, 6.81, and 7.07 μ, which gave a positive silver nitrate test. The crude hydrochloride was suspended in ether and 10% sodium hydroxide solution and was stirred until all of the solid had dissolved. The layers were separated, and the aqueous phase was extracted with ether. The ethereal extracts were washed with saturated sodium chloride solution until the washings were neutral, dried over anhydrous magnesium sulfate, and filtered.

Evaporation of the solvent at reduced pressure afforded the impure *cis-endo* amine XX (0.81 g., 49.6%) as a brown oil; $\lambda_{max}^{CHCl_3}$ 3.0 br., 6.05, 6.22 sh., 6.66 and 6.86 μ.

A mixture of the above amine XX (0.0534 g., 0.000285 mole), 10% sodium hydroxide solution (2 ml.), and freshly distilled benzenesulfonyl chloride (0.5 ml., 0.00391 mole) was shaken for 1 hr. at room temperature. The solid was collected and washed with cold water; yield (0.071 g., 73.5%), m.p. 119–123°. Repeated recrystallization from 95% ethanol gave the pure benzenesulfonamide of *endo*-2-amino-*endo*-3-phenylnorbornane, m.p. 125–126°; λ_{max}^{KBr} 2.99, 3.24, 3.30, 6.16, 6.28, sh., 6.30, 6.44 μ.

Anal. Calcd. for $C_{19}H_{21}NO_2S$: C, 69.69; H, 6.47; N, 4.28. Found: C, 69.54; H, 6.28; N, 4.30.

The hydrochloride of XX was prepared in 93.0% yield by treatment of XX with saturated ethereal hydrogen chloride and had m.p. 240–250° dec. from 95% ethanol; λ_{max}^{KBr} 2.93, 3.30, 3.38, 3.55, 5.10, 6.26, 6.36, 6.64 sh., 6.74, 6.86 μ.

Anal. Calcd. for $C_{13}H_{18}ClN$: C, 69.78; H, 8.11; N, 6.26. Found: C, 69.97; H, 8.32; N, 6.56.

Benzenesulfonamide of exo-2-amino-exo-3-phenylnorbornane (XXII) Treatment of a 1.41-g. (0.00654 mole) sample of the mixture of *cis* acids (m.p. 143–158°; see preparation of XIX) in water (4 ml.) and acetone (30 ml.) with triethylamine (4.0 ml., 0.029 mole) in acetone (20 ml.) followed by ethyl chloroformate (2.0 ml., 0.021 mole) in acetone and then sodium azide (1.5 g., 0.0104 mole) in water (15 ml.) as described above gave 1.61 g. of an oil which was dissolved in dry toluene (15 ml.) and heated on the steam bath for 4 hr. The resulting isocyanate (1.51 g.) was heated under reflux in 20% hydrochloric acid to give 0.630 g. of a basic fraction as a yellow oil. This oil was dissolved in anhydrous ether and was treated with saturated ethereal hydrogen chloride until there was no further precipitation. The ether was removed by decantation, and the oily hydrochloride was washed thoroughly with ether. This oily hydrochloride (0.647 g.) was suspended in 10% sodium hydroxide solution (20 ml.) and freshly distilled benzenesulfonyl chloride (1.0 ml.) was added with cooling. The mixture was shaken for 1 hr. The solid was collected on a filter and was washed with cold water; yield 0.908 g., m.p. 80–85°, of a brown solid. Repeated recrystallization from 95% ethanol (Darco) afforded 0.083 g. of the benzenesulfonamide of XXII, m.p. 130–132°; λ_{max}^{KBr} 2.96, 3.34, 3.42, 6.21, 6.27, 6.65 sh., 6.71, 6.77, 6.86 μ.

Anal. Calcd. for $C_{19}H_{21}NO_2S$: C, 69.69; H, 6.47; N, 4.28. Found: C, 69.80; H, 6.51; N, 4.19.

The infrared spectra (potassium bromide and Nujol) of the two *cis*-benzenesulfonamides were very similar in the 3 to 13 μ region but showed significant differences in the 13 to 15-μ region. An admixture of the two *cis*-benzenesulfonamides melted at 127–128°.

Attempted isomerization of trans-2-nitro-3-phenyl-5-norbornenes IX and X (I). Ten grams (0.0465 mole) of the mixture of nitro adducts I was converted to the soluble potassium salt by addition to 30 ml. of 20% ethanolic potassium hydroxide. The solution was stirred for 15 min. and then cooled to −5°. With good stirring at this temperature, the solution was slowly acidified with a 1:3 sulfuric acid–

ethanol mixture to *p*H 1–2 (Indicator paper). Acidification was accompanied by the immediate precipitation of an oily solid. The resultant thick mixture was diluted with 150 ml. of water and extracted with ether. The extracts were washed four times with a saturated sodium chloride solution. The organic solution was then dried over magnesium sulfate, filtered, and concentrated to dryness *in vacuo*, affording 10 g. of oily product; $\lambda_{max}^{CHCl_3}$ 2.76 w, shl. 3.25, shl. 3.36, 3.43, 5.10 w, 5.30 w, 5.51 w, 5.75 w, 6.24, 6.50, 6.65, 6.86, 7.32, 7.48 μ.

The oil was hydrogenated over 0.05 g. of platinum oxide in 75 ml. of methanol at low pressure. The theoretical 1 mole of hydrogen was consumed in 5 min. The catalyst was filtered, and the filtrate concentrated *in vacuo*. The oily product was dissolved in ether, dried over magnesium sulfate, filtered, and concentrated *in vacuo*.

The 10 g. thus obtained was distilled: Fraction A, 0.74 g., n_D^{19} 1.5290, b.p. 98–108°/0.1 mm., $\lambda_{max}^{CHCl_3}$ 3.37, 3.44, 5.75 w, 6.47, 6.67, 6.87, 7.05 w, 7.27 μ; the vapor phase chromatogram showed three bands in the ratio of 18:1:10 with retention times of 8.6, 10.4, and 19 min.; Fraction B, 6.66 g., n_D^{18} 1.5520, b.p. 110–114°/0.1 mm., $\lambda_{max}^{CHCl_3}$ 3.38, 3.45, 6.25, 6.52, 6.68, 6.76, 6.88, 7.30 μ; the vapor phase chromatogram showed two bands in the ratio of 5:1 with retention times of 19.4 and 20.8 min.; Fraction C, 0.77 g., n_D^{20} 1.5525, b.p. 115–124°/0.25 mm.; the ratios and retention times were the same as for Fraction B.

Fraction B (6.6 g., 0.03 mole) was hydrogenated over 6 g. of 10% palladium-on-carbon in 75 ml. of ethanol. The theoretical amount of hydrogen (0.09 mole) was consumed in 45 min. The hydrogenation mixture was filtered through Supercel, and the catalyst was washed thoroughly with ethanol until it was free of product. The filtrate was concentrated *in vacuo*. The product was dissolved in dilute hydrochloric acid and ether. The layers were separated, and the ethereal solution was extracted twice with dilute acid. The combined acid solutions were washed once with ether, made basic with sodium hydroxide solution, and extracted three times with methylene chloride. The organic solution was washed with water, dried and concentrated *in vacuo*, yielding 4.6 g. of oil (82%), λ_{max}^{Neat} 3.38, 3.46, 6.0, 6.24, 6.68, 6.76, 6.88 μ.

This oily amine (0.02 mole) was combined with 25 ml. of 10% sodium hydroxide and 6.4 g. (0.036 mole) of freshly distilled benzenesulfonyl chloride and shaken for 16 hr. at room temperature. The tan solid was filtered, washed thoroughly with water, and air-dried, m.p. 122–132°. After one recrystallization from ethanol, there was obtained 4.2 g. (69.5%), m. p. 140–142°, alone or when admixed with an authentic sample of the benzenesulfonamide of III; also identical by infrared spectra.

Attempted isomerization of trans-2-nitro-3-phenylnorbornanes XI *and* XII. To a solution of 6 g. (0.092 mole) of 85% potassium hydroxide in 100 ml. of absolute ethanol was added 10 g. (0.046 mole) of hydrogenated I. The resulting mixture from which some insoluble sodium *aci*-nitro salt separated was stirred for 15 min. at room temperature and then cooled to −5° in an ice-salt bath. The resultant mixture was titrated with ethanol–sulfuric acid (3:1) to *p*H 1 which caused an oily solid to separate. The mixture was treated with 250 ml. of water and extracted three times with ether. The ether extracts were washed four times with saturated sodium chloride solution. The extracts were dried over magnesium sulfate, filtered, and concentrated to dryness *in vacuo* to give 10.6 g. of a green oil, λ_{max}^{Neat} 3.0, 3.38, 3.41, 5.70, 6.07 w, 6.21, shl. 6.38, 6.46, 6.67, 6.73 w, 6.85, 7.26 μ. Vapor phase chromatography showed bands with retention times of 10 min. and 18.4 min. in the ratio of 2:3 corresponding to phenylnorcamphor and starting material. The oil was then distilled *in vacuo*. The following four fractions were taken.

Fraction A, 0.63 g., b.p. 106–110°/0.08–0.14 mm., n_D^{19} 1.5518; phenylnorcamphor and nitrophenylnorbornane in a ratio of 12:1 by vapor phase chromatography.

Fraction B, 1.04 g., b.p. 110–116°/0.14 mm., $n_D^{20.5}$ 1.5531; ketone and nitro compound in a ratio of 5:1 by vapor phase chromatography.

Fraction C, 3.15 g., b.p. 116–124°/0.19 mm., n_D^{20} 1.5528; ketone and nitro compound in a ratio of 1:4 by vapor phase chromatography.

Fraction D, 0.49 g., b.p. 125°/0.12 mm., n_D^{20} 1.5534; ketone and nitro compound in a ratio of 1:10 by vapor phase chromatography.

Fraction A was dissolved in 20 ml. of ethanol and treated with a solution prepared by dissolving 0.6 g. of 2,4-dinitrophenylhydrazine in 3 ml. of sulfuric acid, 4.5 ml. of water, and 15 ml. of ethanol. After 4 hr., the crystals were filtered, washed with ethanol, and dried, giving 1.4 g. of yellow crystalline product, m.p. 100–138° dec. After two recrystallizations from ethyl acetate–ethanol, the hydrazone melted at 153–165°; λ_{max}^{Nujol} 3.06, shl. 6.08, 6.19, 6.30, shl. 6.5, shl. 6.58, 6.66. μ.

Anal. Calcd. for $C_{19}H_{18}N_4O_4$: C, 62.28; H, 5.36; N, 15.29. Found: C, 61.71; H, 5.14; N, 15.19.

A sample of XI and XII from reduction of I was converted to 3-phenylnorcamphor *via* the Nef reaction in 81% yield.[8] The oily ketone was converted to the 2,4-dinitrophenylhydrazone. After three recrystallizations from ethanol, the yellow derivative melted at 164.5–167.5° [16]; λ_{max}^{Nujol} 3.05, shl. 6.07, 6.17, 6.29, 6.49, 6.56, 6.67 μ.

Anal. Found: C, 62.46; H, 5.18; N, 15.38.

On mixing the two samples of hydrazones, the melting point was 160–168°; their infrared spectra were very similar.

Fractions C and D containing predominantly nitro compounds were combined (3.6 g., 0.0168 mole) and hydrogenated over 3 g. of 10% palladium-on-carbon in 45 ml. of ethanol. The reduction was complete in 20 min. The catalyst was removed by filtration, and the filtrate was concentrated *in vacuo*. The product was dissolved in ether and dilute hydrochloric acid, and the layers were separated. The ether solution was extracted twice with dilute acid. The combined acid extracts were washed with ether, made basic with aqueous sodium hydroxide, and extracted with methylene chloride. The extracts were evaporated *in vacuo* and dried to afford 2.14 g. (68%) of oily base

The base (0.0112 mole) was combined with 2.4 ml. of freshly distilled benzenesulfonyl chloride and 25 ml. of 10% sodium hydroxide and shaken for 20 hr. The gummy product solidified on scratching. It was filtered, washed thoroughly with water, and air-dried. The product was recrystallized twice from ethanol, affording 1.42 g., m.p. 142.5–144.5°, alone or admixed with the benzenesulfonamide of III; identical by infrared spectra.

Acknowledgment. We are indebted to Mrs. Mary Christie for many of the analyses and spectra.

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(16) Most probably the *exo*-phenyl isomer. See D. C. Kleinfelter and P. von R. Schleyer, *J. Am. Chem. Soc.*, **83**, 2329 (1961).