The Reaction of 2-Chlorocyclohexanone with β-Naphthol. A Novel Synthesis of γ-Brazan

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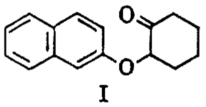
Reaction of 2-chlorocyclohexanone with β-naphthol has been shown to give 7a,8,9,10,11,11a-hexahydrobenzo[*b*]napththo[1,2-*d*]furan-7a-ol which is readily transformed to γ-brazan.

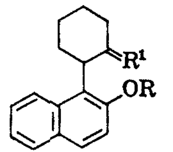
The reaction of 2-chlorocyclohexanone with β-naphthol under basic conditions gives rise to a compound $C_{16}H_{16}O_2$.[2,3] Ebel[2] suggested that the compound, for which he reported the melting point of 135°, was I, while more recently Mousseron[3] considered that the product he obtained, which melted at 138–139°, had the structure II. An examination of the infrared spectrum of the compound indicated that neither of these structures is correct. There is a carbonyl function in both I and II but no corresponding carbonyl band was apparent in the spectrum. Furthermore the compound gave no derivatives with ketonic reagents such as dinitrophenylhydrazine and, since it did not dissolve in cold sodium hydroxide solution, it was apparently not a phenol. The infrared spectrum showed bands at 3356 and 1241 cm^{-1} indicative of an alcohol function and an aryl ether link, respectively. Thus, the compound probably had the hemiketal structure III, 7a,8,9,10,11,11a-hexahydrobenzo[*b*]naphtho[1,2-*d*]furan-7a-ol.

The structure III was confirmed by a series of reactions; with acylating or alkylating agents in the presence of alkali, III yielded phenolic ethers and esters. Thus with methyl iodide 2-(2-methoxy-1-naphthyl)cyclohexanone (IV) was obtained, while benzoyl chloride under Schotten–Baumann conditions gave 2-(2-benzoyloxy-1-naphthyl)cyclohexanone (V). Compound IV yielded a semicarbazone VII and an oxime VIII under the usual conditions. The reaction of III with either butyl isocyanate or with ketene resulted only in the recovery of the starting material.

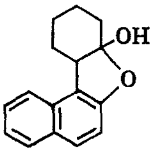
Treatment of III with hydrogen chloride in alcohol gave a crystalline material $C_{16}H_{14}O$. This compound was also obtained when III was treated with benzoyl chloride in benzene. The compound $C_{16}H_{14}O$ showed a band at 249 mμ in the ultraviolet region indicating the conjugation of a double bond with the aromatic nucleus; further, it yielded an orange picrate, mp 143–144°, which appeared to be identical with that described by Ebel[2] for the picrate of a compound obtained from the original condensation product $C_{16}H_{16}O_2$ by treatment with concentrated sulfuric acid. Attempts to hydrogenate the compound $C_{16}H_{14}O$ in the presence of Adams catalyst in ethanol or acetic acid failed. These properties suggested that it was 8,9,10,11-tetrahydrobenzo[*b*]naphtho[1,2-*d*]furan (VI).



I



II, R=H; R^1=O
IV, R=CH_3; R^1=O
V, R=C_6H_5CO; R^1=O
VII, R=CH_3; R^1=$NNHCONH_2$
VIII, R=CH_3; R^1=NOH



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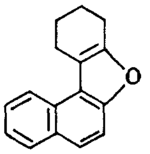
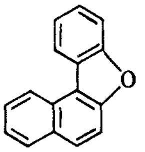
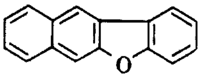


VI



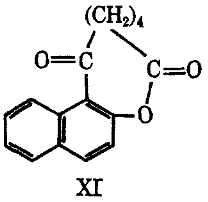
IX



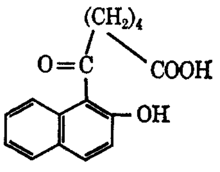
X

When either III or VI was heated with palladium charcoal at 300° a compound $C_{16}H_{10}O$ melting at 31–32° was obtained in high yield. With picric acid this gave a monopicrate melting at 125°. These melting points are in good agreement with those reported by Chatterjea[4] for γ-brazan (benzo[*b*]naphtho[1,2-*d*]furan, IX) and its picrate, respectively. A mixture melting point of the picrates revealed that they were identical.[5]

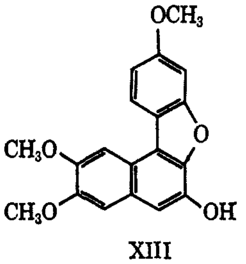
The isolation of γ-brazan (IX) rather than β-brazan (X, benzo[*b*]naphtho[2,3-*d*]furan, mp 208–209°)[6–9] from the above dehydrogenation established that the β-naphthol had reacted at the 1 position in the original condensation. This was readily confirmed by nmr evidence. The aromatic proton in the 3 position of the naphthol was observed in III at δ 7.15 showing a coupling constant of 9 cps which indicated the presence of an adjacent *ortho* proton.



XI



XII



XIII

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[1] Author to whom inquiries should be addressed.

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[4] J. N. Chatterjea, *J. Indian Chem. Soc.*, **33**, 339 (1956).

(5) We wish to thank Professor J. N. Chatterjea for his kindness in comparing the sample of γ-brazan picrate prepared above with his authentic sample.

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Careful oxidation of VI with chromium trioxide in acetic acid gave a crystalline compound $C_{16}H_{14}O_3$ for which the spectral data suggested the structure XI. The infrared spectrum showed two bands in the carbonyl region at 1751 and 1678 cm^{-1} indicative of an aryl lactone and an aryl ketone, respectively. The nmr spectrum showed two proton multiplets centered at δ 2.09 and 2.68; the downfield multiplet results from the methylene groups adjacent to the carbonyl functions. Again the coupling ($J = 9$ cps) of the aromatic protons adjacent to the lactone oxygen revealed an *ortho* arrangement. Hydrolysis of the lactone XI with sodium hydroxide solution gave the expected ketocarboxylic acid XII, 2-hydroxy-1-naphthoylvaleric acid, the structure of which may be deduced from a study of its infrared and nmr spectra.

The series of reactions III → IV → IX constitutes a new and convenient synthesis of γ-brazan, a substance which contains the ring system of α-anhydrotrimethylbrazilone (XIII) obtained by degradation of brazilin.

Experimental Section

Melting points were taken on a Thomas-Hoover capillary melting point apparatus and are uncorrected. The ultraviolet spectra were determined in 95% ethanol solution with a Perkin-Elmer Model 202 spectrophotometer. The infrared spectra were determined in potassium bromide pellets on a Perkin-Elmer Model 21 spectrophotometer. The nmr spectra were determined on a Varian A-60 spectrometer, using deuteriochloroform as solvent with tetramethylsilane as the internal standard.

7a,8,9,10,11,11a-Hexahydrobenzo[*b*]naphtho[1,2-*d*]furan-7a-ol (III). **A.**—To a suspension of 55 g of anhydrous potassium carbonate in 400 ml of dried dioxane was added 60 g of 2-naphthol. The mixture was stirred mechanically and 60 g of 2-chlorocyclohexanone was added dropwise over a 30-min period. The mixture was then boiled under reflux with stirring for 21 hr. After cooling, the mixture was filtered and the filtrate was concentrated to dryness on a rotary evaporator. The residual oil was triturated with benzene and crystallized. The previously removed solid was dissolved in water and was extracted with benzene. On concentration this afforded more material identical with that above: combined yield 57 g (57%), mp 134–135°. Recrystallization from ethanol afforded 47.5 g of III, mp 137–138°.

B.—A mixture of 100 g of 2-naphthol, 90 g of anhydrous potassium carbonate, and 200 ml of xylene was stirred and boiled for 30 min, while any water present was removed by a Dean–Stark apparatus. This was followed by the dropwise addition of 100 g of 2-chlorocyclohexanone (1.5 hr), and the whole was then boiled under reflux for a further 4 hr. After the mixture was allowed to cool to 70° it was filtered. On cooling, the filtrate deposited 28 g of material, mp 137°. The solid residue from the above filtration was treated with 1 l. of cold water when there was obtained 52 g of material, mp 136°. Recrystallization of the combined materials from ethanol afforded 40 g of III: mp 138–139°, undepressed on admixture with material prepared by A; λ_{max} 233, 282 mμ (ϵ 67,400, 4300); infrared spectrum (in KBr), no C=O band in the 1705–1725-cm^{-1} region, characteristic bands at 3356 (OH) and 1241 cm^{-1} (aryl ether); nmr spectrum, δ 3.31 (m), (11a-H), 3.59 (s), (7a-OH), 7.15 (d) (6-H) ($J = 9$ cps).

Anal. Calcd for $C_{16}H_{16}O_2$: C, 79.97; H, 6.71. Found: C, 80.09; H, 6.69.

2-(2-Methoxy-1-naphthyl)cyclohexanone (IV).—To a solution of 3.0 g of sodium metal in 60 ml of absolute ethanol was added with stirring 20 g of III, followed by dropwise addition of 24 g of methyl iodide. The mixture was boiled under reflux for 2 hr and was then concentrated to dryness on a rotary evaporator. The residue was treated with water when an oil separated; this solidified rapidly. Two crystallizations from ethanol afforded IV: 13 g; mp 121°; λ_{max} 231 mμ (ϵ 70,300); infrared spectrum (in KBr), 1695 (C=O), 1258, and 1244 cm^{-1} (doublet, aryl ether); nmr spectrum, δ 4.30 (m), (2-H), 3.85 (s) (OCH_3).

Anal. Calcd for $C_{17}H_{18}O_2$: C, 80.28; H, 7.13. Found: C, 80.24; H, 7.23.

One gram of IV, suspended in ethanol, was treated with a solution of semicarbazide hydrochloride in sodium acetate solution. The semicarbazone after recrystallization from methanol melted at 147–148°.

Anal. Calcd for $C_{18}H_{21}N_3O_2$; C, 69.43; H, 6.80; N, 13.50. Found: C, 69.69; H, 6.79; N, 13.46.

Treatment of IV with hydroxylamine in the usual manner gave 2-(2-methoxy-1-naphthyl)cyclohexanone oxime (VIII) which, after recrystallization from ethanol, melted at 148°.

Anal. Calcd for $C_{17}H_{10}NO_2$: C, 75.81; H, 7.11; N, 5.20. Found: C, 75.54; H, 7.01; N, 5.34.

2-(2-Benzoxy-1-naphthyl)cyclohexanone (V). **A.**—To 50 ml of 3 *N* sodium hydroxide solution was added 12 g of III and the suspension was stirred mechanically. This was followed by the dropwise addition of 8 ml of benzoyl chloride. The mixture became warm and the oil which formed slowly solidified. The solid was washed three times with water and was then recrystallized from ethanol to afford V, mp 153°.

B.—To a solution of 6 g of III in 100 ml of methylene chloride was added 2.5 g of triethylamine followed by 3.5 g of benzoyl chloride. The mixture was boiled under reflux for 2 hr and was then treated with 150 ml of dry benzene which caused precipitation of triethylamine hydrochloride. After filtration the mother liquor was evaporated to dryness to afford 8 g of material, mp 138–139°. Recrystallization from ethanol gave V, identical in all respects with the sample prepared by A: λ_{max} 223 mμ (ϵ 71,400); infrared spectrum (in KBr), bands at 1695 (six-membered ring C=O) and 1739 cm^{-1} (ester C=O).

Anal. Calcd for $C_{23}H_{20}O_3$: C, 80.21; H, 5.81. Found: C, 79.92; H, 5.88.

8,9,10,11-Tetrahydrobenzo[*b*]naphtho[1,2-*d*]furan (VI). **A.**—A mixture of 10 g of III and 100 ml of a 10% ethanolic HCl solution was boiled under reflux for 30 min. The solution was evaporated to dryness on a rotary evaporator, and the residual oil solidified on scratching. The residue was dissolved in petroleum ether (bp 30–60°) and afforded upon cooling in a solid carbon dioxide–acetone bath 7.4 g of VI (78%), mp 44–45°. An analytical sample was obtained by recrystallization from petroleum ether.

B.—A mixture of 6 g of III and 4 ml of benzoyl chloride in 50 ml of dry benzene was boiled under reflux for 3 hr. The solution was evaporated to dryness and the residual oil was dissolved in hot ethanol and cooled. There was obtained 4 g of VI, mp 45°, identical with that prepared by A: λ_{max} 249, 302, 315, 329 mμ (ϵ 25,800, 9600, 9000, 8600); infrared spectrum, absence of OH and C=O bands, presence of band at 1266 cm^{-1} (aryl ether); nmr spectrum, δ 1.87 (m) (9,10-di-CH_2, 2.80 or 3.01 (m) (8-CH_2 or 11-CH_2).

Anal. Calcd for $C_{16}H_{14}O$: C, 86.45; H, 6.35. Found: C, 86.26; H, 6.36.

A small sample of VI was treated with a methanolic solution of picric acid when an orange precipitate was obtained. Recrystallization from ethanol containing picric acid afforded the **picrate**, mp 143–144°.

Anal. Calcd for $C_{16}H_{14}O \cdot C_6H_3N_3O_7$: C, 58.54; H, 3.80; N, 9.31. Found: C, 58.42; H, 3.82; N, 9.25.

Benzo[*b*]naphtho[1,2-*d*]furan (γ-**Brazan, IX**). **A. From III.**—An intimate mixture of 12 g of III and 6 g of 10% palladium on charcoal was heated in a Wood's metal bath at 300° for 2 hr. The mixture was extracted with three 100-ml portions of ether and the charcoal was removed by filtration. The solvent was evaporated and the residual oil was subjected to a vacuum distillation. There was obtained 7.5 g of γ-brazan as a yellow oil, bp 160–161° (0.15 mm). On standing this solidified to give crystals, mp 31–32°. Chatterjea[4] gives the melting point of γ-brazan as 31–32°; λ_{max} 246, 280, 313 mμ (ϵ 46300, 5400, 13,900).

Anal. Calcd for $C_{16}H_{10}O$; C, 88.05; H, 4.62. Found: C, 87.39; H, 4.82.

B. From VI. An intimate mixture of 2 g of VI and 1 g of 10% palladium on charcoal was heated for 2 hr at 300° from which mixture 1.5 g of γ-brazan was isolated, identical in all respects with the material obtained in the above experiment.

A sample of γ-brazan was treated with a methanolic solution of picric acid and warmed on the steam bath for 5 min. On cooling the orange picrate was deposited. Recrystallization from ethanol containing a little picric acid afforded the picrate, mp 125°.

Anal. Calcd for $C_{16}H_{10}O \cdot C_6H_3N_3O_7$: C, 59.06; H, 2.93; N, 9.39. Found: C, 59.13; H, 2.93; N, 9.39.

This material on admixture with the authentic picrate (mp 124°) prepared by Professor J. N. Chatterjea[4] gave no depression of melting point.[5]

8,9,10,11-Tetrahydronaphth[2,1-*b*]oxonine-8,13-dione (XI).—Twenty grams of VI was dissolved in 180 ml of glacial acetic acid and the mixture was stirred and cooled in ice. To this was added dropwise a solution of 28 g of chromium trioxide in 25 ml of water at such a rate that the temperature did not rise above 15° (1.5 hr). After the addition was completed the dark mixture was stirred for a further 3 hr at room temperature and then the crystalline deposit·formed was removed by filtration. Two recrystallizations from ethanol afforded 4.6 g of XI, mp 138–139°, as colorless large square crystals: λ_{max} 218, 301, 236 (sh) mμ (ε 47,100, 4700); infrared spectrum (in KBr), 1751 (C=O, aryl lactone), 1678 cm^{-1} (C=O, aryl ketone); nmr spectrum, δ 2.09 (m) (9,10-di-CH_2, 2.68 (m) 8-CH_2 and 11-CH_2), 7.91 (d) (5-H), (J = 9 cps), 7.32 (d) (6-H) (J = 9 cps).

Anal. Calcd for $C_{16}H_{14}O_3$: C, 75.57; H, 5.55. Found: C, 75.35; H, 5.55.

2-Hydroxynaphthoylvaleric Acid (XII).[10]—One gram of XI was suspended in 8 ml of 40% sodium hydroxide solution. After heating the reaction mixture for a few minutes on a steam bath a brown solution was obtained. Acidification with concentrated hydrochloric acid afforded 1 g of a brown precipitate, mp 79–81°. Recrystallization from cyclohexane gave 0.5 g of colorless crystals: mp 83–84.5°; λ_{max} 225 mμ (ε 55,056); infrared spectrum (in KBr), 1714 (CO_2H), 1625 cm^{-1} (C=O); nmr spectrum, δ 1.76 (m) 3,4-di-CH_2), 2.39 (t) (2-CH_2) (J = 6.5 cps), 3.14 (t) (5-CH_2) (J = 6.5 cps), 7.08 (d) [3-H (ar)] (J = 9 cps).

Anal. Calcd for $C_{16}H_{16}O_4$: C, 70.57; H, 5.92. Found: C, 70.61; H, 5.72.

Acknowledgment.—The authors gratefully acknowledge the help of Dr. E. L. Buhle and Dr. S. J. Childress in the interpretation of the spectra. Thanks are due Mr. L. E. McCardle for his skilled technical assistance.

[10] We wish to thank Dr. A. Santilli who performed this experiment.

The Syntheses, Spectra, and Thermal Isomerizations of *cis*- and *trans*-1-(*para*-Substituted phenyl)-1-cyclopropylprop-1-enes

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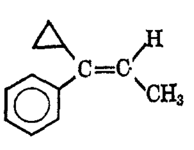
The pmr spectra of the title compounds show that in the *trans* isomers the cyclopropyl group may rotate freely, while in the *cis* isomers free rotation of the cyclopropyl group is severely restricted. In the latter systems, a configuration in which the three-membered ring lies over the π bond is highly unfavorable. Consequently, while the *trans* isomers thermally rearrange *via* a conventional vinylcyclopropane rearrangement to the corresponding cyclopentenes the *cis* isomers give a complex mixture of products which are believed to arise from diradical intermediates.

The thermally induced isomerization of vinylcyclopropanes to the corresponding cyclopentenes is considered to be a truly unimolecular reaction of the "no-mechanism" type.[1-3] Kinetic studies suggest that bond-breaking and bond-making processes are probably synchronous and thus the reaction has little, if any, radical character.[4] It is of interest to know if groups on the π bond *cis* to the cyclopropyl group can sterically inhibit the bond-forming process and thus either decrease the rate of cyclopentene formation or divert the reaction into a free-radical path where bond making and bond breaking are no longer synchronous. Such a path would presumably yield products other than substituted cyclopentenes.

To study the effect of a methyl group *cis* to a cyclopropyl group we prepared 1-phenyl-1-cyclopropylprop-1-ene by a conventional Wittig synthesis from the corresponding ketone. The two geometric isomers were obtained in approximately equal yield and were separated partially by distillation. The pure *trans* I and *cis* II isomers were then isolated by preparative vpc. To observe electronic effects, if present, the corresponding compounds in which the phenyl group was substituted in the *para* position with F, CH_3, and OCH_3 were also prepared.



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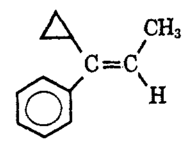

II

Assignment of Structure by Spectroscopic Methods

Literature data on the pmr spectra of styrene and derivatives of styrene indicate that the β-olefinic proton *cis* to the aromatic ring is less shielded than the β-olefinic proton *trans* to the aromatic ring,[5-11] except in *ortho*-substituted derivatives where the plane of the aromatic ring is not nearly parallel to the plane of the double bond.[9]

In a thorough study of five isomeric pairs of *para*-substituted and unsubstituted α,β-dialkylstyrenes, Barbieux and co-workers[8] showed that other differences are present in the pmr spectra of *cis* and *trans* isomers. In the *cis* isomers, the most intense peaks formed by

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