Condensation of β-Cyclocitral with Benzaldehyde

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β-Cyclocitral **1b** condenses with benzaldehyde in the presence of base catalysts giving the 2-benzopyrans **4**, **5** and **6**, and in the presence of acid catalysts giving exclusively the aldehyde **7**. The cyclocitrals **1a** and **1b** are both isomerized by strong base anion exchange resins, but their aldehyde-protected derivatives **2** and **3** are not. Some tests used to characterize the aldehydes and their condensation products are described.

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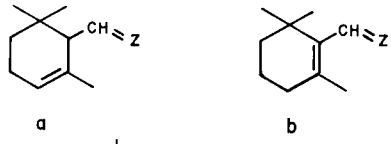
The α- and β-cyclocitrals **1a** and **1b** are useful starting materials for the synthesis of a number of natural products (2).



a b

1, Z = O

2, Z = NPh

3, Z = $\begin{matrix} OCH_2 \\ | \\ OCH_2 \end{matrix}$

In our program on the synthesis of strigol, a witchweed-seed germination stimulant, we considered various methods for extending the carbon-carbon chain at C-2 in β-cyclocitral, and reasoned that an aldol condensation would be suitable provided that: (i) β-cyclocitral could be forced to react as a nucleophile rather than an electrophile, and (ii) reaction did not occur with the methylene group at C-3, which is also activated by the carbonyl group according to the principle of vinylogy.

β-Cyclocitral reacts with acetone (3,4), dimethylacrolein (5), and other active methylene compounds (6-11), giving condensation products in which the other reagent is invariably the nucleophile - a new carbon-carbon bond is formed between the carbonyl group of **1b** and the α-CH_2 group of the other reagent. This paper reports the results of model experiments with a reagent, benzaldehyde, that cannot function as a nucleophile because it possesses no hydrogen on the carbon adjacent to the carbonyl group. The reaction of benzaldehyde with **1b**, a Claisen-Schmidt condensation (12b), was studied under both acid and base catalysis. Also reported are the results of isomerization experiments with the cyclocitrals and their derivatives, and the results of tests used to characterize the aldehydes and their condensation products.

Isomerization of the Cyclocitrals and their Derivatives.

A mixture of α- and β-cyclocitral, prepared by cyclization of citral anil with sulfuric acid (13,14), isomerized to β-cyclocitral **1b** when passed through a strong base anion exchange resin with methanol as the eluant. This procedure was more convenient than Köster's procedure, which requires a treatment with methanolic potassium hydroxide at 0° followed by ether extraction (14,15). One pass through the ion exchange resin gave a product that analyzed 93% β-isomer by nmr (2) and was unchanged by recycling. A sample of 100% β-cyclocitral, freed of α-isomer **1a** by the semicarbazone method (16), also isomerized to 93% β-cyclocitral when passed through the anion exchange resin. Thus, the 93 to 7 ratio is apparently an equilibrium ratio for cyclocitral under the conditions employed. This ratio was a little higher than the approximately 89 to 11 ratio reported by previous investigators (14,15), but their products were all distilled after they were isomerized. Distillation shifts the ratio slightly in favor of the α-isomer.

Efforts to reverse the isomerization by passing 93% β-cyclocitral over a strong acid cation exchange resin (Rexyn 101, H form) (17) with methanol or ether as the eluant were unsuccessful. No dimethyl acetal (18) was detected, but the ratio was unchanged. The ratio was also unchanged when 93% β-cyclocitral was shaken with concentrated hydrochloric acid and ethanol for 3 hours at room temperature or with concentrated sulfuric acid and ether for 1 hour at room temperature. When the solvent was omitted in the latter reaction, the α-cyclocitral was destroyed, leaving the β-cyclocitral intact. β-Cyclocitral, unlike the α-isomer, is stable even to superacids such as fluorosulfonic acid-antimony pentafluoride (19).

The behavior of the aldehyde-protected derivatives **2** and **3** was examined next. The anil **2**, a bright yellow water-sensitive oil, was prepared by condensing β-cyclocitral with aniline in toluene, with azeotropic removal of the water, in 80.9% yield. The β-isomer content, determined by integration of the gem-dimethyl signals in the nmr spectra, was 87%, but it decreased to 71% or below when the product was redistilled. The cyclic acetal **3**, a colorless oil, was prepared by condensing β-cyclocitral with ethylene glycol in benzene, with azeotropic removal of the water, in 62.5% yield. The product, previously believed to be the β-isomer **3b** (20), was mostly the α-isomer **3a**; the β-isomer content, determined by integration of the OCHO signals in the nmr spectra, was 15% before distillation and 8% after distillation. An attempt to circumvent the

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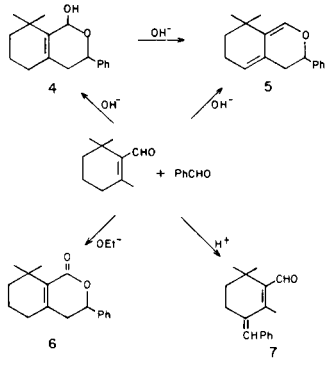
lengthy heating period by complexing the aldehyde with a rare earth salt, europium chloride, as done with citral (21), was unsuccessful. The isomer ratio of both derivatives remained unchanged (nmr, n_D^{20}) when each was dissolved in methanol and passed through the anion exchange resin.

In summation, α- and β-cyclocitral can both be isomerized to a predominantly β-isomer mixture by a strong base anion exchange resin, but their derivatives cannot. The reverse isomerization from β- to α- is induced by distillation but not by acids.

Condensations with Benzaldehyde.

After many trials with various reaction conditions and catalyst ratios, the procedures finally adopted were fairly simple though they differed with each catalyst. In the following discussion, β-cyclocitral refers to the 93% β-product unless stated otherwise.

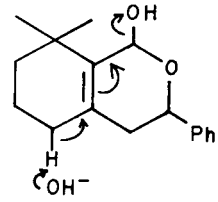
Condensation of β-cyclocitral with benzaldehyde in the presence of sodium hydroxide catalyst gave a mixture of products linked through the C-2 methyl group of the β-cyclocitral. Because the mixture contained two phases at the start, and because there was no pressure build-up, the reaction was best carried out in a stoppered flask purged with argon and shaken for 24 hours on a mechanical shaker. The principal product, isolated in 16.6% yield from the crude reaction mixture by precipitation with hexane, was a white crystalline solid, m.p. 120-122°, identified by ir, nmr, and elemental analysis as the benzopyran-1-ol **4** (Scheme 1). An nmr signal at δ 5.07, a doublet of doublets,



Scheme 1. Products of the Condensation of β-Cyclocitral **1b** with Benzaldehyde.

was identified as the X portion of an ABX spin pattern; the AB portion, located by spin decoupling, was centered at δ 2.05 but was obscured by other CH_2 signals. The ABX signals were assigned to the hydrogens at C-4, C-4, and C-3 respectively. The product is evidently an aldol that is stabilized to dehydration by hemiacetal formation. There seems to be no precedent for this reaction, though side reactions in aldol condensations are common (22,23).

The second major product, isolated from the reaction mixture after steam distillation, was a white crystalline solid, m.p. 76-77°, identified by ir, nmr, and elemental analysis as the benzopyran **5** (Scheme 1). The hydrogens at C-4, C-4, and C-3 again gave an ABX spin pattern in the nmr, but in this instance the CH_2 signals were resolved sufficiently to enable the pattern to be solved, with the aid of spin decoupling. The ir spectrum showed sharp peaks at 1220 and 1600 cm^{-1}, assigned to the conjugated enol ether C=C-O (24). Models of **5** have a planar benzopyran skeleton except for carbons 3 and 7, which can be on the same side of the plane or on opposite sides. The phenyl groups can be axial or equatorial in either conformation. The product is evidently derived from the hemiacetal **4** by base-catalyzed dehydration:



The nmr spectrum of **4** in deuteriochloroform degraded in a few days, producing new signals that corresponded to **5**, thus establishing that **4** is a precursor of **5**. Few compounds possessing the cyclic enol ether ring structure (dihydro-4*H*-pyrans) are described in the literature (25). Some were prepared by dehydration of the cyclic hemiacetals (tetrahydro-4*H*-pyran-2-ols) under acidic or thermal conditions, but not basic conditions (26). The acyclic enol ethers are better known (27,28).

Other products identified in this reaction were benzoic acid (6.5%), β-cyclogeranic acid (2.7%), β-cyclocitral (23.3%), benzaldehyde (15.8%), benzyl alcohol (9.3%), and two condensation products **6** (0.7%) and **7** (2.7%) to be described later. The benzoic acid, β-cyclogeranic acid, and benzyl alcohol were products of Cannizzaro reactions that are commonly encountered in aldol condensations. There was no evidence of any β-cyclogeraniol. The acids were separated from the alkaline reaction mixture together with **6** by extraction with ether. Benzaldehyde, benzyl alcohol, and β-cyclocitral were separated from the other products by steam distillation, and from each other as follows. Benzaldehyde was extracted from an ether solution of the mixture by 10% sodium bisulfite and recovered from the bisulfite addition compound by treatment with sodium carbonate (29). Unlike citral (30), β-cyclocitral does not react with sodium bisulfite or sodium sulfite, even under forcing conditions. β-Cyclocitral is difficult to separate from benzyl alcohol, but the latter resinified when the mixture was shaken with concentrated sulfuric acid (31a). The α-cyclocitral also resinified, leaving the

β-cyclocitral intact.

Increasing the catalyst concentration to 1:1 with respect to **1b** accelerated the disproportionation of the benzaldehyde. Lowering the reaction temperature to 0° suppressed the side reaction leading to β-cyclogeranic acid, but did not diminish the disproportionation of the benzaldehyde. Increasing the benzaldehyde concentration to 5:1 with respect to **1b**, or adding ether to isolate the catalyst, suppressed the aldol condensation itself. No reaction occurred when the condensation was carried out under the conditions of the Knoevenagel reaction (32).

A different product was obtained when β-cyclocitral was condensed with benzaldehyde in anhydrous ethanol with sodium ethoxide as the catalyst. The product, isolated in 13.0% yield from the crude reaction mixture by precipitation with hexane, was a white crystalline solid, m.p. 98-99°, identified by ir, nmr, and elemental analysis as the benzopyran-1-one **6** (Scheme 1). The ir spectrum of **6** showed a strong ester C=O peak at 1680 cm^{-1}. The nmr spectrum showed an ABX pattern similar to **4** and **5**, but the X doublet of doublets at δ 5.24 was now the only signal in the 3 to 7 ppm region. The product is evidently an oxidized aldol that is stabilized to dehydration by lactone formation. Because the reaction was carried out under argon, **6** was probably nor formed by oxidation of **4**. More likely, the β-cyclocitral underwent a crossed Cannizzaro reaction with benzaldehyde, giving β-cyclogeranic acid and benzyl alcohol, after which the β-cyclogeranic acid underwent a Claisen reaction (12a) with the benzaldehyde. The inordinately high yield (29.2%) of benzyl alcohol supported this mechanism.

Condensation of β-cyclocitral with benzaldehyde in the presence of an acid catalyst, hydrochloric acid, proceeded smoothly but in a different direction, giving a high yield (87.5%) of a yellow oil, b.p. 178-179°/0.3 mm, identified by ir, nmr, and elemental analysis as the 3-benzylidene derivative of β-cyclocitral **7** (Scheme 1). The ir spectrum of **7** showed a strong sharp peak at 1655 cm^{-1} for the conjugated C=C and a shoulder at 1700 cm^{-1} for the conjugated C=O. The nmr spectrum featured a singlet for the aldehyde hydrogen at δ 10.27 and a triplet for the vinyl hydrogen at δ 6.97, coupled to the methylene hydrogens at C-4. The couplings and chemical shifts were established by spin decoupling. The geometry of the exocyclic double bond of **7** and its derivatives is unknown.

The only other products identified in this reaction were benzaldehyde (7.7%), benzoic acid (0.5%), β-cyclogeranic acid (1.0%), and a trace of β-cyclocitral. No **1a**, **4**, **5**, **6**, or benzyl alcohol were detected.

The reaction, though clean, was slow. The conversion of **1b** to **7** was 42.0% after 4 hours, 63.0% after 13 hours, and 87.5% after 88 hours at room temperature, or 74.9% after 1.5 hours at reflux.

Attempts to improve the yields of the base-catalyzed condensation products by protecting the aldehyde group of β-cyclocitral were unsuccessful. Reaction of benzaldehyde with the anil **2b** in the presence of sodium ethoxide catalyst under the conditions described for **6** gave no condensation products, though all of the benzaldehyde was consumed. Most of the benzaldehyde underwent an exchange reaction with the **2b** giving *N*-benzylideneaniline and β-cyclocitral, and the remainder underwent Cannizzaro reactions, giving benzyl alcohol (~ 12%), benzoic acid (9.8%), and β-cyclogeranic acid (2.0%). A similar reaction between benzaldehyde and the acetal **3a** in the presence of sodium ethoxide catalyst gave benzyl alcohol (36.3%), benzoic acid (38.9%), β-cyclocitral diethyl acetal (33) (6.3%, formed from **3a** and the solvent by base-catalyzed exchange), and unreacted starting materials.

In summation, β-cyclocitral condenses with benzaldehyde through the lone methyl group or the C-3 methylene group, depending on the catalyst. Base catalysts favor condensation through the methyl group, giving either the hemiacetal **4** that subsequently dehydrates to the enol ether **5**, or the lactone **6**. Acid catalysts act exclusively through the C-3 methylene group, giving the benzylidene derivative **7**.

These model experiments suggest that the aldol condensation does show promise for the strigol synthesis, particularly if the C-3 methylene group, which ultimately requires a hydroxyl substituent, is suitably blocked.

Tests for Aldehydes and α,β-Unsaturated Carbonyl Compounds.

According to Strebel (34), cyclocitral responds to characteristic tests for aldehydes such as a violet color with fuchsin-sulfurous acid (Schiff reagent) and a silver mirror with ammoniacal silver solution (Tollens' reagent). In the present work, positive tests were given by benzaldehyde and α-cyclocitral, but not by β-cyclocitral (Table 1). The aldehyde-protected derivatives **2** and **3** and the

Table 1

Tests for Aldehydes with Schiff or Tollens' Reagent and for α,β-Unsaturated Carbonyl Compounds with Feigl Reagent

Compound	Schiff (a)	Tollens (b)	Feigl (c)
PhCHO	+ + +	+ + +	+ + +
1a	+ +	+ +	+ +
1b	−	−	+ +
2	−	+	+ +
3	+ +	−	−
4	−	−	+ +
5	+	+	+ +
6	−	−	−
7	+	+	+ +

Positive tests: (a)Fuchsin-sulfurous acid (31b), violet color; (b) ammoniacal silver nitrate (31c), silver mirror; (c) alkaline *p*-nitrophenylhydrazine (36), wine-red color. Negative tests are colorless for all three reagents.

condensation products **4**, **5**, and **6** gave variable tests, probably reflecting the extent of hydrolysis of these substances during the testing. The aldehyde **7** gave weak but positive tests. On a preparative scale, oxidation of β-cyclocitral with freshly prepared silver oxide (35) gave only a 22.9% yield of a α-free β-cyclogeranic acid.

A test devised by Feigl (36) for α,β-unsaturated aldehydes and ketones was used as an aid in identification. All the aldehydes and their condensation products gave positive tests except the acetal **3** and the lactone **6**. The hemiacetal **4** and the enol ether **5** possess masked aldehyde groups that could form *p*-nitrophenylhydrazones under the test conditions, whereas **6** does not. α-Cyclocitral, which does not have a conjugated double bond, probably isomerized to the β-isomer when the potassium hydroxide was added.

The aldehyde **7** formed well-defined crystalline derivatives with semicarbazide, 2,4-dinitrophenylhydrazine, and hydroxylamine. Efforts to prepare a phenyl isocyanate derivative of **4** or semicarbazide derivatives from **4** or **5**, however, were unsuccessful.

EXPERIMENTAL

Methods.

Melting points are uncorrected. Elemental analyses were performed by Galbraith Laboratories, Inc., Knoxville, Tenn. All ether extractions were performed three times, followed by rinsing once with water and once with saturated sodium chloride, drying with anhydrous sodium sulfate, and stripping under reduced pressure. Infrared (ir) spectra were taken on a Perkin-Elmer 137B (w = weak, m = medium, s = strong, vs = very strong, br = broad). Nuclear magnetic resonance (nmr) spectra were taken on a Varian EM360L equipped with a spin decoupler, with TMS or DSS as an internal lock (s = singlet, d = doublet, m = multiplet, br = broad).

Reagents.

α,β-Cyclocitral was prepared from citral anil (20) by cyclization with sulfuric acid (13,14). The separation of water from the mixture of citral and aniline occurs much more rapidly if the ether solution is shaken with anhydrous sodium sulfate. An attempt to cyclize the anil by passing the ether solution through a strong acid cation exchange resin (Rexyn 101, H form) was unsuccessful. β-Cyclocitral semicarbazone, m.p. 166-167° (2-PrOH, 3 ml./g.) was prepared from 93% β-cyclocitral as described by Tiemann (3) and hydrolyzed to 100% β-cyclocitral with sulfuric acid (16). The semicarbazone was α-free even before recrystallization; nmr (deuteriochloroform): δ 1.20 (s, 6H, Me_2), 1.3-2.3 (m, 6H, CH_2), 1.79 (s, 3H, Me), 6.00 (s, 2H, NH_2), 7.75 (s, 1H, CH), and 10.13 (s, 1H, NH) ppm. Other reagents were used as obtained; the benzaldehyde and benzyl alcohol were chlorine free.

Isomerization of α,β-Cyclocitral (**1a,b**).

A 19 × 600-mm chromatographic column with a sealed-in coarse fritted disk was filled with methanol and charged to a 12-in depth with Rexyn 201 (OH form), a strong base anion exchange resin. A solution of α,β-cyclocitral (10.00 g., 57% β) in methanol (10 ml.) was transferred to the column, eluted with methanol at a flow rate of 60 ml./minute, and stripped under vacuum in a rotary evaporator. The product (9.61 g.) was a pale-yellow oil, n_D^{20} 1.4943, that analyzed 93% β-cyclocitral by nmr (2).

This method was subsequently used to isomerize large quantities (150 g. or more) of α,β-cyclocitral. A single pass was sufficient. With repeated use there was a gradual build-up of α- and β-cyclogeranic acid. The resin was regenerated by elution with a solution of potassium hydroxide (10 g.) in methanol (190 ml.), followed by rinsing with methanol until the effluent was neutral. The cyclogeranic acids were recovered from the eluate by dilution with ice water, extraction with ether to remove neutral impurities, acidification with concentrated hydrochloric acid (25 ml.), and extraction with ether, giving 4.44 g. of a white solid that analyzed 75% β-cyclogeranic acid by nmr [ratio of Me_2 signals at δ 1.17 (s, β-isomer) to 1.00 (d, J 4.0 Hz, α-isomer) ppm].

N-(β-Cyclocitrylidene)aniline (**2b**).

A mixture of β-cyclocitral (15.22 g., 0.1 mole), aniline (18.63 g., 0.2 mole), and toluene (75 ml.) was heated to reflux in an apparatus fitted with a Dean-Stark trap for azeotropic removal of the water, and held at a reflux until the evolution of water subsided (2 hours). The solution was stripped under vacuum and distilled, giving 9.04 g. (97.1%) of aniline, b.p. below 60°/0.4 mm, and 18.39 g (80.9%) of the anil **2b** as a bright-yellow oil, b.p. 130-134°/0.4 mm, n_D^{20} 1.5700; ir (neat): ν max 692 s (Ph), 762 s (Ph), 1165 m, 1470 s, 1580 vs (C=C), 1600 s and 1660 s (C=N), and 2900 vs cm^{-1}; nmr (deuteriochloroform): δ 1.32 (s, 6H, Me_2), 1.4-2.8 (m, 6H, CH_2), 1.92 (s, 3H, Me), 6.9-7.5 (m, 5H, Ph), and 8.34 (s, 1H, NCH) ppm. Signals at δ 0.98 (s, 6H, Me_2), 5.60 (br s, 1H, 3-CH), and 7.57 (d, 1H, NCH, J 8.0 Hz) ppm were assigned to the α-isomer **2a**.

Anal. Calcd. for $C_{16}H_{21}N$: C, 84.53; H, 9.31; N, 6.16. Found: C, 84.96; H, 8.94; N, 5.83.

Addition of a few drops of deuterium oxide to a solution of **2b** in acetone-d_6 caused extensive hydrolysis (nmr).

α-Cyclocitral Ethylene Acetal (**3a**).

A mixture of β-cyclocitral (30.45 g., 0.2 mole), ethylene glycol (15.52 g., 0.25 mole), *p*-toluenesulfonic acid (0.10 g.), and benzene (100 ml.) was heated to reflux in an apparatus fitted with a Dean-Stark trap for azeotropic removal of the water, and held at reflux until the evolution of water subsided (13 hours). The solution, now homogeneous, was extracted with 5% sodium bicarbonate to remove the catalyst, rinsed with water, stripped, and distilled, giving 24.55 g. (62.5%) of the acetal **3a** as a colorless oil, b.p. 98-106°/2.4 mm, n_D^{20} 1.4846 [lit. (20)b.p. 107-108°/12 mm, n_D^{20} 1.4841]; ir (neat): ν max 828 m, 943 s, 956 s, 1040 vs, br, 1130 vs, br, 1350 m, 1445 m, 1670 m, and 1705 w cm^{-1}; nmr (deuteriochloroform): δ 0.92 (s, 3H, 6-Me), 1.02 (s, 3H, 6-Me), 1.78 (d, 3H, 2-Me, J 2.0 Hz), 1.0-2.3 (m, 4H, 4- and 5-CH_2), 3.5-4.1 (m, 4H, OCH_2CH_2O), 4.92 (d, 1H, OCHO, J 3 Hz), and 5.5 (br s, 1H, 3-CH) ppm. Signals at δ 1.08 (s, 6H, Me) and 5.32 (s, 1H, OCHO) ppm were assigned to the β-isomer **3b**.

8,8-Dimethyl-3-phenyl-3,4,5,6,7,8-hexahydro-1*H*-2-benzopyran-1-ol (**4**) and 8,8-dimethyl-3-phenyl-3,4,6,7-tetrahydro-8*H*-2-benzopyran (**5**).

A solution of β-cyclocitral (15.23 g., 0.1 mole), benzaldehyde (10.61 g., 0.1 mole), and ethanol (25 ml.) was treated with a solution of sodium hydroxide (1.00 g., 0.025 mole) in water (10 ml.), purged with argon, and shaken for 24 hours in a stoppered flask by means of a mechanical shaker. The mixture contained two phases at the start, but after 4 hours it was homogeneous. After being shaken the mixture was diluted with water, extracted with ether, acidified with hydrochloric acid and extracted again with ether. The first extract yielded 1.45 g. of an off-white solid comprised (nmr) of benzoic acid (6.5%), β-cyclogeranic acid (2.7%), and the benzopyran-1-one **6** (0.7%). The second extract yielded 24.40 g. of yellow oil that partly crystallized on standing. The oil was shaken with hexane and filtered, giving 4.28 g. (16.6%) of the benzopyran-1-ol **4** as white needles, m.p. 120-122° after two recrystallizations from hexane (35 ml./g.); ir (Nujol): ν max 695 s (Ph), 752 s (Ph), 991 s 1035 s, 1105 s, 1165 s, 1630 m (C=C), and 3350 vs (OH) cm^{-1}; nmr (acetone-d_6): δ 1.10 (s, 3H, Me), 1.18 (s, 3H, Me), 1.3-1.7 (m, 2H, 7-CH_2), 1.7-2.2 (m, 6H, 4-, 5-, and 6-CH_2), 3.73 (br s, 1H, OH, vanishing with deuterium oxide), 5.07 (d of d, 1H, 3-CH, X portion of ABX spin pattern, ν_{AB} 2.05), 5.25 (br s, 1H, 1-CH), and 7.30 (br s, 5H, Ph) ppm.

Anal. Calcd. for $C_{17}H_{22}O_2$: C, 79.03; H, 8.59. Found: C, 79.37; H, 8.86.

The hemiacetal **4** is soluble in 2-propanol, chloroform, carbon tetra-

chloride, acetone, and cyclohexane and insoluble in water and hexane.

The hexane filtrate was stripped and steam distilled until 500 ml. of distillate was collected. The distillate was extracted with ether, giving 6.38 g. of a pale yellow liquid comprised (nmr) of β-cyclocitral (23.3%), benzaldehyde (15.8%), and benzyl alcohol (37a) (9.3%). The nonvolatile fraction was also extracted with ether, giving 12.61 g. of a thick yellow oil. The oil was distilled, giving 8.76 g. of a bright-yellow oil, b.p. 152-158°/0.4 mm, that partly crystallized on cooling. The oil was rubbed with ethanol and filtered, giving 1.91 g. (7.9%) of the benzopyran **5** as white needles, m.p. 76-77° after one recrystallization from ethanol (5 ml./g.); ir (Nujol): ν max 697 s (Ph), 764 s (Ph), 810 m, 870 m, 1040 s, 1055 s, 1100 vs, 1125 vs, 1220 s (C-O), 1600 s (C=C), and 1635 w cm^{-1}; nmr (deuteriochloroform): δ 1.05 (s, 3H, Me), 1.10 (s, 3H, Me), 1.45 (d of t, 2H, 7-CH_2, J^2 2.0, J^3 6.0 Hz), 2.13 (m, 2H, 6-CH_2, coupled to 7-CH_2 and 5-CH), 2.53 (m, 2H, 4-CH_2, AB portion of ABX spin pattern, ν_A 154.5, ν_B 149.5, J_{AB} 15.5, $J_{AH,\ 5H}$ 2.0 Hz), 4.78 (t of d, 1H, 3-CH, X portion of ABX spin pattern, ν_X 287.0, J_{AX} 12.0, J_{BX} 2.0 Hz), 5.25 (m, 1H, 5-CH, coupled to 4-CH_2, 6-CH_2, and 1-CH), 6.54 (d, 1H, 1-CH, J^5 1.5 Hz), and 7.31 (br s, 5H, Ph) ppm.

Anal. Calcd. for $C_{17}H_{20}O$: C, 84.95; H, 8.39; MW, 240.33. Found: C, 85.06; H, 8.50; MW (osmometric in chloroform), 229.

The enol ether **5** is soluble in most of the common organic solvents, partially soluble in the lower alcohols, and insoluble in water. A small (2.7%) quantity of the aldehyde **7** was identified (nmr) in the reaction mixture both before and after steam distillation.

8,8-Dimethyl-3-phenyl-3,4,5,6,7,8-hexahydro-1*H*-2-benzopyran-1-one (**6**).

A solution of sodium (2.3 g., 0.1 g.-atom) in ethanol (75 ml.) was purged with argon, treated with β-cyclocitral (15.23 g., 0.1 mole) and benzaldehyde (12.74 g., 0.12 mole), and stirred for 3 hours at room temperature under an argon atmosphere. There was a mild exotherm, and the mixture turned muddy. The mixture was diluted with water and worked up as described for the hemiacetal **4**, giving 3.34 g. (13.0%) of the benzopyran-1-one **6** as a white crystalline solid, m.p. 98-99° after recrystallization from hexane (9 ml./g.); ir (Nujol): ν max 694 m (Ph), 763 m (Ph), 1040 m, 1135 s, 1165 s, 1360 s, 1625 s (C=C), and 1680 vs (C=O) cm^{-1}; nmr (deuteriochloroform): δ 1.27 (s, 3H, Me), 1.33 (s, 3H, Me), 1.4-1.9 (m, 2H, 7-CH_2), 1.9-2.9 (m, 6H, 4-, 5-, and 6-CH_2), 5.24 (d of d, 1H, 3-CH, X portion of ABX spin pattern, ν_{AB} 2.38), and 7.33 (br s, 5H, Ph) ppm.

Anal. Calcd. for $C_{17}H_{20}O_2$: C, 79.65; H, 7.86. Found: C, 79.66; H, 7.72.

The lactone **6** is soluble in ethanol, chloroform, carbon tetrachloride and acetonitrile, partially soluble in 2-propanol and cyclohexane, and insoluble in water and hexane.

The neutral extract yielded 6.77 g. of steam-volatile liquid comprised of β-cyclocitral (23.8%) and benzyl alcohol (29.2%), but no benzaldehyde. The remainder of the neutral extract, a yellow oil (10.82 g.), was a mixture of unidentified condensation products linked through the C-2 methyl group (nmr).

3-Benzylidene-2,6,6-trimethyl-1-cyclohexene-1-carboxaldehyde (**7**).

A mixture of β-cyclocitral (15.23 g., 0.1 mole), benzaldehyde (10.61 g., 0.1 mole), 37% hydrochloric acid (10 ml., 0.12 mole), and ethanol (25 ml.) was stirred under argon for 88 hours, diluted with water and extracted with ether. The ether extract was rinsed with 10% sodium hydroxide, water and saturated sodium chloride, and was then dried over anhydrous sodium sulfate and stripped. The residue (23.59 g.), which contained no β-cyclocitral (nmr), was distilled, giving 0.82 g. (7.7%) of benzaldehyde, b.p. 65°/0.3 mm, and 21.03 g. (87.5%) of the aldehyde **7** as a yellow oil, b.p. 178-179°/0.3 mm, n_D^{20} 1.6165; ir (Nujol): ν max 695 m (Ph), 1150 m, 1170 m, 1655 s ($C=C_{conj.}$), and 1700 m, sh ($C=O_{conj.}$) cm^{-1}; nmr (deuteriochloroform): δ 1.26 (s, 6H, Me_2), 1.45 (m, 2H, 5-CH_2), 2.31 (s, 3H, Me), 2.60 (m, 2H, 4-CH_2), 6.97 (t, 1H, CHPh, J 1.5 Hz), 7.30 (br s, 5H, Ph), and 10.27 (s, 1H, CHO) ppm.

Anal. Calcd. for $C_{17}H_{20}O$: C, 84.95; H, 8.39. Found: C, 84.75; H, 8.61.

Aldehyde Derivatives of **7**.

These were prepared by standard methods (31d) and recrystallized to constant m.p. Crude yields are given in parentheses. The semicarbazone (87.1%) was obtained as lemon-yellow needles, m.p. 200-203° (ethanol, 30 ml./g.); ir (Nujol): ν max 694 m (Ph), 745 m (Ph), 1340 s, 1560 s, 1680 s (C=C), and 3170 s (NH) cm^{-1}; nmr (DMSO-d_6): δ 1.21 (s, 6H, Me_2), 1.3-1.7 (m, 2H, 5-CH_2), 2.02 (s, 3H, Me), 2.5 (br s, 2H, 4-CH_2), 6.12 (br s, 2H, NH_2), 6.70 (t, 1H, CHPh, J 1.5 Hz), 7.30 (br s, 5H, Ph), 7.98 (s, 1H, CH=N), and 9.97 (br s, 1H, NH) ppm.

Anal. Calcd. for $C_{18}H_{23}N_3O$: C, 72.69; H, 7.79; N, 14.13. Found: C, 72.83; H, 7.81; N, 14.10.

The 2,4-dinitrophenylhydrazone (95.4%) was obtained as a brown-red solid, m.p. 175-177° (carbon tetrachloride, 33 ml./g.); ir (Nujol): ν max 1130 m, 1300 s, 1320 vs, 1540 s ($C=C_{arom.}$), 1560 s ($C=C_{conj.}$), and 3300-3400 s (NH) cm^{-1}; nmr (deuteriochloroform): δ 1.38 (s, 6H, Me_2), 1.4-1.7 (m, 2H, 5-CH_2), 2.21 (s, 3H, Me), 2.4-2.8 (m, 2H, 4-CH_2), 4.3 (br s, 1H, NH), 6.82 (t, 1H, CHPh, J 1.5 Hz), 7.3 (br s, 5H, Ph), 8.26 (s, 1H, CH=N), 7.88, 8.31 and 9.10 (ABX octet, 3H, $C_6H_3(NO_2)_2$, J_{AB} 9.0, J_{AX} −0.1, J_{BX} 2.6 Hz, where A, B, and X are 6-, 5-, and 3-H, respectively) ppm; compare acetone 2,4-dinitrophenylhydrazone (37b).

Anal. Calcd. for $C_{23}H_{24}N_4O_4 \cdot \frac{1}{2}H_2O$: C, 64.32; H, 5.87; N, 13.05. Found: C, 63.60; H, 5.84; N, 13.09.

The oxime was obtained in 86.2% yield, cream plates, m.p. 119-120° (MeCN, 6 ml./g.); ir (Nujol): ν max 693 s, 857 m, 885 m, 952 s, and 3250 s (OH) cm^{-1}; nmr (deuteriochloroform): δ 1.19 (s, 6H, Me_2), 1.4-1.7 (m, 2H, 5-CH_2), 2.06 (s, 3H, Me), 2.4-2.8 (m, 2H, 4-CH_2), 6.68 (t, 1H, CHPh, J 1.5 Hz), 7.27 (br s, 5H, Ph), 8.12 (s, 1H, CH=N), and 9.00 (br s, 1H, OH, vanishing with deuterium oxide) ppm.

Anal. Calcd. for $C_{17}H_{21}NO$: C, 79.96; H, 8.29; N, 5.49. Found: C, 80.30; H, 8.39; N, 5.62.

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