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(4) We have no proof for the competitive reduction of **2** and hydrogenolysis of **4**. However, the quantitative conversion of **5** to **6** demonstrates that the enol ether functionality is quite receptive to catalytic reduction; and thus it seems that some of the alkene bond of **2** might suffer similar reduction.

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Studies Directed toward a Practical Synthesis of Brevicomin. V. Isomer Enrichment of Bicyclic Ketals in the 6,8-Dioxabicyclo[3.2.1]octane Series by Complexation with Titanium Tetrachloride

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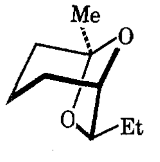
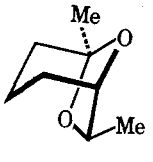
Received June 24, 1975

As part of a continuing effort directed toward a practical synthesis of brevicomin (1),[1] the aggregating sex pheromone of the pine bark beetle, *Dendroctonus brevicomis*, we initiated a study of methods for effecting isomer enrichment. Since it is well documented that powerful synergistic effects are noted for compound mixtures in testing, an effective method to remove unwanted isomers became quite important.[2] In our synthetic methodologies to date, we have always prepared a mixture isomeric about C-7.

Since 1 has proven to be relatively difficult to obtain in quantity at this time, we chose to study the readily available 2 for our isomer enrichment study.[3]



exo-1



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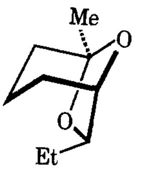
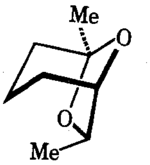


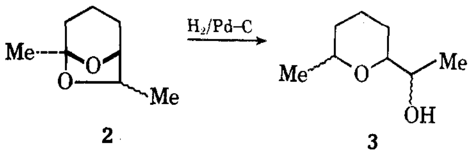
endo-1



endo-2

Substituted 1,3-dioxolane and dioxane derivatives have been generally observed to suffer cleavage and rearrangement to an appropriate ester in the presence of titanium tetrachloride.[4] Though this is a well-known Lewis acid capable of complexing ligands having heteroatom functionality,[5] *no ketal complexation has been reported.* We have observed, however, that titanium tetrachloride readily forms a complex with **2**, and this complex can be hydrolyzed with water to recover 93% of the initial bicyclic ketal.

We had previously noted[6] that hydrogenolysis of *endo*-**2** proceeded much faster than *exo*-**2** (**2** → **3**). This was rationalized as a steric effect of the exo methyl group on the catalyst surface. Taking advantage of this observation we envisioned preparing a $TiCl_4$ "surface" on which one isomer might selectively interact. This was accomplished by preparing a dilute $TiCl_4$–CCl_4 frozen matrix at liquid nitrogen temperature. Typically, 0.005 mol of $TiCl_4$ in 20 ml of carbon tetrachloride was frozen in liquid nitrogen. To the surface formed was added 0.01 mol of ketal, and the solution was allowed to warm, unperturbed, to room temperature. The complex was filtered through a fritted glass filter and the filtrate was reduced in volume. GLC analysis indicated, that as expected, the endo isomer was selectively complexed. Hydrolysis of the filtered complex with water, followed by extraction with methylene chloride, yielded an enriched endo-isomer mixture. If the experiment is carried out without solvent, selectivity is decreased. This enrichment procedure can be repeated as many times as necessary to reach a desired isomeric purity. Starting with 2 having an exo–endo ratio of 15.9:9.4, three cycles increased the ratio to 16:2.7. This constitutes an enrichment of 71.5% by an experimentally simple procedure.



2 3

Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this work.

Registry No.—1, 20290-99-7.

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Radical Decomposition of α-Hydroperoxy Ketones. A Facile Scission of Benzoyl Radical[1]

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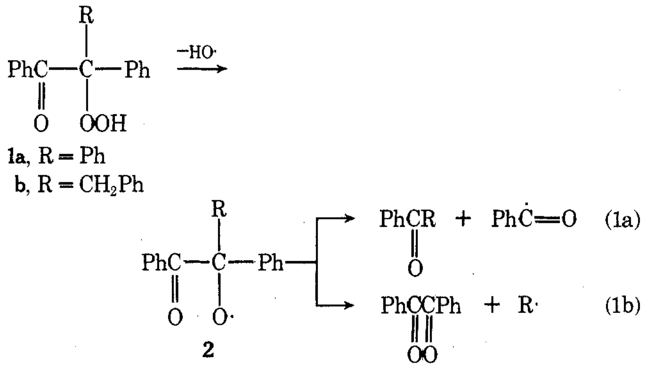
Received June 17, 1975

The β-scission of *tert*-alkoxy radicals has been established,[2] and previous reports include the information on the scission of halomethyl,[2a,h] alkoxymethyl,[2h,i] and alkoxycarbonyl radicals,[2h,i] and of acyl radical.[3,4] In the course of our study on the basic decomposition of α-hydroperoxy ketones,[5] **1**, the facile fission of benzoyl radical was observed.

Table I
Radical Decomposition of α-Hydroperoxy Ketones (1)

Peroxide	Conditions	Products,[a] % $\mathrm{Ph\underset{\overset{\|}{O}}{C}R}$	 $PhCO_2H$	 Ph_2	 $\mathrm{Ph\underset{\overset{\|}{O}}{C}\underset{\overset{\|}{O}}{C}Ph}$	 Others
		A. Pyrolysis GLC (250°)[b]				
1a	in PhH	95–100	68–80	1–6	0	None
1a	in PhMe	99	97	0	0	$PhCH_2CH_2Ph$ (7%); $PhCH_2OH$ (7%); PhCHO (17%)
1b	in PhH	90–95	75–90	1–7	6	None
		B. Fe^{2+}-Catalyzed Decomposition (70% MeOH, 25°)[c]				
1a	$FeSO_4$	96	d	0	16[e]	None
1a	$FeSO_4$–$FeCl_3$	100	d	0	<1[e]	$PhCO_2Me$ (61%)
1b	$FeSO_4$	80	d	0	18[e]	None
1b	$FeSO_4$–$FeCl_3$	82	d	0	3.9[e]	$PhCO_2Me$ (55%); $PhCH_2Cl$ (4.9%)

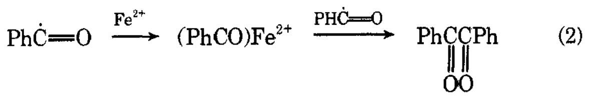
[a] Products were determined by GLC. [b] See Experimental Section. [c] $[1] = 0.01\ M$, $[FeSO_4] = 0.1\ M$, and $[FeCl_3] = 0.05\ M$. [d] Not determined. [e] Mol/mol %. According to eq 2, this value should be duplicated.


1a, R = Ph
b, R = CH_2Ph
2
(1a)
(1b)

Pyrolysis GLC of α-hydroperoxy-α,α-diphenylacetophenone (**1a**) at 250° as a solution in benzene gave benzophenone and benzoic acid together with a smaller amount of biphenyl (Table IA). When **1a** in toluene was pyrolyzed, bibenzyl, benzyl alcohol, and benzaldehyde were detected in place of biphenyl, suggesting a radical reaction. Biphenyl is formed probably via a sequence $Ph\dot{C}{=}O \rightarrow Ph\cdot \rightarrow Ph_2$ in benzene.[6] These results suggest the predominant scission of benzoyl radical from **2** (eq 1a). Benzaldehyde may be produced by the hydrogen abstraction of $Ph\dot{C}{=}O$ and/or oxidation of benzyl alcohol.

The thermal decomposition of α-hydroperoxy-α-phenyl-α-benzylacetophenone (**1b**) afforded benzil (6%) together with deoxybenzoin, benzoic acid, and biphenyl. The yield of benzil was unchanged even by a tenfold increase in the amount of **1b**, and its formation was not detected from **1a** or other α-benzoyl hydroperoxides. This suggests that the scission of benzyl radical (eq 1b) also occurs.

The reactions of eq 1a and 1b can be confirmed by the redox reaction of **1a** and **1b** with ferrous sulfate (Table IB). It is well known that the Fenton reaction of ROOH produces RO·.[2d,7] The predominant formation of monoketones shows the facile fission of $Ph\dot{C}{=}O$ from **2.** The reaction of **1** with $FeSO_4$ afforded a considerable amount of benzil, much of which is formed by the dimerization of benzoyl radicals (eq 2). The reaction of **1** with Fe^{2+} is instantaneous, but the yield of benzil was not influenced by one-time or dropwise addition. Probably, $Ph\dot{C}{=}O$ is efficiently trapped by Fe^{2+} to form a metastable complex[8,9] and benzil is formed by ligand transfer to another $Ph\dot{C}{=}O$.



$$Ph\dot{C}{=}O \xrightarrow{Fe^{2+}} (PhCO)Fe^{2+} \xrightarrow{PH\dot{C}=O} \mathrm{Ph\underset{\overset{\|}{O}}{C}\underset{\overset{\|}{O}}{C}Ph} \qquad (2)$$

Addition of $FeCl_3$ to the redox system reduced the yield of benzil but instead produced methyl benzoate (eq 3), substantiating the formation of free $Ph\dot{C}{=}O$. The formation of benzyl chloride from **1b** demonstrates the scission of benzyl radical (eq 1b).

$$Ph\dot{C}{=}O \xrightarrow{FeCl_3} PhCOCl \xrightarrow{MeOH} PhCO_2Me \qquad (3)$$

These results at 25 or 250° together with no formation of α-hydroxy ketones clearly show that the scission of benzoyl radical from **2** is very facile and ca. 15–20 times faster than that of benzyl radical in view of the product ratio of PhCOR and PhCOCOPh: 90:6–80:3.9 in Table I. Since the scission of benzyl radical is known to be very fast,[2d,k,n] the scission of $Ph\dot{C}{=}O$ (eq 1a) is probably the fastest one thus far known. This seems to be comprehensible, if it is considered that acyl radicals are stable and easily formed from aldehydes.[10] The scission of acyl radicals have been shown for a few cases,[2j,3,4] and its facility suggests a probable mechanism for the autoxidative α-fission of ketones.

Experimental Section

Materials. α-Hydroperoxy ketones, **1a** and **1b**, were prepared by basic autoxidation of ketones as described elsewhere.[5]

Pyrolysis GLC. Ca. 4 μl of a 0.01 M solution of **1** was injected into GLC (injection temperature 250°; column temperature 80–250°). Since the solvent was vaporized immediately, the thermal decomposition of **1** occurs in the vapor phase. Products were identified and determined by the usual GLC technique with three different columns (1 m): (1) Apiezon grease L, 15% on Celite 545; (2) PEG 20M, 2% on Chamelite CK; (3) PEG succinate, 13% on Chromosorb. Propiophenone or biphenyl were used as an internal standard.

Fe^{2+}-Catalyzed Decomposition. A methanolic solution of **1** (0.02 M, 5 ml) was added to the mixture of MeOH (2 ml), aqueous $FeSO_4$ (0.5 M, 2 ml), and H_2O (1 ml) at 25°. The reaction was instantaneously completed. Products were extracted with $CHCl_3$ after dilution with aqueous NaCl, and analyzed by GLC.

Acknowledgments. We are grateful to Dr. Shin Tsuge for the relevant discussions about pyrolysis GLC.

Registry No.—**1a,** 57196-77-7; **1b,** 57196-78-8; benzoyl radical, 2652-65-5.

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Synthesis of (±)-3-Methoxy-*N*-acetylnornantenine

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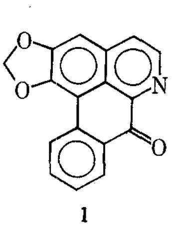
Received July 14, 1975

The heartwood of *Liriodendron tulipifera* has previously yielded two antimicrobial alkaloids, liriodenine (1) and dehydroglaucine (2),[1] and two nonbasic noraporphine alkaloids, one of which has been identified as (+)-*N*-acetylnornantenine (3) by direct comparison with an authentic sample.[2] A structure for the second alkaloid was tentatively assigned as (+)-3-methoxy-*N*-acetylnornantenine (4) based on spectroscopic evidence.[2] A total synthesis confirming this assignment has now been achieved.

Decomposition of ω-diazo-3,4-methylenedioxy-6-nitroacetophenone (5) in the presence of 2,3,4-trimethoxy-β-phenylethylamine (6) and silver oxide afforded the crystalline amide 7. Compound 7 was smoothly cyclized in the Bishler–Napieralski reaction using phosphorus oxychloride in acetonitrile to the dihydroisoquinoline 8. Reduction of 8 with sodium borohydride and acetylation with acetyl chloride produced the *N*-acetyl derivative 9. The NMR spectrum of 9 clearly showed signals for each conformer which is characteristic of hindered rotation in 1-benzyl-1,2,3,4-tetrahydroisoquinolines.[3] Reduction of 9 with zinc dust and sulfuric acid gave 10, which upon Pschorr cyclization following the method utilized by Weisbach and Douglas[4] gave (±)-3-methoxy-*N*-acetylnornantenine (4) which gave TLC, NMR, solution ir, and MS data identical with those of natural (+)-3-methoxy-*N*-acetylnornantenine (4).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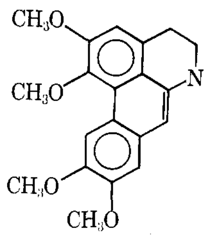
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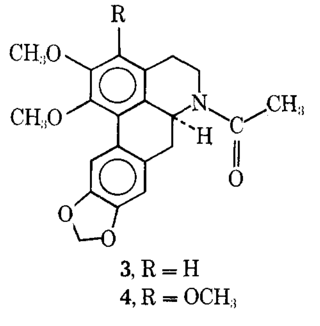
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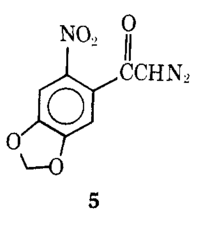
4, R = OCH₃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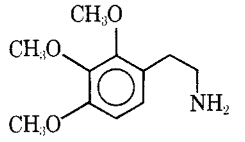
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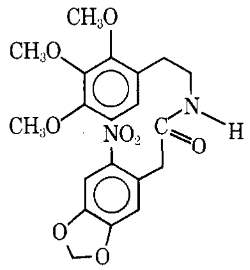
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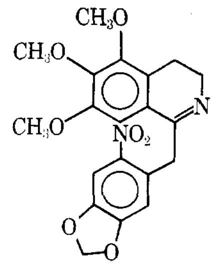
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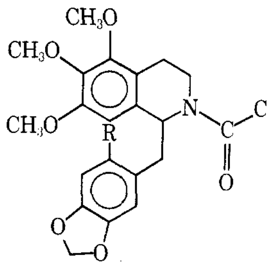
9, R = NO₂
10, R = NH₂

Experimental Section

All melting points were determined on a Thomas-Hoover Unimelt and are uncorrected. The infrared spectra were taken on a Perkin-Elmer 257 or Beckman IR-33 infrared spectrometer. Elemental analyses were performed by Scandinavian Microanalytical Laboratory, Herlev, Denmark. NMR spectra were recorded on a Jeol C-60HL spectrometer using deuterated chloroform as solvent and Me_4Si as internal standard, with chemical shifts recorded in δ (ppm) units. Uv spectra were obtained in methanol on a Beckman Acta III spectrophotometer. Mass spectral data were obtained on a Du Pont CEC 492 spectrometer.

***N*-(2,3,4-Trimethoxy-β-phenylethyl)-3′,4′-methylenedioxy-6′-nitrophenylacetamide (7).** To a solution of 7.2 g of ω-diazo-3,4-methylenedioxy-6-nitroacetophenone (5)[5] in 75 ml of dry benzene at 60° was added, with stirring, a solution of 7.4 g of 2,3,4-trimethoxy-β-phenylethylamine (liberated from 8.5 g of hydrochloride salt, obtained from Aldrich) in 30 ml of dry benzene and 513 mg of freshly prepared Ag_2O. The suspension was stirred at 60° for 0.5 hr and then an additional 300 mg of Ag_2O was added, followed by 1 hr of refluxing. After cooling, the solution was concentrated under reduced pressure to remove most of the benzene and then dissolved in boiling acetonitrile, filtered through Celite while hot, and evaporated to dryness to leave 10.2 g of amide 7. Crystallization from acetonitrile gave 9.1 g: mp 181–182°; ir (KBr) 3300 (NH) and 1645 cm^{-1} (C=O).

Anal. Calcd for $C_{20}H_{22}N_2O_8$: C, 57.40; H, 5.30; N, 6.70. Found: C, 57.33; H, 5.27; N, 6.89.

1-(3′,4′-Methylenedioxy-6′-nitrobenzyl)-5,6,7-trimethoxy-3,4-dihydroisoquinoline (8).[6] Amide 7 (300 mg) was dissolved in 20 ml of acetonitrile at 60° and with stirring 3 ml of phosphorus oxychloride was added. After 2 hr at 60° the solution was evaporated under reduced pressure to give a red gum which yielded 77 mg of 8 upon crystallization from alcohol, mp 144–145°. Chromatography of the mother liquor on silica gel using benzene–acetone (8:1) as eluent gave an additional 69 mg: NMR ($CDCl_3$) δ 7.43, 6.95, and 6.85 (1 H each, PhH), 5.98 (2 H, s, OCH_2O), 4.30 (2 H, s, $NO_2PhCH_2C{=}N$), 3.87 (3 H, s, OCH_3), 3.80 (6 H, s, OCH_3), 3.55 (2 H, dd, J = 8, 8 Hz, $C{=}NCH_2CH_2$), 2.58 (2 H, dd, J = 8, 8 Hz, $-C{=}NCH_2CH_2$).