The second compound eluted was 8,13-dioxo-13a-hydroxy-2,3,10,11-tetramethoxyberbine (**9**): 430 mg, 1.08 mmol (46%); mp 150 °C dec (lit.[9] mp 160–161 °C); UV 251 nm (ϵ 25000); NMR δ 7.63 (s, 1 H), 7.42 (s, 1 H), 7.04 (s, 1 H), 6.58 (s, 1 H), 4.84 (m, 1 H, C-6), 4.02 (s, 3 H), 3.99 (s, 3 H), 3.86 (s, 3 H), 3.84 (s, 3 H), 2.4–3.7 (m, 3 H); MS, *m/e* 399 (relative intensity) (parent, 10.4), 383 (–16, 20), 368 (–31, 12).

Anal. Calcd for $C_{21}H_{21}NO_7$: C, 63.15; H, 5.30; N, 3.51. Found: C, 62.91; H, 5.25; N, 3.42.

Method B. Compound **8** (770 mg, 1.81 mmol) and 3.0 g of lead tetraacetate were stirred in 100 mL of chloroform at room temperature for 18 h. After being quenched with glycerine, the solution was washed 3 times with water and dried with sodium sulfate. The solution was diluted with 30 mL of absolute ethanol, and a few crystals of *p*-toluenesulfonic acid monohydrate were added. After 18 h, TLC (1:1 ethyl acetate:toluene) indicated complete conversion to the ethyl ether **15**. After being quenched with 1 mL of triethylamine, the solution, after addition of 50 mL of chloroform, was washed 3 times with water, dried with sodium sulfate, and evaporated. The residue was crystallized from ether:petroleum ether to yield 690 mg (1.62 mmol, 90%) of **15**.

Lead Tetraacetate Oxidation of 13-Acetoxy-2,3-(methylenedioxy)-9,10-dimethoxyoxyprotoberberine (12). Compound **12** (800 mg, 1.95 mmol) was oxidized according to method B above. Methanol was used, however, in place of ethanol. The residue, after workup, was flash chromatographed by using 5:95 ethyl acetate:methylene chloride to yield 709 mg (1.79 mmol, 92%) of 8,13-dioxo-2,3-(methylenedioxy)-9,10,13a-trimethoxyberbine (**13**): mp 129–130.5 °C dec (lit.[9] mp 125–126 °C).

13β-Hydroxy-2,3,10,11-tetramethoxyberbine (13β-Hydroxyxylopinine) (10). To a solution of 1.4 g of lithium aluminum hydride in 100 mL of tetrahydrofuran under argon was added 1.40 g (3.29 mmol) of acetoxylated oxyprotoberberine **8**. After stirring for 23 h at room temperature, excess hydride was quenched with a saturated solution of Rochelle salt. After separation of the layers, the Rochelle salt solution was further extracted with methylene chloride. The combined extracts were dried with sodium sulfate and the methylene chloride and a portion of the THF evaporated under reduced pressure. The remaining solution was diluted with 200 mL of methanol, 3 g of sodium borohydride were added, and the resultant mixture was stirred overnight. The majority of the solvent was removed, then diluted with water, and extracted with chloroform. After being dried with sodium sulfate, the solvent was evaporated and the residue flash chromatographed by using 4:96 methanol:methylene chloride to yield 730 mg (1.97 mmol, 60%) of 13β-hydroxyxylopinine (**10**): mp 202–205 °C (acetone–water) (lit.[16] 197–198 °C); IR 3460 cm^{-1}, 1517; NMR δ 6.92 (s, 1 H), 6.75 (s, 1 H), 6.58 (s, 1 H), 6.55 (s, 1 H), 4.75 (br s ($w_{1/2}$ = 3 Hz), 1 H, 13α-H), 3.88 (s, 6 H), 3.86 (s, 6 H), 2.4–3.8 (m, 7 H).[2c,17]

Anal. Calcd for $C_{21}H_{25}NO_5$: C, 67.91; H, 6.78; N, 3.77. Found: C, 67.48; H, 6.78; N, 3.96.

(±)-Ophiocarpine (1). The 13-acetoxylated oxyprotoberberine **12** (521 mg, 1.27 mmol) was reduced sequentially as illustrated for compound **8** to yield 223 mg (0.63 mmol 52%) of ophiocarpine (**1**), mp 249–251 °C (methanol) (lit.[3,4b] mp 254–256 °C), and whose NMR spectrum agreed with published spectra (C-13α δ 4.71 (br s, $w_{1/2}$ = 3 Hz)).[3c,4b]

(±)-Chilenine (14). A deep red-violet solution of compound **13a** (119 mg) in 18 mL of concentrated hydrochloric acid was poured into 1.2 L of water and extracted with three portions of chloroform. The combined extracts were dried with magnesium sulfate, filtered, and concentrated to yield 103 mg (88%) of a chromatographically homogeneous, but dark red, 13a-hydroxy derivative of **13b**: NMR δ 7.81, 7.14 (AB q, J = 9 Hz, 2 H), 6.90 (s, 1 H, C1), 6.58 (s, 1 H, C4), 5.91 (s, 2 H), 4.71–5.01 (m, 1 H), 3.95 (s, 3 H), 3.94 (s, 3 H), 2.46–3.13 (m, 3 H).

A solution of 98 mg of **13b** in 64 mL of chloroform was vigorously shaken with 64 mL of 10% aqueous ammonia for 0.5 h. The organic layer was separated, dried with magnesium sulfate, filtered, and evaporated. Radial preparative thick layer chromatography (Chromatotron) on silica (1:4 ethyl acetate:methylene chloride) afforded 65 mg (66%) of chilenine (**14**) as a foam. Two recrystallizations from methanol gave an analytical sample: mp 114.5–116 °C (lit.[18] 155 °C); IR (chloroform) 1710, 1685, 1610 cm^{-1}; NMR δ 7.03, 7.30 (AB q, J = 8 Hz, 2 H), 6.68 (s, 1 H), 6.63 (s, 1 H), 5.91 (s, 2 H), 4.05 (br s, 1 H), 3.98 (s, 3 H), 3.85 (s, 3 H), 2.78–4.38 (br m, 4 H); MS, *m/e* (relative intensity) 383 (parent, 11), 367 (39), 352 (13), 338 (44), 308 (16), 220 (45), 176 (79), 148 (100).

Anal. Calcd for $C_{20}H_{17}NO_7$: C, 62.66; H, 4.47; N, 3.65. Found: C, 62.40; H, 4.28; N, 3.61.

Registry No. (±)-**1**, 18090-55-6; **5**, 32255-47-3; **6**, 90553-68-7; **7**, 10211-78-6; **8**, 90553-69-8; (±)-**9**, 75091-35-9; (±)-**10**, 59373-39-6; **11**, 549-21-3; **12**, 66054-87-3; (±)-**13a**, 71733-96-5; (±)-**13b**, 71766-69-3; (±)-**14**, 71700-15-7; (±)-**15**, 90553-70-1; **16**, 90553-67-6; lead tetraacetate, 546-67-8.

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(17) Battersby, A. R.; Spenser, H. *J. Chem. Soc.* **1965**, 1087.
(18) Moniot, J. L.; Hindenlang, D. M.; Shamma, M. *J. Org. Chem.* **1979**, *44*, 4343. The substantial differences in melting point between our sample of chilenine and that reported is ascribed to a difference in crystalline form since the solution spectra and mass spectrum are identical with those reported.

Oxidation of β-Diketones with (Diacetoxyiodo)benzene

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In an earlier paper[1] we reported that the ethyl esters of aroylpyruvic acids undergo an oxidative cleavage reaction with (diacetoxyiodo)benzene (PIDA) in acetic acid–water. These investigations were continued in order to determine the pathway of the oxidative cleavage of the β-dicarbonyl compounds. We now report on the oxidation of some β-diketones with PIDA. This reaction has been investigated by Neiland[2] and Mizukami[3] who employed anhydrous conditions. The end products were the corresponding α-acetoxy derivatives.

In this paper we describe the oxidations of dibenzoylmethane, benzoylacetone, 4,4,4-trifluoro-1-phenyl-1,3-butanedione, 1,3-indandione, 2-phenyl-1,3-indandione, methyldibenzoylmethane, and, as a support for the suggested pathway of oxidative cleavage, the oxidations of acetoxydibenzoylmethane, acetoxy-4,4,4-trifluoro-1-phenyl-1,3-butanedione, 2-acetoxy-2-phenyl-1,3-indandione, dibenzoylmethanol, 1,3-diphenylpropanetrione, dibenzoyl, phenylglyoxaldehyde, phenylglyoxalic acid, and ninhydrin.

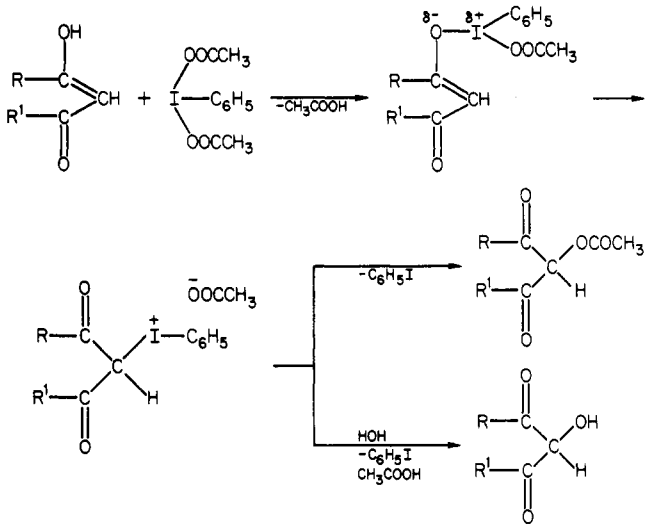
Results and Discussion

The oxidations were conducted for various molar ratios of substrate–PIDA in acetic acid containing water. The reactions proceed at room temperature and, in some cases, are even exothermic. However, in order to increase the rate of reaction, the temperature was maintained at 80–100 °C. Under these conditions, the oxidations of β-diketones with an unsubstituted methylene group at substrate–PIDA molar ratios of 1:1, 1:2, and 1:3, proceeded with CO_2 evolution and gave the corresponding α-acetoxy derivatives and carboxylic acids. When the amount of PIDA was increased, the yields of the α-acetoxy derivatives decreased and the yields of the carboxylic acids increased. At a molar

(1) Podolešov, B. *God. Zb., Prir.-Mat. Fak. Univ. Skopje, Mat. Fiz. Hem.* **1974**, *24*, 51; *Chem. Abstr.* **1975**, *82*, 124993p.
(2) Neiland, O.; Vanag, G. *Dokl. Akad. Nauk SSSR* **1960**, *131*, 1351; *Chem. Abstr.* **1960**, *54*, 21080g.
(3) Mizukami, F.; Ando, M.; Tanaka, T.; Imamura, J. *Bull. Chem. Soc. Jpn.* **1978**, *51*, 335.

0022-3263/84/1949-2644$01.50/0

Scheme I



ratio of 1:4, oxidative decomposition was almost quantitative, and only the carboxylic acids were obtained. Similar oxidations of substituted β-diketones yielded a mixture of the corresponding α-acetoxy derivatives and carboxylic acids (regardless of the substrate–PIDA molar ratio).

These results suggest that the β-diketones undergo acetoxylation and oxidative cleavage via parallel reactions. It seems likely that acetoxylation and oxidative cleavage proceed through *C*-iodonium intermediates which are subject to nucleophilic displacement of iodobenzene. In one case, acetoxylation of the methylene group occurs, and, in another, hydroxylation (with water) of the methylene group occurs (Scheme I).

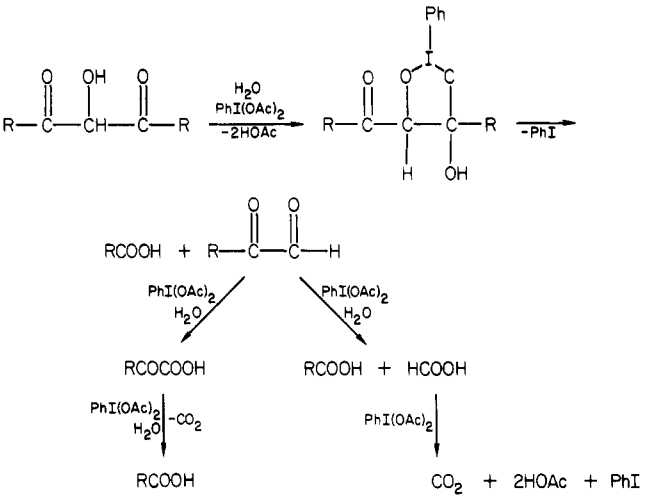
The process of acetoxylation is supported by the isolation and identification of corresponding α-acetoxy derivatives for some of the β-diketones. Our results and those of Neiland demonstrate that acetoxylation does not require the presence of sulfuric acid as Mizukami has claimed.

The isolation and identification of the expected *C*-hydroxy derivatives under the given conditions has not been achieved. Apparently, the *C*-hydroxy derivatives immediately undergo oxidative cleavage. This assumption is supported by a study of the direct and quantitative oxidation of dibenzoylmethanol with PIDA under the same conditions to CO_2 and benzoic acid. The oxidative cleavage of dibenzoylmethanol (and of the *C*-hydroxy derivatives in general) probably proceeds similarly to the well-known oxidative cleavage of glycols.[4-6] The glycol grouping necessary for this kind of cleavage may be provided by hydrated forms of the *C*-hydroxy compounds (Scheme II).

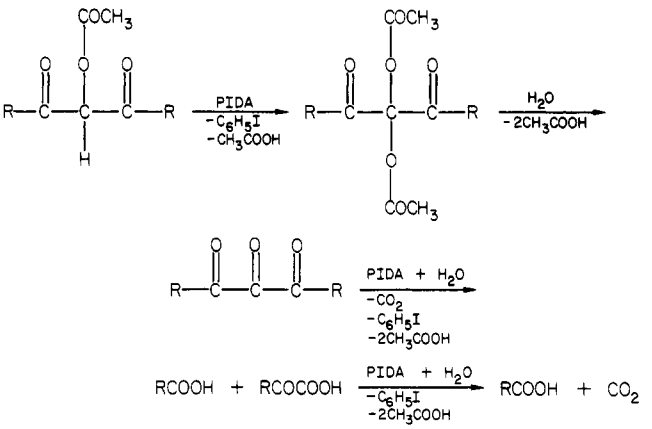
The phenylglyoxaldehyde and phenylglyoxalic acid that should result from such oxidative cleavage were not isolated since they can easily undergo further oxidation. This was proved by the oxidations of authentic phenylglyoxaldehyde and phenylglyoxalic acid with PIDA which give benzoic acid and CO_2. We suggest that phenylglyoxaldehyde is initially oxidized to phenylglyoxalic acid, the hydrate of which undergoes glycolytic cleavage. The oxidation of the aldehyde to the carboxylic acid may follow the same pathway as the hydroxalation of the methylene group of the β-diketones. Alternatively, the oxidation of the aldehyde can also proceed directly to carboxylic acid and formic acid. This formic acid is immediately further oxidized to CO_2 and H_2O.

(4) Griegee, R.; Beucker, H. *Ann. Chim.* **1939**, *541*, 218.
(5) Pausacker, K. *J. Chem. Soc.* **1953**, 107.
(6) Dyall, L.; Pausacker, K. *J. Chem. Soc.* **1958**, 3950.

Scheme II



Scheme III. Oxidative Decomposition of the α-Acetoxy Derivatives



The α-acetoxy derivatives can also undergo oxidative decomposition. We propose that the monoacetoxy derivative is acetoxylated again and that the diacetoxy derivative is subsequently hydrolyzed to the corresponding triketone. The hydrate of the triketone then undergoes glycolytic cleavage to the corresponding carboxylic acids and CO_2 (Scheme III).

This possibility was confirmed by studies of the oxidations of authentic diphenylpropanetrione and ninhydrin, both of which were rapidly and quantitatively decomposed to CO_2 and benzoic acid and phthalic acid, respectively.

The second mechanism is not acceptible for β-diketones with a substituted methylene group since there is no possibility for the formation of a diacetoxy derivative. For β-diketones with a substituted methylene group, such as methyldibenzoylmethane and 2-phenyl-1,3-indandione and which undergo the same parallel reactions, the acetoxy derivatives are end products and cannot be further oxidized. This was confirmed by an attempt to oxidize 2-phenyl-2-acetoxy-1,3-indandione, which, under the given reaction conditions, remained unchanged.

Experimental Section

All the melting points are uncorrected.

The infrared spectra were obtained on a Perkin Elmer 581 spectrophotometer.

The NMR spectra were obtained on a Varian FT 80A spectrometer.

The PIDA was synthesized according to the procedure given by Pausacker.[5]

General Procedure. To 0.01 mol of the β-diketone dissolved in 20–30 mL of acetic acid–water (9:1), 0.01–0.04 mol PIDA are

Table I. Results of the Oxidative Cleavage of β-Diketones and Other Keto Compounds

substrate	product	% yield for mr[d] 1:4	1:3	1:2	1:1	mp, °C	found, % C	H	calcd, % C	H
dibenzoylmethane	benzoic acid	95	68.5	41.5	18	121				
	acetoxydibenzoylmethane		24	22	20	94	72.66	4.70	72.32	4.98
	CO_2									
benzoylacetone	benzoic acid	96	72	43	19	121				
	CO_2									
4,4,4-trifluoro-1-phenyl-1,3-butanedione	benzoic acid	94	70	40	19	121				
	trifluoroacetic acid[a]	94	70	40	19	121				
	CO_2									
	acetoxy-4,4,4-trifluoro-1-phenyl-1,3-butanedione		22	21	18	90–91	52.15	3.60	52.56	3.30
methyldibenzoylmethane	benzoic acid[b]		37	28	21	121				
1,3-indandione	phthalic acid[c]	92	67	35	17	203				
	CO_2									
2-phenyl-1,3-indandione	phthalic acid		38	26	18	203				
	benzoic acid		36	25.5	17	121				
	2-acetoxy-2-phenylindandione		35	28	23	164	71.60	4.31	71.33	4.20
acetoxydibenzoylmethane	benzoic acid		95			121				
	CO_2									
acetoxy-4,4,4-trifluoro-1-phenyl-1,3-butanedione	benzoic acid		95			121				
	trifluoroacetic acid									
	CO_2									
2-acetoxy-2-phenyl-1,3-indandione	unchanged									
dibenzoylmethanol	benzoic acid		97			121				
	CO_2									
1,2-diphenylpropanetrione	benzoic acid	97				121				
	CO_2									
dibenzoyl	benzoic acid				96	121				
phenylglyoxaldehyde	benzoic acid			96		121				
	CO_2									
phenylglyoxalic acid	benzoic acid				96	121				
	CO_2									
ninhydrin	phthalic acid			94		203				
	CO_2									

[a] Determined qualitatively only by gas chromatography with authentic CF_3COOH. [b] Oily product, probably the acetoxy derivative, does not undergo further oxidation. [c] Unidentified solid product. [d] mr = molar ratio.

Table II. IR and ^1H NMR Data for the Acetoxylated Compounds

compound	IR[a](CO, cm^{-1})	NMR[b]
acetoxydibenzoylmethane	1691 (s), 1751 (s)	2.25 (CH_3COO), 6.98 (COCHCO), 7.2–8.1 (C_6H_5)
2-acetoxy-4,4,4-trifluoro-1-phenyl-1,3-butanedione	1690 (s), 1750 (s)	2.1 (CH_3COO), 6.4 (COCHCO), 7.4–8.2 (C_6H_5)
2-acetoxy-2-phenyl-1,3-indandione	1725 (s), 1744 (s)	2.21 (CH_3COO), 7.1–7.5 (C_6H_5), 7.7–8.05 (C_6H_4)

[a] s = strong. [b] In $CDCl_3$.

added. The reaction takes place immediately at room temperature and, in some cases, was exothermic. In order to increase the rate of reaction, the reaction mixture is heated to 80–100 °C for 6 h. For the β-diketones with an unsubstituted methylene group, the reaction proceeds with the evolution of CO_2 (determined as $BaCO_3$; the gas gave a negative reaction for CO with $PdCl_2$ solution). In order to remove the excess PIDA, 1–2 mL of ethyleneglycol are added and the reaction mixture is completely evaporated at reduced pressure. From the dry residue, which is a mixture of the acetoxylated β-diketone and the corresponding carboxylic acid, the carboxylic acids are first separated by extraction with hot water. From this water solution, after several recrystallizations, we identified benzoic acid and phthalic acid. The residue, insoluble in hot water after several recrystallizations, was identified as the corresponding α-acetoxy derivative.

The results of the oxidative cleavage of the β-diketones are given in Table I. The spectroscopic data for the obtained α-acetoxy derivatives are given in Table II.

The same procedure was also used for the oxidation of acetoxydibenzoylmethane, acetoxy-4,4,4-trifluoro-1-phenyl-1,3-butanedione, 2-acetoxy-2-phenyl-1,3-indandione, dibenzoylmethanol, 1,2-diphenylpropanetrione, dibenzoyl, phenylglyoxaldehyde, phenylglyoxalic acid, and ninhydrin. The results are also given in Table I. In the oxidation of formic acid under the same conditions, only CO_2 and H_2O were obtained.

Registry No. Dibenzoylmethane, 120-46-7; benzoylacetone, 93-91-4; 4,4,4-trifluoro-1-phenyl-1,3-butanedione, 326-06-7; methyldibenzoylmethane, 1846-29-3; 1,3-indandione, 606-23-5; 2-phenyl-1,3-indandione, 83-12-5; acetoxydibenzoylmethane, 13054-83-6; 2-acetoxy-4,4,4-trifluoro-1-phenyl-1,3-butanedione, 65921-31-5; 2-acetoxy-2-phenyl-1,3-indandione, 90269-22-0; dibenzoylmethanol, 4720-56-3; 1,3-diphenylpropanetrione, 643-75-4; dibenzoyl, 134-81-6; phenylglyoxaldehyde, 1074-12-0; phenylglyoxalic acid, 611-73-4; ninhydrin, 485-47-2; (diacetoxyiodo)-benzene, 3240-34-4.