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REACTION OF C-ACETYL COMPOUNDS WITH PHENYLIODOSODIACETATE

By the reaction of C-acetyl compounds with phenyliodosodiacetate in acetic acid, corresponding ω-acetoxy-C-acetyl derivatives were obtained.

In aqueous acetic acid, phenyliodosodiacetate effects oxidative cleavage of the C-acetyl compounds and forms the corresponding carboxylic acids in high yield.

Based on these results and the results of oxidative cleavage of ω-acetoxy-C-acetyl and ω-hydroxy-C-acetyl compounds and that of benzoin, possible pathway for this reaction are presented.

In a previous paper[1], we described the oxidation of β-diketones with phenyliodosodiacetate (PIDA). As a continuation of investigations of the properties of polyoxo compounds[2], we have now examined the reactions of C-acetyl compounds with PIDA.

The action of PIDA on C-acetyl compounds has already been investigated by Mizukami[3], Pati[4] and Mahalingam[5] and their coworkers. Mizukami employed anhydrous conditions and obtained acetoxy derivatives as final products. Pati and Mahalingam examined the kinetics of oxidation of ketones in aqueous acetic acid. Other hypervalent iodine compounds such as iodosylbenzene[6] and hydroxy(tosyloxy)iodo benzene[7] have been also used in the reactions with ketones.[10]

We have examined the C-acetyl compounds given in Tables I and II.

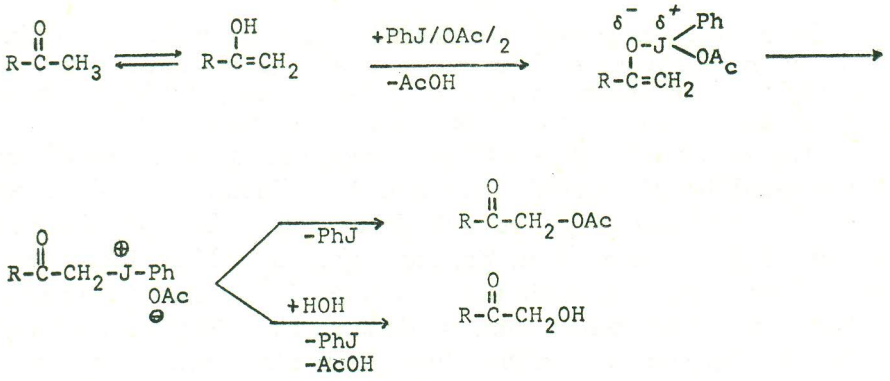
Reactions were conducted in both glacial acetic acid and in aqueous acetic acid at 90—95°C for over 15—20 hrs. At room temperature, no reaction occurs. In glacial acetic acid and with 1 : 1 molar ratios of reactants, only ω-acetoxy-C-acetyl compounds were obtained (Table I), these being identified by elemental, IR and NMR analyses and from their hydrolysis products.

RESULTS AND DISCUSSION

In contrast to the results reported by Mizukami et al.[3], all C-acetyl compounds studies by us gave ω-acetoxy derivatives in high yield and purity.

In aqueous acetic acid under the same conditions and with C-acetyl: PIDA molar ratios of 1 : 4, CO_2 evolution was observed and the carboxylic acids given in Table II were obtained in high yield. With molar ratios of 1 : 1, 1 : 2 and 1 : 3, besides carboxylic acids, the corresponding ω-acetoxy-C-acetyl and ω-hydroxy-C-acetyl compounds were detected.

The acetoxylation reaction probably proceeds through an ω-C-iodonium intermediate. Displacement of iodobenzene from that intermediate with acetate ion as the nucleophile would give ω-acetoxy-C-acetyl derivatives while nucleophile displacement of iodobenzene with water would give ω-hydroxy-C-acetyl derivatives (Scheme I). Under aqueous conditions, the ω-acetoxy-C-acetyl and ω-hydroxy-C-acetyl apparently undergo oxidative cleavage. This assumption is supported by the direct reactions of authentic ω-acetoxy-C-acetyl and ω-hydroxy-C-acetyl compounds with PIDA in aqueous acetic acid (molar ratio 1 : 3) to give CO_2 and the corresponding carboxylic acids.

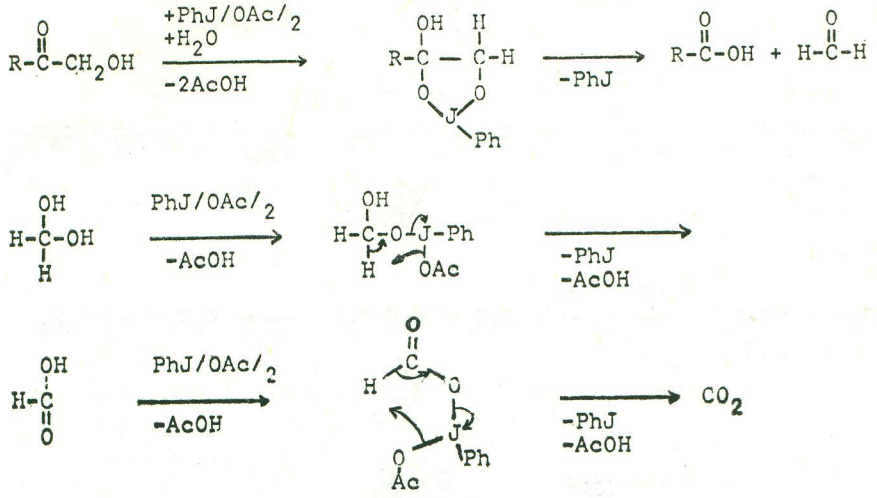


R = C_6H_5-; 4-ClC_6H_4-; 4-BrC_6H_4-; 4-$NO_2C_6H_4$-; 4-$C_6H_5C_6H_4$-; 4-$CH_3OC_6H_4$-; 2-fluorenyl; 3-phenanthryl

Scheme I

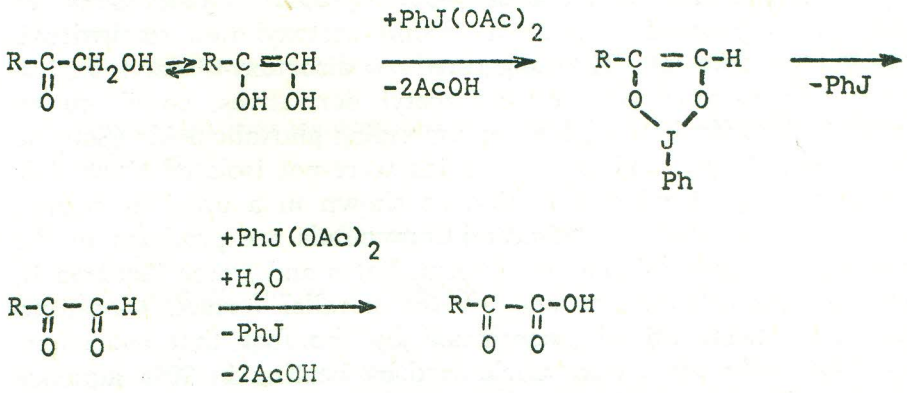
The oxidation of ω-hydroxy-C-acetyl derivatives (Scheme II) with PIDA probably proceeds through a glycol cleavage[8], the

"glycol" being provided by hydration of the ω-hydroxy-C-acetyl compounds. Thus, when ω-hydroxy-C-acetyl compounds were treated with PIDA (1 : 1, 90—95°, 90% acetic acid, 1 hr), the corresponding carboxylic acids were isolated, and formaldehyde was detected as its 2,4-dinitrophenyl hydrazone (Table III). With an excess of PIDA, formaldehyde is oxidized to CO_2, this being confirmed by the direct oxidation of authentic formaldehyde in water solution with PIDA.



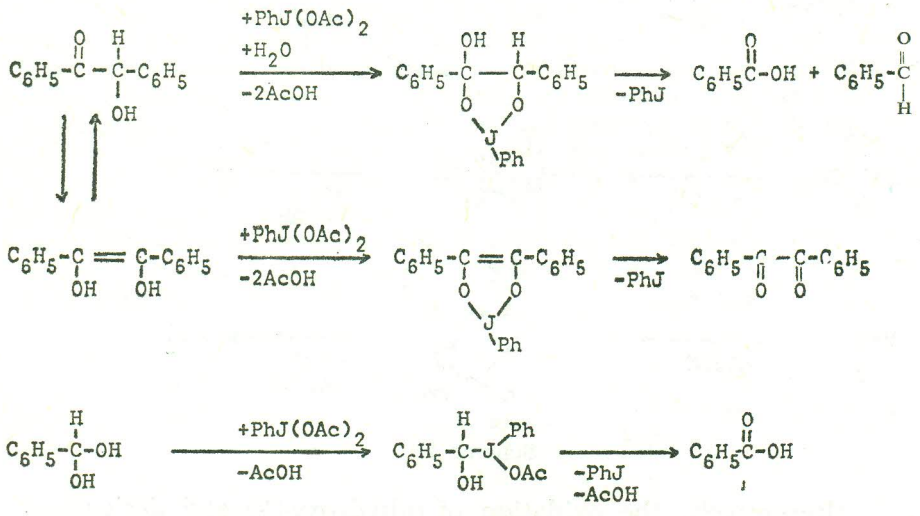
Scheme II

Alternatively, the oxidation of ω-hydroxy-C-acetyl derivatives with PIDA may proceed through the endiol tautomers to give glioxaldehydes and glyoxalic acids (Scheme III).



Scheme III

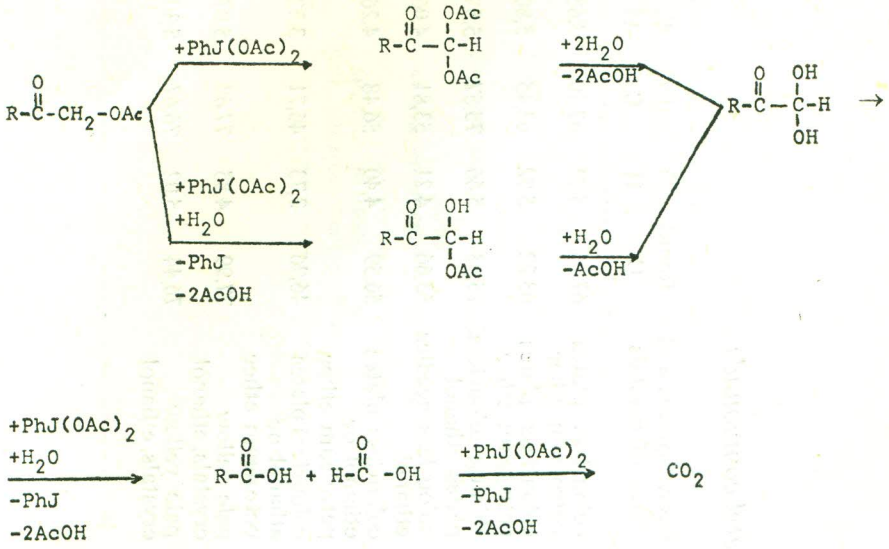
These two modes of oxidation have been confirmed by studies of the oxidation of benzoin (Scheme IV). In aqueous acetic acid with benzoin: PIDA molar ratios of 1 : 1 besides benzoic acid as main product, benzaldehyde and benzyl were obtained. However in a molar ratio 1 : 2 only benzoic acid was obtained. In an excess of PIDA, benzaldehyde and benzyl are oxidized to benzoic acid. This was confirmed by the direct oxidation of authentic benzaldehyde and benzyl with PIDA.



Scheme IV

The oxidative cleavage of ω-acetoxy-C-Acetyl derivatives we suggest to proceed through a second acetoxylation or hydroxilation (Scheme I). The suggested ω,ω-diacetoxy-C-acetyl derivatives and ω-hydroxy-ω-acetoxy-C-acetyl derivatives could subsequently be hydrolized to the corresponding glioxalic acids (Scheme V). Glioxaldehyds and glioxalic acids were not isolated since they easily undergo further oxidation as shown in a previous paper[1].

That the ω-hydroxy-C-acetyl compounds are products in the reaction between C-iodonium intermediates and water (Scheme I), but not hydrolizing products of the parallel formed ω-acetoxy-C-acetyl compounds is confirmed by the fact that ω-acetoxy-C-acetyl compounds were unchanged by heating in 90% aqueous acetic acid at 90—95°C during 15—20 hrs.



Scheme V

The previously obtained results[1] by the reaction of β-diketones with PIDA compared with these of C-acetyl compounds indicate that the oxidative cleavage of the former is faster. This could be explained by the greater activity of the metilen group in β-diketones than the metil group in C-acetyl compounds.

EXPERIMENTAL PART

All the melting points are uncorrected.

The IR spectra were obtained on a Perkin Elmer 581 Spectrophotometer.

The NMR spectra were obtained on Varian FT-80A Spectrometer.

The PIDA was synthetized according to the procedure given by Pausacker.[7]

General procedures

Acetoxylation of C-acetyl compounds

To 0.01 mole of a C-acetyl compound dissolved in 10 ml glacial acetic acid, 0.01 mole of PIDA are added. The reaction mixture is heated at 90—95°C for 15—20 hours, and then evapo-

TABLE I

Results of the acetoxylation of C-acetyl compounds

Substrate	Product	% yield	mp. °C	Recr. solvent and form of crystals	found % C	found % H	calcd. % C	calcd. % H
acetophenone	ω-acetoxy-acetophenone	55,4	52	colourless plates petroleum ether	67,26	5,74	67,40	5,65
4-metoxy-acetophenone	ω-acetoxy-4-metoxy-acetophenone	70	58	colourless plates petroleum ether	63,22	5,92	63,45	5,80
4-phenyl-acetophenone	ω-xydrohy-4-phenil-acetophenone	55	123	shining colourless, plates ethanol	75,68	5,66	75,57	5,55
4-nitro-acetophenone	ω-acetoxy-4-nitro-acetophenone	66	123	colourless needles ethanol	53,66	4,21	53,81	4,06
4-chloro-acetophenone	ω-acetoxy-4-chloro-acetophenone	76	68	colourless plates ethanol or petroleum ether	56,59	4,40	56,48	4,26
4-bromo-acetophenone	ω-acetoxy-4-bromo-acetophenone	75	84	colourless plates ethanol or petroleum ether	46,96	3,73	46,71	3,52
3-acetyl-phenantrene	ω-acetoxy-3-acetyl-phenantrene	51	126	pale yellow crystals, ethanol	77,99	4,85	77,68	5,07
2-acetyl-fluorene	ω-acetoxy-2-acetyl-fluorene	53	149	pale yellow crystals, ethanol	76,44	5,02	76,67	5,30

TABLE Ia

Results of hydrolisis of ω-acetoxy-C-acetyl compounds

Substrate	Product	% yield	mp. °C	Recr. solvent and form of crystals
ω-acetoxy-acetophenone	ω-hydroxy-acetophenone	60	85	colourless plates water
ω-acetoxy-p-metoxy-acetophenone	ω-hydroxy-p-metoxy-acetophenone	60	108	colourless needles water
ω-acetoxy-p-bromo-acetophenone	ω-hydroxy-p-bromo-acetophenone	63	136	colourless needles ethanol water
ω-acetoxy-p-chloro-acetophenone	ω-hydroxy-p-chloro-acetophenone	65	122	colourless crystals ethanol or water

TABLE II

Results of the oxidative cleavage of C-acetyl, ω-C-acetyl and ω-hydroxy compounds

Substrate	Product	% yield	mp. °C	Recr. solvent and form of crystals
acetophenone	benzoic acid; CO_2	70	122	colourless crystals
ω-acetoxy-acetophenone	benzoic acid; CO_2	78		water
ω-hydroxy-acetophenone	benzoic acid; CO_2	81		
4-metoxy-acetophenone	4-metoxy-benzoic acid; CO_2	78	185	colourless needles
ω-acetoxy-4-metoxy-acetophenone	4-metoxy-benzoic acid; CO_2	80		water
ω-hydroxy-4-metoxy-acetophenone	4-metoxy-benzoic acid; CO_2	80		
4-phenil-acetophenone	4-phenil-benzoic acid; CO_2	65	217	colourless crystals
ω-acetoxy-4-phenil-acetophenone	4-phenil-benzoic acid; CO_2	68		ethanol
4-nitro-acetophenone	4-nitro-benzoic acid; CO_2	73	239	pale yellow
ω-acetoxy-4-nitro-acetophenone	4-nitro-benzoic acid; CO_2	75		ethanol or water
ω-hydroxy-4-nitro-acetophenone	4-nitro-benzoic acid; CO_2	75		
4-chloro-acetophenone	4-chloro-benzoic acid; CO_2	84	243	colourless needles
ω-acetoxy-4-chloro-acetophenone	4-chloro-benzoic acid; CO_2	91		
ω-hydroxy-4-chloro-acetophenone	4-chloro-benzoic acid; CO_2	91		
4-bromo-acetophenone	4-bromo-benzoic acid; CO_2	83	250	colourless crystals
ω-acetoxy-4-bromo-acetophenone	4-bromo-benzoic acid; CO_2	90		ethanol
ω-hydroxy-4-bromo-acetophenone	4-bromo-benzoic acid; CO_2	93		
3-acetyl-phenantren	phenantrene-3-carboxylic-acid; CO_2	90	261	pale yellow crystals
ω-acetoxy-3-acetyl-phenantren	phenantrene-3-carboxylic-acid; CO_2	93		ethanol
2-acetyl-fluorene	fluorene-2-carboxylic-acid; CO_2	70	276	colourless needles
ω-acetoxy-2-acetyl-fluorene	fluorene-2-carboxylic-acid; CO_2	75		aceticacid—water

TABLE III

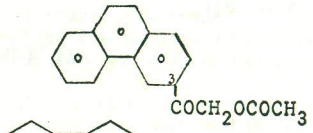
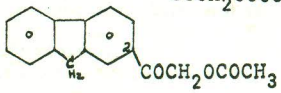
Results of the oxidative cleavage of ω-hydroxy-C-acetyl compounds with PIDA in molar ratio 1 : 1

Substrate	Product	% yield	mp. °C	Recr. solvent and form of crystals
ω-hydroxy-acetophenone	benzoic acid	18	121	colourless crystals
	formaldehyde*	21		water
ω-hydroxy-4-metoxy-acetophenone	4-metoxy benzoic acid	30	185	colourless needles
	formaldehyde	24		water
ω-hydroxy-4-bromo-acetophenone	4-bromo-benzoic acid	41	250	colourless crystals
	formaldehyde	27		ethanol
ω-hydroxy-4-chloro-acetophenone	4-chloro-benzoic acid	35	243	colourless needles
	formaldehyde	26		benzen

* Formaldehyde indentified as formaldehyde 2,4-dinitro-phenyl hidrazone, in form of yellow crystals mp. 155°C.

TABLE IV

IR and ^1H NMR Data for the ω-acetoxy and ω-hydroxy-C-acetyl compounds

Compound	IR[a] ($OH_4C = O$, $C — O$, cm^{-1})	^1H NMR
1	2	3
$C_6H_5COCH_2OCOCH_3$	1750 (vs), 1705 (vs), 1235 (vs), 1215 (vs)	7.20—7.90 (C_6H_5), 5.28— (CH_2O), 2.18 (CH_3CO)
p-$CH_3OC_6H_4COCH_2OCOCH_3$	1735 (vs), 1690 (vs) 1222 (vs)	6.75—8.0 (C_6H_4), 5.25 (OCH_2) 3.9 (OCH_3), 2.2 (CH_3CO)
p-$C_6H_5C_6H_4COCH_2OCOCH_3$	1750, 1741 (vs), 1696 (vs) 1215 (vs)	7.2—8 (C_6H_5—C_6H_4), 5.33 (OCH_2), 2.27 (CH_3CO)
p-$NO_2C_6H_4COCH_2OCOCH_3$	1733((vs); 1687 (vs) 1205 (vs), 1235 (vs)	7.9—8.5 (C_6H_4), 5.3 (CH_2O) 2.2 (CH_3CO)
p-$ClC_5H_4COCH_2OCOCH_3$	1735 (vs), 1690 (vs) 1220 (vs), 1235 (vs)	7.3—7.9 (C_6H_5), 5.26 (CH_2O) 2.21 (CH_3CO)
p-$BrC_6H_4COCH_2OCOCH_3$	1739 (vs), 1688 (vs) 1221 (vs), 1230 (vs)	7.5—7.8 (C_6H_4), 5.25 (CH_2O) 2.2 (CH_3CO)
	1732 (vs), 1692 (vs) 1240 (vs), 1200 (vs)	7.5—9 (Ar), 5.45 (CH_2O) 2.2. (CH_3CO)
	1750 (vs), 1690 (vs) 1230 (vs), 1210 (vs)	7.25—8.1 (Ar), 5.35 (CH_2O) 3.93 (CH_2), 2.18 (CH_3CO)

	2	3
p-$BrC_6H_4COCH_2OH$	3370 (vs), 3420 (vs) 1680 (vs), 1225 (vs)	7,5—7,65 (C_6H_4), 4.5—4.75 (CH_2O), 3.25—3.5 (OH)
p-CH_3O—$C_6H_4COCH_2OH$	3395 (vs), 3420 (vs) 1690 (vs), 1680 (vs) 1240 (vs), 1230 (vs)	6.75—7.95 (C_6H_4), 4.6—4.75 (CH_2O), 3.85 (CH_2O), 3.4—3.6 (OH)
$C_6H_5COCH_2OH$	3400 (vs), 1690 (vs), 1230 (vs)	7.35—8.0 (C_6H_5) 4.5—4.7 (CH_2O) 3.35—3.6 OH)
p-$ClC_6H_4COCH_2OH$		7.5—7.6 (C_6H_4) 4.55—4.7 (CH_2O) 3.25—3.5(OH)

a) KBr, vs — very strong, strotehings

rated under reduced pressure. From the dry residue the resulting ω-acetoxy-C-acetyl derivatives were isolated by recrystallization from suitable solvent.

The results of the acetoxylation of the C-acetyl compounds are given in Table I. The spectroscopic data for the obtained ω-acetoxy-C-acetyl compounds are given in Table IV.

Hydrolysis of ω-acetoxy-C-acetyl compounds

A suspension of 0.005 mole of ω-acetoxy-C-acetyl derivatives and 0.0025 mole of barium carbonate in 100 ml water was refluxed during 3 hours. The solution was filtered hot and the resulting ω-hydroxy-C-acetyl compounds, after cooling, were isolated as colorless crystals. In this way, the hydrolysis of ω-acetoxyacetophenone, ω-acetoxy-p-chloroacetophenone, ω-acetoxy-p-bromoacetophenone, and ω-acetoxy-p-methoxyacetophenone was achieved. The results of the obtained ω-hydroxy-C-acetyl compounds are given in Table Ia. The spectroscopic data of the obtained ω-hydroxy-C-acetyl compounds are given in Table IV.

Oxidative cleavage of C-acetyl compounds

To 0.01 mole of C-acetyl compound dissolved in 10 ml 90% aqueous acetic acid, 0.04 mole PIDA are added. The reaction mixture is heated at 90—95°C for 15—20 hrs. The reaction proceeds with the releasing of CO_2. The end of the releasing of CO_2 indicated the end of the reaction. In order to remove the unreacted PIDA, few drops of ethylenglycol were added and the reaction mixture was completely evaporated at reduced pressure. From the dry residue the corresponding carboxylic acids were obtained in high yield by recrystallization from suitable solvent (Table II). The gas evolved by this reaction was detected as CO_2 in a form of $BaCO_3$. The gas gave negative reaction for CO with $PdCl_2$-solution.

The same procedure was also used for the oxidative cleavage of ω-acetoxy-C-acetyl compounds and ω-hydroxy-C-acetyl compounds with PIDA in molar ratio 1 : 3. The reaction proceeds with CO_2 releasing and as reaction product only carboxylic acids were isolated. The results are given in Table II.

Oxidative cleavage of ω-hydroxy-C-acetyl compounds with PIDA in molar ratio 1 : 1

a. Isolation of carboxylic acid. To 0.01 mole of ω-hydroxy-C-acetyl compounds dissolved in 5 ml of 90% aqueous acetic acid 0.001 mole of PIDA was added. The mixture was kept for

an hour at 90—95°C, and was evaporated in vacuo. From the dry residue corresponding carboxyllic acid was isolated by recrystallization from suitable solvent. In this way by oxidative cleavage of ω-hydroxy-acetophenone, ω-hydroxy-bromoacetophenone, ω-hydroxy-4-chloroacetophenone and ω-hydroxy-4-methoxy-acetophenone, a corresponding carboxylic acid was obtained. The results are given in Table III.

b. Identification of formaldehyde. To 0.001 mole of ω-hydroxy-C-acetyl compounds dissolved in 5 ml of 90% aqueous acetic acid, 0.001 mole of PIDA was added. After heating at 90—95°C for an hour the mixture was diluted with 20 ml water. The mixture was cooled in ice and the supernatant liquid was added to a solution of lukewarm dilute hydrochloric acid that contained 0.2 g of 2,4-dinitro-phenyl hydrazine. The mixture was kept at 70°C for 30 minutes, and after cooling in ice the precipitate was filtered with suction, washed with dilute hydrochloric acid and dried. After recrystallization from ethyl alcohol, yellow crystals of formaldehyde 2,4-dinitrophenylhydrazone with m.p. 155°C was obtained.

In this way, formaldehyde as 2,4-dinitrophenyl-hydrazone was obtained by oxidative cleavage of ω-hydroxy-acetophenone, ω-hydroxy-bromoacetophenone, ω-hydroxy-4-chloroacetophenone and ω-hydroxy-4-methoxy-acetophenone. The yield in % is given in Table III.

The oxidative cleavage of benzoin

To 1.06 g (0.005 mole) of benzoin dissolved in 6 ml of 90% aqueous acetic acid, 1.6 g (0.005 mole) of PIDA was added. The mixture was kept for an hour at 90—95°C. After adding 5 ml of water, the mixture was evaporated in vacuo. In order to remove benzaldehyde from the residue, 10 ml of water was added and evaporation was repeated. From the dry residue (which is a mixture of the benzoic acid, benzyl and unreacted benzoin) the benzoic acid was first separated by extraction with hot water. 0.250 g pure benzoic acid with m.p. 121°C was obtained. From the yellow colored solid (0.450 g) which is undissolved in water, benzyl was isolated in form of quinoxaline derivative as follows: the yellow solid was dissolved in 5 ml alcohol and 0.3 g of o-phenylenediamine was added. The solution was warmed for 30 minutes on a water bath. After cooling, the mixture was diluted with water, and the separated solid was recrystallized from alcohol. 0.27 g (19%) 2,3-diphenylquinoxaline as yellow needles m.p. 122°C was obtained.

From the combined destilate obtained by the vacuum evaporation of the reaction mixture, the benzaldehyde was identified as p-nitrophenylhydrazone.

Identification of benzaldehyde as p-nitrophenylhydrazone. To the combined destilate obtained by the vacuum evaporation of the reaction mixture, 0.3 g of p-nitrophenylhydrazine was added and the solution was warmed to 70°C. After 30 minutes the preparation was diluted with 40 ml of water and kept in ice for 3 hours. The izolated crude product after recrystallization from ethyl alcohol yielded 0.230 g (16%) of benzaldehyde-p-nitrophenylhydrazone with m.p. 191°C.

Oxidation of benzaldehyde with PIDA

A. In the presence of water. To 0.530 g (0.005 mole) of benzaldehyde dissolved in 5 ml of 90% aqueous acetic acid, 1,6 g (0.005 mole) PIDA are added. The mixture was heated at 90—95°C for 3 hours. In order to remove unreacted PIDA, 0.5 ml of ethylen glycol is added and the reaction mixture is evaporated at reduced pressure. From the dry residue, after recrystallization from water, 0.4 g of benzoic acid of m.p. 120°C was obtained.

B. In the absence of water. When the oxidation of benzaldehyde with PIDA was carried out in acetic acid—acetic anhydryde, no benzoic acid was obtained.

Oxidation of formaldehyde hydrate

To a solution of 5 ml 90% aqueous acetic acid containing 0.24 g (0.01 mole) formaldehyde hydrate, 3.2 g (0.01 mole) PIDA was added. The reaction mixture was heated at 90—95°C. During the reaction of 5 hrs only CO_2 was released as a reaction product.

The oxidative cleavage of benzyl

The cleavage of benzyl and the isolation of the cleavage product, were carried out in the same way as described for the cleavage of benzoin. From 1.05 g (0.005 mole) of benzyl 0.5 g of benzoic acid of m.p. 121°C was obtained.

REFERENCES

1. B. Podolešov, *J. Org. Chem.*, 1984, 49, 2644.
2. B. Podolešov, *God. Zb., Prir.-Mat. Fak. Univ. Skopje*, Mat. Fiz. Hem., 1974, 24, 51 (Chem. Abstr, 1975, 82 124,993 p).
3. F. Mizukami, M. Ando, T. Tanaka, J. Imamura, *Bull. Chem. Soc. Jpn.*, 1978, 51, 335,
4. C. S. Pati, B. R. Dev, *Indian J. Chem. Sect. A.* 1979, 18 A, 262.

5. V. Mahalingam, N. Vencatasubramanian, *Indian J. Chem., Sect. B*, 1979, 18 B. (1) 95.
6. R. M. Moriarty, H. Hu, *Tetrahedron Lett.*, 1981, 22, 1283.
7. G. F. Koser et al., *J. Org. Chem.*, 1982, 47, 2487.
8. R. Griegee, H. Bieucker, *Ann. Chem.*, 1939, 541, 218.
9. Pausacker, K., *J. Chem. Soc.*, 1953, 107.
10. A. Varvoglis, *Synthesis*, 1984, № 9, 709.

БОЈАН ПОДОЛЕШОВ

РЕАКЦИЈА НА С-АЦЕТИЛ СОЕДИНЕНИЈА СО ФЕНИЛЈОДОЗОДИАЦЕТАТ

(Резиме)

При реакцијата на С-ацетил соединенијата со фенилјодозодиацетат во глацијална оцетна киселина, се добиваат соодветни ω-ацетокси-С-ацетил соединенија.

Ако оваа реакција се изведува во оцетна киселина — вода, С-ацетил соединенијата претрпуваат разложување до соодветни карбоксилни киселини.

Врз основа на овие резултати и резултатите од оксидацијата на ω-хидрокси-С-ацетил, ω-ацетокси-С-ацетил соединенија и на бензоинот предложен е механизам на оваа реакција.

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