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APPLICATION OF OZONOLYSIS TO THE STUDY OF SUBSTITUTED DERIVATIVES OF VULPINIC ACID

CONSTITUTION OF PINASTRIC AND ISOPINASTRIC ACIDS

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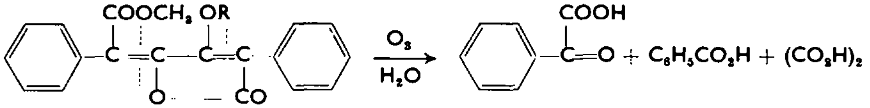
Abstract—Ozonolysis of vulpinic acid (V) yields the methyl ester of benzoylformic acid as the neutral product indicating the possibility of identifying the ester half of the molecule. In this reaction pinastric acid and isopinastric acid gave methyl benzoylformate and methyl *p*-methoxybenzoylformate respectively and these results confirm the revised structures I and II assigned to them as position isomers.[9]

THE final stage in the elucidation of the structure of unsymmetrical derivatives of vulpinic acid is the location of the substituent group in either of the two phenyl rings with reference to the carbomethoxyl group. The earlier methods employed for this purpose were (a) reduction with zinc and acetic acid[7,8] and (b) condensation with *o*-phenylenediamine.[1–6] It was observed that the isomers pinastric acid (I) and isopinastric acid (II) yielded the same product on condensation with *o*-phenylenediamine.[4,5] The method is, therefore, unsuitable for this study.[9] Though reduction with zinc and glacial acetic acid is suitable, the synthesis of authentic samples of degradation products for comparison is tedious.[9] The need for a simple, yet dependable method is provided by ozonolysis.

In the ozonolysis of vulpinic acid methyl ether (III), Karrer *et al.*[10] subjected the ozonide to hydrolytic decomposition and obtained oxalic acid, benzoic acid and probably benzoylformic acid (IV).



III R = CH_3
V R = H

IV

In a preliminary study, the ozonolysis of vulpinic acid (V) yielded methyl benzoylformate (VI), benzoylformic acid (IV), benzoic acid and oxalic acid. If the ozonization is prolonged, the yield of benzoylformic acid is decreased and that of benzoic

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[1] A. Schönberg and A. Sina, *J. Chem. Soc.* 601 (1946).

[2] O. P. Mittal and T. R. Seshadri, *J. Chem. Soc.* 1734 (1956).

[3] O. P. Mittal and T. R. Seshadri, *J. Chem. Soc.* 3053 (1955).

[4] P. K. Grover and T. R. Seshadri, *Tetrahedron* **6**, 312 (1959).

[5] P. K. Grover and T. R. Seshadri, *Tetrahedron* **4**, 105 (1958).

[6] P. K. Grover and T. R. Seshadri, *J. Chem. Soc.* 2134 (1960).

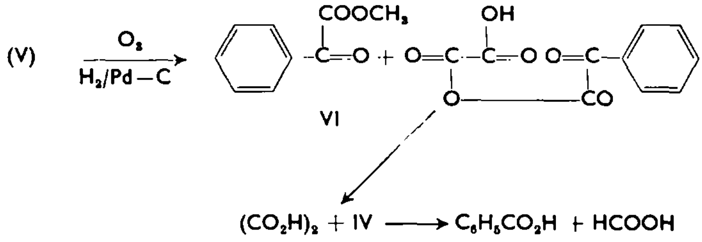
[7] M. Asano and Y. Kameda, *Ber. Dtsch. Chem. Ges.* **67B**, 1522 (1934).

[8] M. Asano and Y. Kameda, *Ber. Dtsch. Chem. Ges.* **68B**, 1565 (1935).

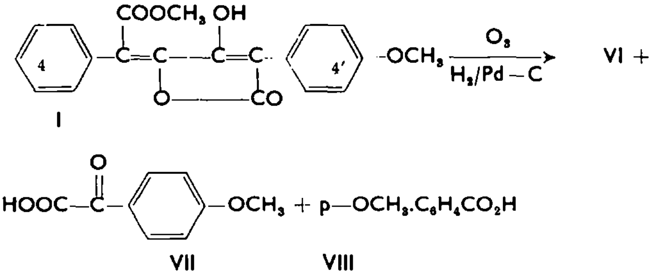
[9] S. C. Agarwal and T. R. Seshadri, *Indian J. Chem.*, in press.

[10] P. Karrer, K. A. Gehrckens and W. Heuss, *Helv. Chim. Acta* **9**, 446 (1926).

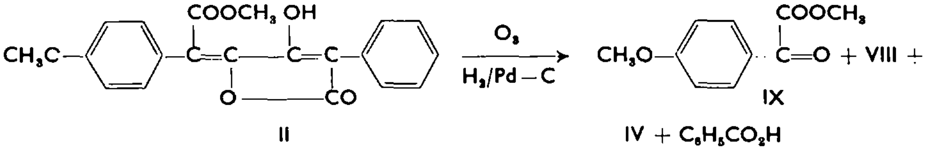
acid increased due to oxidative decomposition. The formation of methyl benzoylformate suggests that the method is capable of distinguishing between the two phenyl groups and can be applied to locate the position of the nuclear methoxyl group in pinastric and isopinastric acids.



In the above reaction pinastric acid (I) gave methyl benzoylformate (VI) as the neutral fragment and *p*-methoxybenzoylformic (VII) and anisic (VIII) acids as the acidic products. The identity of the ester was proved by comparison with an authentic sample and also by alkaline degradation whereby a mixture of benzoylformic acid and benzoic acid were formed.



Ozonolysis of isopinastric acid (II) furnished methyl *p*-methoxybenzoylformate (IX) in the neutral fraction and anisic acid (VIII), benzoylformic acid (IV) and benzoic acid in the acid fraction. Compounds IX and IV are obviously the primary fission products which give rise to others by further changes.



The above results are in agreement with the structure of pinastric acid[7–9] (I) and of isopinastric acid[5] (II) proposed earlier and support the conclusion that they are position isomers.

EXPERIMENTAL

Ozonolysis of vulpinic acid (V)

A stream of ozonized oxygen (3%; 150 ml/min) was bubbled through a solution of vulpinic acid (methyl pulvinate: 1·0 g) in dry ethyl acetate (40 ml) maintained at ca. −15° till the yellow colour almost faded (30 min). The cold solution was transferred to a hydrogenation vessel containing a suspension of palladized charcoal catalyst (5% Pd, 0·8 g) in dry ethyl acetate (20 ml) and shaken with H_2 at atm press. till the absorption ceased (15 min). The catalyst was filtered off and the filtrate extracted repeatedly with $NaHCO_3$ aq. (5%; acid fraction A) and the residual ethyl acetate solution (B) contained the neutral fraction

Acid fraction. The $NaHCO_3$ extract (A) was acidified with cooling and extracted with ether (5 × 75 ml). The dried ether extract on evaporation yielded a sticky residue which was macerated with ice-cold water (2 ml) and filtered (filtrate C); the residue after drying crystallized from light pet ether (60–80°) as colourless flakes, m.p. 120–121° alone or mixed with benzoic acid. The aqueous filtrate (C) was extracted exhaustively with ether and ether recovered from the extract; the oily residue gave a yellow 2,4-dinitrophenylhydrazone which crystallized from aqueous alcohol as yellow shining needles, m.p. 194–196° (dec), undepressed on admixture with an authentic sample of 2,4-dinitrophenylhydrazone of benzoylformic acid.

In another experiment, after the decomposition of the ozonide, ethyl acetate was removed (red press) and the residue taken up in ether. The ether solution was washed successively with distilled water (aqueous extract D) and $NaHCO_3$ aq. (5%). The residual ether solution contained the neutral fraction. The extract (D) was evaporated and the residue was found to be oxalic acid by its characteristic properties. The $NaHCO_3$ extract gave the same results, as described in the above experiment.

Neutral fraction. The residual ethyl acetate solution (B) was dried ($MgSO_4$) and the solvent removed (red. press.). The oily residue did not crystallize and was converted into the oxime by refluxing with hydroxylamine hydrochloride, abs ethanol and pyridine. On working up, it gave a semisolid mass which was extracted repeatedly by refluxing with light petroleum. The extract on concentration and cooling, deposited colourless needles which after recrystallization from water melted at 138–139° alone or mixed with an authentic sample of methyl benzoylformate oxime.

Ozonolysis of pinastric acid (I)

A solution of pinastric acid (methyl 4′-methoxy-pulvinate; 0·74 g) in dry ethyl acetate (175 ml) was ozonized for ca. 55 min as mentioned in the case of vulpinic acid. Fractionation of the ethyl acetate solution gave the following:

Acid fraction. This was obtained as a brownish semisolid, was boiled with water (4 ml; animal charcoal) and filtered. The filtrate on cooling deposited colourless needles, m.p. 181–182°, alone or mixed with anisic acid. The mother liquor was extracted with ether and the extract evaporated; the semisolid residue was examined as follows: (i) It gave an orange 2,4-dinitrophenylhydrazone (from alcohol), m.p. 195–197° (dec.) alone or on admixture with 2,4-dinitrophenylhydrazone of *p*-methoxybenzoylformic acid. (ii) It gave a semicarbazone which crystallized from methanol as colourless tiny needles, m.p. 198–199° (dec.); mixed m.p. with an authentic sample of semicarbazone of *p*-methoxybenzoylformic acid was undepressed. (iii) It was warmed with a few drops of conc H_2SO_4 when it turned brown with the evolution of CO ; the other product was found to be anisic acid. (iv) When subjected to vacuum sublimation, no sublimate was obtained up to 120° proving the absence of benzoic acid.

Neutral fraction. Evaporation of the residual ethyl acetate solution (red. press.) gave a sweet smelling yellow oil. Its IR spectrum was similar to that of methyl benzoylformate; IR (CCl_4): 3450 (w), 2985 (m), 2326 (w), 1961 (w), 1898 (w), 1727 (s), 1681 (s), 1588 (s), 1497 (m), 1441 (s), 1419 (m), 1370 (w), 1250 (s) cm^{-1}. Its identity was confirmed as follows: (i) It was converted into the oxime which crystallized from benzene–light petroleum (charcoal) as tiny colourless needles, m.p. 124–125°. It was shown to be the oxime of methyl benzoylformate as follows: (a) Its IR spectra in $CHCl_3$ and KBr were indentical in all details with those of an authentic sample; IR (KBr): 3334 (s), 1739 (s), 1431 (m), 1405 (m), 1398 (m) cm^{-1}; (b) Elemental analysis agreed (Found: C, 60·6; H, 5·4. Calc. for $C_9H_9NO_3$: C, 60·3; H, 5·0%); (c) it was different from the oxime of methyl *p*-methoxybenzoylformate, m.p. 132–134°, the mixed m.p. being depressed to 100–105°. (ii) The 2,4-dinitrophenylhydrazone crystallized from ethanol (charcoal) as yellow needles, m.p. 171–173° (sinters at 161°) alone or mixed with 2,4-dinitrophenylhydrazone of methyl benzoylformate. (iii) When heated (15 min) with KOH aq. (10%) at 100°, it gave benzoylformic acid and benzoic acid.

Ozonolysis of isopinastric acid (II)

A solution of isopinastric acid (methyl 4-methoxy-pulvinate; 0·37 g) in dry ethyl acetate (35 ml) was ozonized as before. The ethyl acetate solution on fractionation gave the following:

Acid fraction. This was obtained as an oil; it was treated with ice cold water (5 ml) and filtered. (a) The residue was dried (P_2O_5) and sublimed in vacuum at 80°; the sublimate crystallized from water as colourless needles, m.p. 120–121° alone or mixed with benzoic acid while the unsublimed part crystallized from water as colourless needles, m.p. 180–182° undepressed by anisic acid. (b) The filtrate was extracted with ether (4 × 40 ml) and ether evaporated; the oily residue gave 2,4-dinitrophenylhydrazone of benzoylformic acid, m.p. and mixed m.p. 193–195° (dec).

Neutral fraction. The residual ethyl acetate solution was dried ($MgSO_4$) and the solvent distilled (red. press.). The IR spectrum of the oily residue was similar to that of methyl *p*-methoxybenzoylformate; IR (CCl_4): 3040 (m), 1739 (m), 1684 (m), 1600 (m), 1506 (m), 1468 (w), 1418 (m), 1307 (w), 1261 (m) cm^{-1}. Its identity was further confirmed as follows: (i) It was converted into the oxime which crystallized from light petroleum as colourless needles, m.p. 81–83°. Its identity as the oxime of methyl *p*-methoxybenzoylformate was shown by (a) its IR spectrum which was similar to that of authentic sample; IR (Nujol): 3400 (s), 1709 (s), 1610 (m), 1513 (m), 1326 (s), 1250 (s) cm^{-1}, (b) elemental analysis (Found: C, 57·3; H, 5·4. $C_{10}H_{11}O_4N$ requires: C, 57·4; H, 5·3%) and (c) non-identity with methyl benzoylformate oxime, the mixed m.p. being depressed considerably. (ii) The other portion of the crude neutral product was heated with KOH aq. (10%) at 100°. The solution was cooled and acidified; the precipitated brown solid crystallized from hot water (charcoal) as colourless needles, m.p. 179–181° undepressed by anisic acid.