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ON THE REACTION OF ORSELLINIC ACID CARBANION WITH PYRYLIUM SALTS

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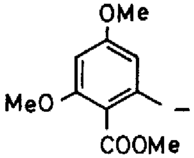
Summary From the reaction of methyldimethyl orsellinate anion 1 with the pyrylium salt 2 the isocoumarin 5 was isolated in addition to the pyrones 3 and 4 Reaction intermediates could be trapped as pyridines 6 and 7

Staunton et al. recently described highly convergent syntheses of various naphthopyrons, biphenyls and anthracenes related to natural products, starting from orsellinic acid and triacetic acid lactone as polyketide synthons [1-4] Although the conversion of the starting materials as well as the yields seem to be moderate in these reactions, they have certainly an advantage over alternate multistep routes

We thus used the reaction of the methyl orsellinate anion 1 with pyrylium salt 2 for the preparation of a sample of γ-pyron 3 During the work up we observed in addition to 3 and the corresponding α-pyron 4 a third major product characterized by a bright blue fluorescence on t l c upon irradiation at 366 nm Dry column chromatography [5] afforded



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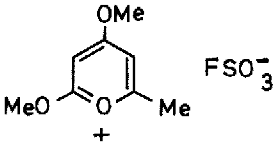

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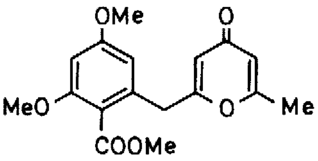

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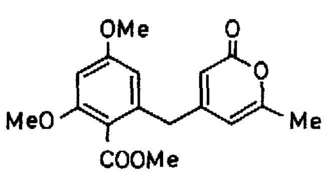

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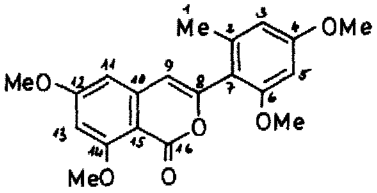

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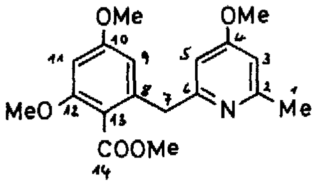

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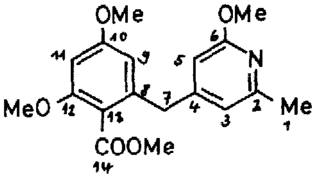

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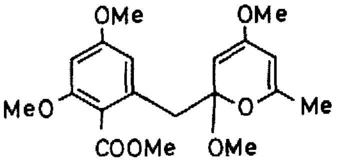

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colourless crystals, m p 168^{0} in 17 % yield [6] They were identified by molecular composition, $C_{20}H_{20}O_6$ [7], i.r spectrum (1720, 1660 cm^{-1}) and ^{1}H- and ^{13}C n.m r spectra (Table 1 and 2) as the isocoumarin 5 We assume that the formation of 5 is connected to the main side reaction in the system which is the proton transfer from 2 and possibly from some reaction products to 1 leading to the recovery of large amounts of methyl orsellinate During the reaction the electrophilic methyl orsellinate undergoes condensation with the remaining anion 1 to form eventually 5 Interestingly Hauser et al [8] recently observed a similar self condensation of ortho-toluate carbanions to isocoumarins With the orsellinic acid derivative 1 no dimer was observed however. In a biosynthetic view the isocoumarine 5 represents the cyclisation product of an octaacetic acid chain with a mode of folding not observed among natural products until now

Since we were also interested in the structure of possible reaction intermediates we quenched the reaction mixture of 1 and 2 with an excess of saturated ammonium chloride solution at 0^{0}C followed by immediate extraction with ethyl acetate In this case we isolated in addition to 5 two new isomeric compounds, 6 (22 %, m p 90^{0}) and 7 (2 %, b p. 140^{0}, 10^{-6}mbar)

Table 1 ^{13}C-Chemical shifts and ^{13}C - ^{1}H coupling constants of 5, 6, 7 and methyl dimethyl orsellinate 9 in $CDCl_3$ 9)

	5			6	7	9
C	δ(ppm)		J_{CH}(Hz)	δ(ppm)		
1	20.3	qd	128, 5	24.3	24.1	19.9
2	140.2	q	6	159.0^{a}	156.1	138.3
3	106.6	dq	160, 5	107.0^{b}	116.7	106.8
4	165.3^{a}	m		166.6	151.9	161.4
5	96.1	dd	160; 5	106.4^{b}	107.2	96.2
6	159.2^{b}	p	4	161.0^{a}	164.1	158.3
7	103.4	m		42.3	38.7	116.5
8	152.6	d	6	139.7	139.5	168.7
9	108.2	dd	166; 6	106.8	107.0	
10	142.4	s		161.6	161.7	
11	100.1	dd	161, 4	97.1	97.0	
12	161.3^{a}	m		158.3	158.5	
13	98.6	dd	160; 6	116.8	116.8	
14	163.3^{b}	p	4	168.4	168.0	
15	115.5	q	5			
16	160.0	s				
OMe	55.3	q	144	52.0	52.1	51.9
	55.6	q	144	54.9	53.3	55.3
	55.8	q	144	55.4	55.4	55.9
	56.3	q	144	56.0	56.0	

a, b may be interchanged

by dry column chromatography 5) having the molecular composition $C_{18}H_{21}NO_5$ 7)

6 and 7 gave almost identical i.r. spectra (1715 cm^{-1} in $CHCl_3$) and very similar n.m.r. spectra (Table 1, 2), which indicate the presence of an orsellinic acid and a pyron moiety. From the combined spectral data pyridine structures related to the pyrones 3 and 4 can easily be deduced. A rigorous proof of 6 to be the γ-methoxy pyridine isomer was obtained from the proton coupled ^{13}C n.m.r. spectrum showing vicinal coupling of carbon C-7 to H-5 (2.5 Hz) and H-9 (4.5 Hz) but not to H-3. Since one methoxy group of 2 is retained in 6 and 7 we assume that the addition products of 1 and 2, e.g. 8, are present in the reaction medium. They are either hydrolysed to 3 and 4 during the acidic work up or trapped by ammonia at pH 8 to give the pyridines 6 and 7.

Table 2 ^{1}H - N m r spectral data of 5, 6 and 7 in $CDCl_3$ 9) (δ in ppm)

	H-1	H-3	H-5	H-7	H-9	H-11	H-13	OMe
5	δ 2 28 s	6 36 sbr	6.34 sbr		6 31 s	6.48 d 2Hz	6 40 d 2Hz	3 74,3 82,3.90,3 98
6	δ 2 49 s	6.40 d 2Hz	6 45 d 2Hz	4 05 sbr	6.37 d 2Hz	6.31 d 2Hz		3 74,3.76,3 81,3 82
7	δ 2 38 s	6 50 sbr	6 29 sbr	3.83 sbr	6 33 d 2Hz	6 21 d 2Hz		3.76,3 78,3 81,3 88

Acknowledgement

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References and notes

1) F.J Leeper and J Staunton, J C S Chem Comm , 1978, 406

2) G E Evans, F J Leeper, J A Murphy and J Staunton, J C S Chem. Comm , 1979, 205

3) F J Leeper and J Staunton, J. C S Chem Comm , 1979, 206

4) G E Evans, M J Garson, D A Griffin, F.J Leeper and J Staunton in "Further Perspectives in Organic Chemistry", Ciba Foundation Symposium 53, Elsevier Amsterdam (1978)

5) Column dimensions 180 cm long, 2 cm in diameter, Kieselgel 60 Merck, eluent diethylether/methanol 99 1

6) Yield of isolated pure compound based on unrecovered starting material

7) All new compounds gave correct elemental analyses and the expected high resolution mass spectral data.

8) F.M Hauser, R.P Rhee, S Prasanna, S M Weinreb and J H Dodd, Synthesis 1980, 72.

9) Proton n m r. spectra were run on a Varian XL-100 or Bruker WH-270, carbon spectra on a Varian CFT-20 or XL-100 instrument, assignments are based on homo- and heteronuclear decoupling experiments

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