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A STRAIGHTFORWARD SYNTHESIS OF PYRENOPHORIN

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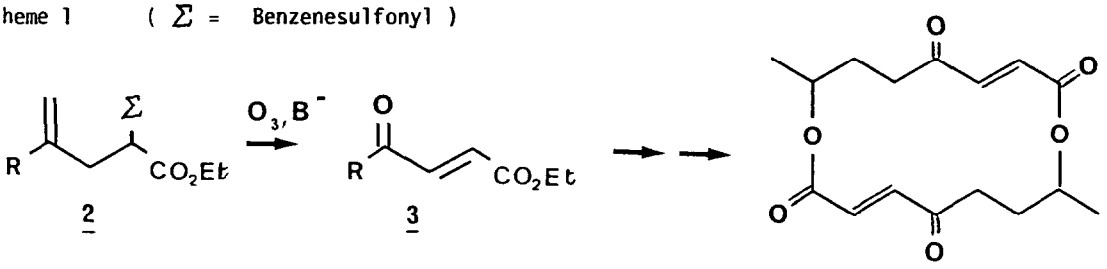
A b s t r a c t : *A very simple method to prepare 4-oxo-2 alkenoates and an application to the synthesis of a natural fungicidal, pyrenophorin, 1, are described.*

The γ-keto acrylate synthon is common to many biologically interesting natural products [1d]. Most of the numerous [1,2] preparations of this unit involve relatively delicate, mainly carbanionic, chemistry.

As part of a programm aiming at designing efficient fungicidals related to 1 we have examined the possibility to prepare such compounds by a more convenient procedure summarized below (scheme 1).

Scheme 1 (Σ = Benzenesulfonyl)



2 3 PYRENOPHORIN 1

2a, R = CH_3

2b, R = CH_3-CO-CH_2-CH_2

In a model experiment, the ester 2a [3] (R=methyl) was treated by ozone in methylene chloride then triethylamine at -78°C, according to the Isobe's procedure [4], to afford the γ-acetyl acrylate 3a (R=Me) in an almost quantitative yield [5].

The suitability of the process now established we turned to the preparation of

pyrenophorin, 1, and hence, of the suitable ester 2b.

Treatment of 2a by acetone in a slurry of cupric and manganic acetates according to the Heiba's procedure [6] at 80°C in acetic acid for 20 hours afforded a mixture of only two components with quite distinct Rf in T.L.C. (5% ethyl acetate in hexane) and therefore easy to separate by a fast flash - chromatography on silica gel with a gradient of ethyl acetate in hexane : the unreacted ester 2a (41%) was eluted first then the more polar homologated ester 2b (27% yield), free of isomers as evidenced by NMR spectroscopy [7a]. Cupric acetate was essential to get the observed [8] selectivity.

Classical chemical manipulations involving :

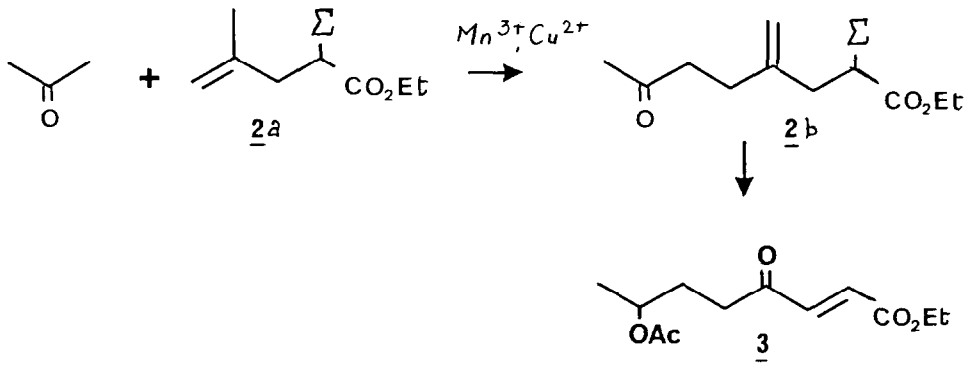
a - sodium borohydride reduction of the keto group ;

b - acetylation by acetic anhydride in pyridine with a trace of 4-dimethylaminopyridine [1b]

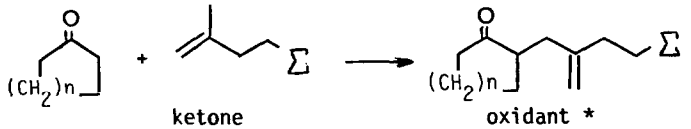
c - ozonolysis then treatment by triethylamine as above afforded the keto-ester 3 [7b] in a 64% overall yield from 2b (scheme 2).

Since 3 has been converted into pyrenophorin 1 [1] this constitutes a formal synthesis of 1 .

Scheme 2



The homologation of an isopentenyl residue described here could of course be useful to prepare vinylketones. We have examined this possibility :



	ketone	oxidant *	yield (%)
1	n = 1	A	30
2	"	B	20
3	n = 2	A	54
4	"	B	45

* A : 2 molar équivalents of $Cu(OAc)_2$ and $Mn(OAc)_3$;

B : 2 molar equivalents of $Cu(OAc)_2$ plus 0.2 molar equivalent of $Mn(OAc)_3$, plus 2 molar equivalents of PbO_2.

Results clearly show the feasibility of such a way [9]. Furthermore, the possibility to use the manganic acetate in a catalytic amount was demonstrated (entry 2 and 4).

In summary, a formal synthesis of pyrenophorin has been established. The key step- i.e. selective oxidative addition of a ketone to an isopentenyl sulfone- appears as general and hencecould be applied elsewhere. Some applications are under current investigation and will be published in due course.

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REFERENCES

(1) a) R.S. Mali, M. Pohmakotr, B. Weidmann and D. Seebach, Liebigs Ann. Chem., 1981, 2272, and references therein,
b) P.G. Baraldi, A. Barco, S. Benetti, M. Moroder, G.P. Pollini and D. Simoni, J. Org. Chem, 1983, 48, 1297,
c) J.W. Labadie, D. Tueting, J.K. Stille, J. Org. Chem., 1983, 48, 4634,
d) G.S. Bates, S. Ramaswamy, Can. J. Chem., 1983, 61, 2466,
e) F. Derguini and G. Linstrumelle, submitted to this journal,
f) W. Dumont, C. Vermeyen and A. Krief, Tetrahedron Lett., 1984, 25, 2883

(2) a) T.A. Hase, A. Ourika and C. Holmberg, J. Org. Chem., 1981, 46, 3137,
b) P.A. Bartlett, J. Am. Chem. Soc., 1976, 28, 3305 and ref. therein,
c) H.M. Walton, J. Org. Chem., 1957, 22, 308.

(3) Easily prepared by alkylation of ethyl α-phenylsulfonyl acetate by methallyl chloride according to W.C. Ashley, R.H. Shriner, J. Am. Chem. Soc., 1932, 54, 4410 ; m.p. 35°C (ether - hexane) ; NMR : (80MHz, $CDCl_3$) : 1,1 (t,J=8Hz, 3H) ; 1,7 (bs, 3H) ; 2,7 (d, J=8Hz, 2H) ; 3,9-4,3 (m,3H) ; 4,7 (bs, 2H) ; 7,2-7,9 (m,5H).

(4) M. Isobe, M. Kitamura and T. Goto, J. Am. Chem. Soc., 1982, 104, 4997

(5) I.R. (film) : 1680, 1720 cm^{-1} ; NMR (80MHz, $CDCl_3$) : 1,3 (t, J=8Hz, 3H) ; 2,4 (s,3H) ; 4,2 (q, J=8Hz, 2H) ; 6,5-6,9 (2d, J=16Hz,2H)

(6) E.I. Heiba, R.M. Dessau, J. Org. Chem., 1974, 39, 3456 ; J. Am. Chem. Soc., 1971, 93 524 ;
general conditions : the sulfone (10 mmol) and the ketone (50 mmol) were added to a slurry of manganic acetate (20 mmol) and cupric acetate (20 mmol) in acetic acid (30 ml) containing some potassium acetate (50 mmol) and previously made anhydrous by treatment with the required amount of acetic anhydride. The mixture was stirred at 80°c under nitrogen for 20 hours, poured into water and extracted with methylene chlo -

ride. Flash-chromatography on silica gel of the dried extract was performed using a gradient of ethyl acetate in petroleum ether.
Rf. in T.L.C. (5% of ethyl acetate in hexane)of the starting material and of the condensation product were respectively about 0,7-0,8 and 0,1 - 0,15

(7) a) IR (film) : 1720 cm^{-1} ; NMR ($CDCl_3$) : 1-1,5 (m,3H) ; 1,9 - 2,8 (m,9H) ; 3,9-4,2 (m,3H) ; 4,7 (bs, 2H) ; 7,2-7,9 (m,5H) ;
b) IR (film) :1680, 1720 cm^{-1} ; NMR (80MHz, $CDCl_3$) : 1,2 (t, 3H) ; 1,6-2,2 (m, 5H) ; 2,4-2,8 (m,2H) ; 4,2 (q, 2H) ; 6,5 (d,J=16Hz; 1H) ; 7 (d,J=16Hz, 1H).

(8) The unique role of cupric acetate on the selectivity of these additions has already been pointed out : F.J. Quillin, M. Wood, J. Chem. Soc. Perkin 1, 1976, 1763

(9) Ozonolysis of these substrates followed by basic treatment to get vinylic diketones is presently studied.

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