The Pyrethrins and Related Compounds. Part XI.[1] Synthesis of Insecticidal Esters of 4-Hydroxycyclopent-2-enones (Nor-rethrins)

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2-Benzylcyclopent-2-enones, obtained by rearrangement of the corresponding benzylidenecyclopentanones, are brominated by *N*-bromosuccinimide at the 4-position; the products upon treatment with silver chrysanthemate give new analogues of the natural pyrethrins.

ESTERS in which the alkadienyl side-chain of the natural insecticide, pyrethrin I,[2] [I; R^1 = (+)-*trans*-chrysanthemoxy, $R^2 = CH^{c}{=}CH{-}CH{=}CH_2$] is replaced by an allyl [3] ($R^2 = CH{=}CH_2$) or a benzyl [4] (R^2 = Ph) group still retain considerable insecticidal activity; with the benzyl side-chain, toxicity to insects is greatly enhanced by substituting the 3-furylmethyl nucleus for the methyloxocyclopentenyl ring to give esters such as [II; R = (+)-*trans*-chrysanthemoxy].[5] Since the 3-furylmethyl ring has no substituent sterically equivalent to the 2-methyl group of the natural oxocyclopentenyl compounds, we synthesised benzyloxocyclopentenyl chrysanthemates (III) to indicate whether the methyl

[1] Part X, M. Elliott, N. F. Janes, and K. A. Jeffs, *Pesticide Sci.*, 1970, **1**, 49.

[2] For a review of pyrethrin chemistry, see L. Crombie and M. Elliott, *Fortschr., Chem. org. Naturstoffe*, 1961, **19**, 121.

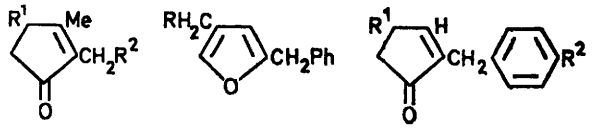
[3] M. S. Schechter, N. Green, and F. B. La Forge, *J. Amer. Chem. Soc.*, 1949, **71**, 3165.

[4] Y.-L. Chen and W. F. Barthel, *J. Amer. Chem. Soc.*, 1953, **75**, 4287.

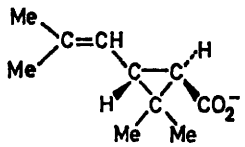
[5] M. Elliott, A. W. Farnham, N. F. Janes, P. H. Needham, and B. C. Pearson, *Nature*, 1967, **213**, 493.

group in pyrethrin I was important for toxicity. This account of chemical aspects of the work is prompted by a recent discussion [6] of benzylcyclopentenones and related compounds.

Whereas McWatt *et al.*[6] could demonstrate no tendency for 2-benzylidenecyclopentanone to rearrange to 2-benzylcyclopentenone (III; $R^1 = R^2 = H$), Conia and Amice [7] earlier achieved this isomerisation in polyphosphoric acid at 150°. We found that reaction was complete even at 90° in this medium, but that on a larger scale much resin (70—90%) was frequently obtained. Of many alternative reagents tested (see Experimental section) dry hydrogen chloride in refluxing methoxyethanol was most satisfactory and convenient on a large scale, because isolation of the product did not involve extraction from excess of acid. This procedure gave satisfactory yields of benzyl-, *p*-chlorobenzyl-, and *p*-methylbenzyl-cyclopentenones (III; $R^1 = H$). The



(I) (II) (III)
R^2=H,Cl,or Me



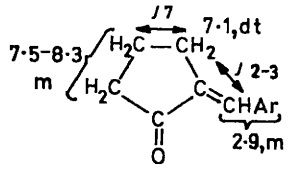
(+)-*trans*-chrysanthemoxy

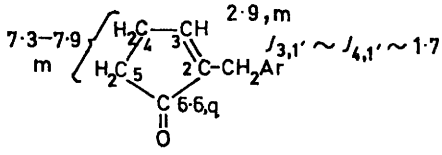
n.m.r. spectra of the *exo*- and *endo*-isomers agreed with the structures assigned (see below). The benzylic protons appeared at τ 6·6 as a quartet (not a doublet *cf.* ref. 7) through coupling with the methylene group at C-4 and the olefinic proton. When coupling with the olefinic proton was removed by irradiation at τ 2·9 this quartet changed to a triplet, confirming the interpretation and indicating that the allylic ($J_{3.1'}$) and homoallylic ($J_{4.1'}$) couplings are approximately equal.

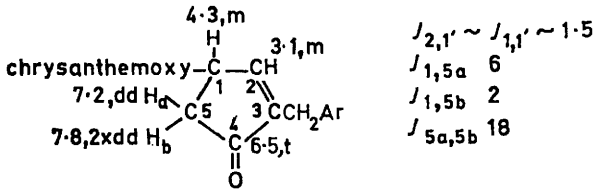
Like 2-alkyl-3-methylcyclopentenones,[8] the 2-benzylcyclopentenones (III; $R^1 = H$) prepared here reacted with *N*-bromosuccinimide to give 4-bromo-compounds, which, although too unstable to be isolated, reacted satisfactorily *in situ* with silver chrysanthemate to give 3-benzyl-4-oxocyclopent-2-enyl (+)-*trans*-chrysanthemates (III; R^1 = (+)-*trans*-chrysanthemoxy). This behaviour of the benzyl substituted compounds contrasted with the reaction of 2-alkenyl-3-methylcyclopentenones where side-chain substitution, rearrangement, and polymerisation blocked the *N*-bromosuccinimide route to 3-alkenyl-2-methyl-4-oxocyclopent-2-enyl chrysanthemates.[8]

[6] I. McWatt, D. Phillips, and G. R. Proctor, *J. Chem. Soc.* (*C*), 1970, 593.
[7] J. M. Conia and P. Amice, *Bull. Soc. chim. France*, 1968, 3327.

Evidence for substitution at C-4 of the benzylcyclopentenones and not at other positions, such as the 1′-CH_2 group, was provided by the n.m.r. spectra of the







derived chrysanthemates, for the side-chain benzylic CH_2 signal at τ 6·6 persisted, and was a triplet, through approximately equal coupling to the olefinic proton and to the *single* proton now remaining on the attacked carbon, now numbered C-1. The origins of both splittings that produced this triplet were confirmed by spin decoupling, when irradiation at either τ 3·1 (olefinic H) or at 4·3 (1-H) collapsed it to a doublet, in each case with a coupling constant of *ca.* 1·5 Hz. Attempts to measure the value of $J_{1.1'}$ in the natural pyrethrins are frustrated by the broadness of the corresponding peak for the methylene group at C_1'. Additional evidence that the products made here are formed by attack at C-4, and are therefore closely related to the natural pyrethrins, is that the peaks at τ 4·3, 7·2, and 7·8 appear in the same place and with the same coupling constants as the signals from the three alicyclic protons (at C-1 and C-5) in the natural pyrethrins.[9] The signal at τ 7·8 showed additional complexity because the product was a mixture of two diastereoisomeric esters from a racemic alcohol and an optically active acid. The situation is similar to that observed in (±)-jasmolin I, and other synthetic pyrethroids,[9] where the upfield 5-H signal is more complex than in the natural, stereochemically pure, compounds.

The benzyl-substituted esters synthesised here (conveniently called nor-rethrins, *cf.* Harper [10]) have considerable insecticidal activity. Thus, 3-benzyl-4-oxocyclopent-2-enyl (+)-*trans*-chrysanthemate is approximately 3 times as toxic as pyrethrin I [11] to a normal

[8] L. Crombie, M. Elliott, and S. H. Harper, *J. Chem. Soc.*, 1950, 971.
[9] A. F. Bramwell, L. Crombie, P. Hemesley, G. Pattenden, M. Elliott, and N. F. Janes, *Tetrahedron*, 1969, **25**, 1727.
[10] S. H. Harper, *Chem. and Ind.*, 1949, 636.
[11] M. Elliott and N. F. Janes, *Chem. and Ind.*, 1969, 270.

strain of houseflies,[12] and has significant knockdown action and response to synergists. Therefore, the methyl group on the oxocyclopentenyl ring of the natural esters is probably not essential for insecticidal activity.

EXPERIMENTAL

N.m.r. spectra were determined on a Perkin-Elmer R10 spectrometer, with spin-decoupling accessory, for dilute solutions in carbon tetrachloride with tetramethylsilane as internal standard; the J values quoted refer to the observed separations between appropriate lines. All compounds were homogeneous by g.l.c. (Varian Aerograph 1200; 5 ft × $\frac{1}{8}$ in stainless-steel column; 5% QF1 on chromosorb W).

2-Benzylcyclopent-2-enone.—To 2-benzylidenecyclopentanone [13] [τ 2·4—2·9 (6H, m, C_6H_5 + $-CH=$) 7·1 (2H, dt, 3-CH_2, J 7, 2 Hz) 7·5—8·3 (4H, m, $4CH_2$ + $5CH_2$)] (152 g) in boiling 2-methoxyethanol (1·5 l), was added dropwise 2-methoxyethanol (100 ml) previously saturated at 20° with hydrogen chloride; the mixture was heated under reflux for 2 hr. Distillation of the reaction mixture, at 10 mmHg (to remove solvent) then at 0·1 mmHg (Vigreux column) gave 2-benzylcyclopent-2-enone (65·3 g, 43%), b.p. 130—140°/0·1 mmHg, n_D^{20} 1·5630, τ 2·8 (5H, m, C_6H_5) 3·0 (1H, m, =CH) 6·6 (q, 2H, $PhCH_2$, J 1·7 Hz) 7·3—7·9 (4H, m, $4CH_2$ + $5CH_2$) [Conia and Amice [7] give τ 4·0 (5H, m, C_6H_5), 2·90 (1H, m, =CH) and 6·65 [2H, (!), d $PhCH_2$, J 1·5 Hz] for the product (50% yield) by isomerisation in polyphosphoric acid].

Acid-catalysed Rearrangements of 2-Benzylidenecyclopentanone.—The following reagents and conditions were investigated (g.l.c. analysis) (*a*) Polyphosphoric acid—rearrangement complete at 90°, but product contaminated by various amounts of resin. (*b*) Catalytic amount of polyphosphoric acid in hot diglyme—no rearrangement. (*c*) Aqueous hydrochloric acid—resin only. (*d*) Iodine—no rearrangement, hot or cold. (*e*) Toluene-*p*-sulphonic acid in boiling benzene or methanol—no rearrangement. (*f*) Aqueous hydrobromic acid—reaction, but not required product. (*g*) Dry hydrogen chloride in warm acetic acid, or in diglyme—rearrangement, but with much resin. In methanol, rearrangement always incomplete. (*h*) Aqueous hydrochloric acid in 2-methoxyethanol—resin + product. (*i*) Dry hydrogen chloride in 2-methoxyethanol at 20° (saturated solution)—resin + product. (*j*) Dry hydrogen chloride in boiling 2-methoxyethanol (130°)—rearrangement incomplete because hydrogen chloride lost from solution. Successful when hydrogen chloride continually replaced (see above). Hassner and Mead,[14] used dry hydrogen chloride in cyclohexanol at 60—65° for a 5-substituted benzylidenecyclohexanone.

(±)-3-*Benzyl*-4-*oxocyclopent*-2-*enyl* (+)-trans-*Chrysanthemate*.—2-Benzylcyclopent-2-enone (8·0 g) and *N*-bromosuccinimide (8·0 g, recrystallised) in carbon tetrachloride (50 ml) were boiled under reflux until reaction was just complete (disappearance of the *N*-bromosuccinimide). The mixture was cooled, filtered, and heated under reflux with dry silver chrysanthemate [15] (12·0 g) for 5 h. After filtration, hexane (100 ml) was added and the solution was shaken with 2N-sodium hydroxide (2 × 50 ml) and saturated brine (50 ml), and was then dried (Na_2SO_4) and evaporated at reduced pressure. Distillation gave the *ester* (3·8 g, 19%), b.p. 178—186°/0·001 mmHg, n_D^{20} 1·5400 (Found: C, 78·2; H, 7·6. $C_{22}H_{26}O_3$ requires C, 78·1; H, 7·7%); τ 2·6—2·9 (5H, m, C_6H_5), 3·1 (1H, m, $-CH=$), 4·3 (1H, m, 1-H) 6·5 (2H, t, $PhCH_2$, J 1·5 Hz, 7·2 (1H, dd, one 5-H, J 18, 6Hz) 7·8 (1H, 2 × dd, other 5-H, J 18, 2 Hz) (oxocyclopentenyl signals) and at 5·1 (1H, broad d) 8·0(1H, dd), 8·3 (6H, s) 8·7 (1H, d, 8·8 (3H, s), and 8·9 (3H, s) similar to those in other chrysanthemate esters.[9]

2-p-*Chlorobenzylidenecyclopentanone* (cf. *ref.* 13).—Cyclopentanone (19·2 g) and *p*-chlorobenzaldehyde (10·55 g) were added dropwise during 1½ h to sodium hydroxide (4·0 g) in water (150 ml); the mixture was stirred at 20° for 4 h and then neutralised with conc. hydrochloric acid. An ether extract of this mixture was washed with aqueous sodium carbonate and saturated brine and was then dried (Na_2SO_4) and distilled to give a fraction, b.p. 163—165°/0·1 mmHg (4·8 g, 30%). Recrystallisation from pentane gave the *ketone* m.p. 78—80° (Found: C, 69·6; H, 5·3; Cl, 16·9. $C_{12}H_{11}ClO$ requires C, 69·7; H, 5·4; Cl, 17·2%); τ 2·7(4H, m, C_6H_4), 2·9 (1H, t, $-CH=$), 7·1 (2H, dt, 3 CH_2, $J_{3,4}$ 7 Hz, $J_{3,1'}$ 3 Hz), 7·5—8·2 (4H, m, $4CH_2$ + $5CH_2$).

2-(p-*Chlorobenzyl*)-*cyclopent*-2-*enone*.—This *ketone* was prepared from 2-(*p*-chlorobenzylidene)cyclopentanone (48·6 g) using HCl–2-methoxyethanol as above (27·3 g, 56%) and had b.p. 100—106°/0·1 mmHg, n_D^{20} 1·5698 (Found: C, 70·2; H, 4·8; Cl, 17·5) τ 2·6—3·0 (5H, m, C_6H_4 + $-CH=$) 6·6 (2H, q, $ArCH_2$, J 1·6 Hz) 7·3—7·8 (4H, m, $4CH_2$ + $5CH_2$).

(±)-3-(p-*Chlorobenzyl*)-4-*oxocyclopent*-3-*enyl* (+)-trans-*Chrysanthemate*.—Reaction of 2-(*p*-chlorobenzyl)cyclopent-2-enone (4·14 g) and *N*-bromosuccinimide (3·56 g) and then silver (+)-*trans*-chrysanthemate (5·5 g), gave the *ester* (1·6 g, 19%), b.p. 180—195°/0·01 mmHg, n_D^{20} 1·5498 (Found: C, 71·1; H, 6·7; Cl, 9·6. $C_{22}H_{25}ClO_3$ requires C, 70·9; H, 6·8; Cl, 9·5%); τ 2·5—3·1 (5H, m, C_6H_4 + $-CH=$), 4·3 (1H, m, 1-H), 6·6 (2H, t, $ArCH_2$, J 1·5 Hz), 7·2 (1H, dd, one 5-H, J 6, 18 Hz), 7·7 (1H, 2 × dd, other 5-H, J 2, 18 Hz), (oxocyclopentenyl) and 5·1 (1H, broad d), 8·0 (1H, dd), 8·3 (6H, s), 8·7 (1H, d), 8·8 (3H, s) and 8·9 (3H, s) chrysanthemoxy).

2-(p-*Methylbenzylidene*)*cyclopentanone*.— Cyclopentanone (101 g) and *p*-methylbenzaldehyde (72 g) condensed as above (*cf.* ref. 13), to give 2-(*p*-methylbenzylidene)cyclopentanone, m.p. 63—68° (lit.,[15] m.p. 62—63°), b.p. 124—127°/0·01 mmHg (Found: C, 83·4; H, 7·6. Calc. for $C_{13}H_{14}O$: C, 83·8; H, 7·6%); τ 2·5—2·9 (5H, m, C_6H_4 + $-CH=$), 7·1 (2H, dt, $3CH_2$, J 7, 2·5 Hz) 7·7 (3H, s, $ArCH_3$), and 7·6—8·2 (4H, m, $4CH_2$ + $5CH_2$).

2-(p-*Methylbenzyl*)*cyclopent*-2-*enone*.—Rearrangement of the above product with hydrogen chloride in 2-methoxyethanol gave 2-(*p*-methylbenzyl)cyclopent-2-enone (33%), b.p. 89—91°/0·1 mmHg, n_D^{20} 1·5520, (Found: C, 83·6; H, 7·6%); τ 3·1 (5H, m, C_6H_4 + $=CH-$), 6·7 (2H, q, $ArCH_2$, J 1·7 Hz), 7·7 (3H, s, $ArCH_3$), and 7·4—7·9 (4H, m, $4CH_2$ + $5CH_2$).

(±)-3-(p-*Methylbenzyl*)-4-*oxocyclopent*-2-*enyl* (+)-trans-*Chrysanthemate*.—2-*p*-Methylbenzylcyclopent-2-enone (3·72

[12] A. W. Farnham, personal communication.
[13] A. P. Phillips and J. Mentha, *J. Amer. Chem. Soc.*, 1956, **78**, 140.
[14] A. Hassner and T. C. Mead, *Tetrahedron*, 1964, 2201.
[15] A. Maccione and E. Marongui, *Ann. Chim.* (*Italy*), 1958, **48**, 557.

g) with *N*-bromosuccinimide (3·56 g) and then silver (+)-*trans*-chrysanthemate (5·5 g) gave the *ester* (1·0 g, 15%), b.p. 176—194°/0·01 mmHg, n_D^{20} 1·5395 (Found: C, 77·9; H, 8·0. $C_{23}H_{28}O_3$ requires C, 78·4; H, 8·0%); τ 2·7—3·1 (5H, m, C_6H_4 + $-CH=$), 4·3 (1H, m, 4-H), 6·6 (2H, broad s, $ArCH_2$), 7·2 (1H, dd, one 5-H, *J* 6, 18 Hz) 7·7 (4H, m, $ArCH_3$ + other 5-H) (oxocyclopentenyl) and at 5·1 (1H, broad d), 8·0 (1H, dd), 8·3 (6H, s), 8·7 (1H, d) 8·8 (3H, s) and 8·9 (3H, s) (chrysanthemoxy).

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