# 116. *Preparation of 3-Alkylchromones. Effect of Substitution on the Reactivity of the 2-Methyl group in Chromones.*

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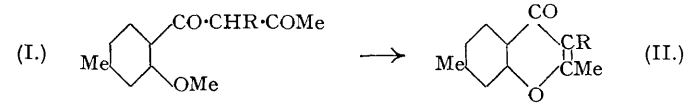
The method of Bloch and Kostanecki has been used in the preparation of a number of 3-alkyl-2-methylchromones.

2-*Methoxy*-4-*methylbenzoylacetone* (I, R = H) and a number of its α-alkyl derivatives (I, R = Me, Et, *n*-Pr, *n*-Bu, *n*-amyl, and $CH_2Ph$) have been converted into the corresponding *chromones* (II) by boiling hydriodic acid, in yields varying from 83% in the case of (I, R = H) to 66% in the case of (I, R = $CH_2Ph$) (cf. Bloch and Kostanecki, *Ber.*, 1900, **33**, 471, 1998; Kostanecki and Lloyd, *ibid.*, 1901, **34**, 2942). In all the 2-methylchromones (II) thus produced, the methyl group is reactive and condenses with aromatic aldehydes to give *styryl* derivatives. Thus substitution of alkyl groups in positions 3 and 7 does not affect the usual reactivity of the 2-methyl group (cf. Chakravarti, *J. Indian Chem. Soc.*, 1931, **8**, 25; Heilbron, J., 1934, 1311).




In the case of the *benzoyl* derivative of (I, R = COPh) the reaction leads to 7-methylflavone, thus showing that the acetyl group is eliminated in preference to the benzoyl group.

## Experimental.

2-*Methoxy*-4-*methylbenzoylacetone*.—2-Methoxy-4-methylacetophenone (16·4 g.; 1 mol.) was dissolved in pure ethyl acetate (26·5 g.; 3 mols.), sodium (2·3 g.; 1 mol.) added, and the mixture cooled in ice with occasional shaking. The thick brown broth was left in the ice-box overnight, ice then added, the sodium salt dissolved in cold water, and the solution acidified with the required amount of acetic acid. The oil which separated was extracted in ether and shaken with cold 5% sodium hydroxide solution. The alkaline extract on treatment with carbon dioxide gave a crystalline mass, which was washed with water and recrystallised from alcohol, forming yellowish plates of 2-*methoxy*-4-*methylbenzoylacetone*, m. p. 52° (Found: C, 69·8; H, 7·0. $C_{12}H_{14}O_3$ requires C, 69·9; H, 6·85%).

2 : 7-*Dimethylchromone* (cf. Wittig, *Annalen*, 1926, **446**, 155).—2-Methoxy-4-methylbenzoylacetone (10·6 g.) was boiled with hydriodic acid (40 c.c., *d* 1·96) for 3 hours, and the mixture then poured on ice (100 g.). The oil that separated and soon solidified was dissolved in ether, and the solution washed successively with sodium bisulphite, 5% sodium carbonate and 2% sodium hydroxide solutions. After drying over sodium sulphate, the ether was distilled, and the chromone crystallised from light petroleum (b. p. 80—90°), forming colourless needles, m. p. 98°. Yield, 7·2 g. (83%) (Found: C, 75·6; H, 5·7. Calc. for $C_{11}H_{10}O_2$: C, 75·85; H, 5·8%).

4′-*Methoxy*-2-*styryl*-7-*methylchromone*.—A solution of 2 : 7-dimethylchromone (1·74 g.; 1 mol.) and anisaldehyde (1·36 g.; 1 mol.) in absolute alcohol (10 c.c.) was cooled in ice, sodium ethoxide solution (0·23 g. of sodium in 20 c.c. of absolute alcohol) added, and the mixture left in the ice-box for 24 hours. The brownish-yellow mass was collected, washed with water containing a few drops of acetic acid, and crystallised from light petroleum (b. p. 80—90°), giving small yellow plates of 4′-*methoxy*-2-*styryl*-7-*methylchromone*, m. p. 150° (Found: C, 77·8; H, 5·5. $C_{19}H_{16}O_3$ requires C, 78·05; H, 5·5%).

α-2-*Methoxy*-4-*methylbenzoyl*-α-*methylacetone*.—2-Methoxy-4-methylbenzoylacetone (20·6 g.) was dissolved in absolute alcohol (60 c.c.), and sodium ethoxide solution (2·3 g. of sodium in 40 c.c. of absolute alcohol) added, followed after 10 minutes by methyl iodide (20 g.); the mixture was refluxed until it was neutral to litmus (about 20 mins.). The solution was filtered, alcohol and the excess of methyl iodide distilled off, and the residual oil distilled under diminished pressure. α-2-*Methoxy*-4-*methylbenzoyl*-α-*methylacetone* was obtained as a thick yellow oil, b. p. 190—192°/20 mm. (Found: C, 70·7; H, 7·2. $C_{13}H_{16}O_3$ requires C, 70·9; H, 7·3%).

2 : 3 : 7-*Trimethylchromone*.—This chromone (Robertson, Waters, and Jones, J., 1932, 1681) was prepared in the general way described above, from α-2-methoxy-4-methylbenzoyl-α-methylacetone (11 g.). Yield, 7·3 g. (78%). Recrystallised from petrol, it formed colourless needles, m. p. 89° (Found: C, 76·5; H, 6.4. Calc.: C, 76·6; H, 6·4%).

4′-*Methoxy*-2-*styryl*-3 : 7-*dimethylchromone*, prepared from 2 : 3 : 7-trimethylchromone (1·88 g.), crystallised from alcohol in long, yellow, silky needles, m. p. 123° (Found: C, 78·2; H, 6·0. $C_{20}H_{18}O_3$ requires C, 78·4; H, 5·9%).

α-2-*Methoxy*-4-*methylbenzoyl*-α-*ethylacetone* was obtained as a thick yellow oil, b. p. 197—200°/20 mm. (Found: C, 71·3; H, 7·8. $C_{14}H_{18}O_3$ requires C, 71·75; H, 7·75%).

2 : 7-*Dimethyl*-3-*ethylchromone*, obtained as a liquid by Robertson, Waters, and Jones (*loc. cit.*), was prepared by the general method described above from α-2-methoxy-4-methylbenzoyl-α-ethylacetone (11·7 g.). After removal of the ether a reddish oil was obtained (7·8 g.), which was distilled; the portion, b. p. 300—305°, solidified on cooling and crystallised from light petroleum (b. p. 30—50°) in small colourless needles, m. p. 51°; yield, 78% (Found: C, 77·0; H, 7·15. Calc.: C, 77·2; H, 7·0%).

4′-*Methoxy*-2-*styryl*-7-*methyl*-3-*ethylchromone*, prepared from 2 : 7-dimethyl-3-ethylchromone (2 g.), separated from acetic acid in yellow crystals, m. p. 114° (Found: C, 78·6; H, 6·25. $C_{21}H_{20}O_3$ requires C, 78·7; H, 6·3%).

α-2-*Methoxy*-4-*methylbenzoyl*-α-n-*propylacetone*.—This and the following alkyl diketones could not be obtained by the method used for the methyl analogue. The sodium salt precipitated from the alcoholic solution of the diketone by the addition of sodium ethoxide solution was therefore collected, washed with absolute alcohol, dried in a desiccator, and suspended in a large excess of *n*-propyl iodide and the mixture was refluxed until it was neutral to litmus. After filtration and distillation of the excess of propyl iodide the residual oil was fractionated under diminished pressure; the fraction, b. p. 206—210°/20 mm., consisted mainly of α-2-*methoxy*-4-*methylbenzoyl*-α-n-*propylacetone* (Found: C, 72·2; H, 8·0. $C_{15}H_{20}O_3$ requires C, 72·5; H, 8·1%).

2 : 7-*Dimethyl*-3-n-*propylchromone* was prepared from α-2-methoxy-4-methylbenzoyl-α-*n*-propylacetone (12·4 g.). The viscous oil (7·6 g.) obtained crystallised from light petroleum in colourless needles, m. p. 56—57°. Yield, 71% (Found: C, 77·5; H, 7·35. $C_{14}H_{16}O_2$ requires C, 77·7; H, 7·5%).

4′-*Nitro*-2-*styryl*-7-*methyl*-3-n-*propylchromone*, prepared from 2 : 7-dimethyl-3-*n*-propylchromone (2·2 g.) and 4-nitrobenzaldehyde (1·5 g.), crystallised from acetic acid in small yellow plates, m. p. 176—177° (Found: C, 71·8; H, 5·4; N, 4·0. $C_{21}H_{19}O_4N$ requires C, 72·2; H, 5·5; N, 4·0%).

α-2-*Methoxy*-4-*methylbenzoyl*-α-n-*butylacetone*, a thick yellow oil, b. p. 207—210°/10 mm. (Found : C, 73·1; H, 8·6. $C_{16}H_{22}O_3$ requires C, 73·2; H, 8·4%), was converted into 2 : 7-dimethyl-3-*n*-butylchromone, a viscous reddish oil (yield, 73%), which was identified as its styryl derivative, 4′-*nitro*-2-*styryl*-7-*methyl*-3-n-*butylchromone*; this crystallised from acetic acid in long, yellow, silky needles, m. p. 168—170° (Found : C, 72·45; H, 5·75; N, 3·9. $C_{22}H_{21}O_4N$ requires C, 72·7; H, 5·8; N, 3·8%).

α-2-*Methoxy*-4-*methylbenzoyl*-α-n-*amylacetone*, a yellow thick oil, b. p. 215—220°/10 mm. (Found : C, 73·9; H, 8·9. $C_{17}H_{24}O_3$ requires C, 73·9; H, 8·8%), was converted into 2 : 7-dimethyl-3-*n*-amylchromone (yield, 72%), a viscous reddish oil identified in the form of 4′-*nitro*-2-*styryl*-7-*methyl*-3-n-*amylchromone*, which crystallised from benzene–light petroleum in yellow needles, m. p. 173—174° (Found : C, 73·7; H, 6·12; N, 3·8. $C_{23}H_{23}O_4N$ requires C, 73·2; H, 6·15; N, 3·7%).

α-2-*Methoxy*-4-*methylbenzoyl*-α-*benzylacetone*.—The dry sodium salt of the diketone was suspended in dry benzene and refluxed with benzyl bromide until the mixture was neutral to litmus. After removal of sodium bromide by filtration and of benzene by distillation the residual oil solidified on cooling. It crystallised from light petroleum (b. p. 50—60°) in long colourless needles, m. p. 67—68° (Found : C, 77·3; H, 7·0. $C_{19}H_{20}O_3$ requires C, 77·0; H, 6·8%).

3-*Benzyl*-2 : 7-*dimethylchromone*, prepared from α-2-methoxy-4-methylbenzoyl-α-benzylacetone (14·8 g.), crystallised from benzene–light petroleum in colourless needles, m. p. 95°. Yield, 66% (Found : C, 81·8; H, 6·0. $C_{18}H_{16}O_2$ requires C, 81·8; H, 6·1%).

4′-*Methoxy*-2-*styryl*-3-*benzyl*-7-*methylchromone* crystallised from alcohol in yellow needles, m. p. 176° (Found : C, 81·4; H, 5·9. $C_{26}H_{22}O_3$ requires C, 81·6; H, 5·8%).

α-*Benzoyl*-α-2-*methoxy*-4-*methylbenzoylacetone*.—To a solution of 20·6 g. of 2-methoxy-4-methylbenzoylacetone in 75 c.c. of absolute alcohol, cooled in ice, 50 c.c. of sodium ethoxide solution (4·6 g. of sodium) and 12 c.c. of benzoyl chloride were alternately added in ten successive portions, the flask being removed from the ice for 5 minutes after each addition. After 12 hours ice-cold water was added, and the solution acidified with acetic acid. The thick oil which separated was taken up in ether and shaken with cold 5% sodium hydroxide solution, the benzoyl derivative, being more acidic than the original diketone, dissolving first in the alkali. The alkaline solution was acidified with acetic acid and the oil formed was taken up in ether. The ethereal solution was left overnight with anhydrous sodium sulphate. A portion of the compound crystallised; it was filtered off together with the sodium sulphate, from which it was separated by water. After crystallisation from light petroleum colourless crystals were obtained, m. p. 141—148°. From the ethereal solution a mixture of a solid and an oil was obtained. The solid, crystallised from light petroleum, had m. p. 137—139°. Neither solid gave a colour with ferric chloride, but the liquid gave a violet colour. It seems that the liquid is the enolic form and the two solids are enantiomorphic keto-forms of α-*benzoyl*-α-2-*methoxy*-4-*methylbenzoylacetone*. On standing, and after repeated crystallisation, the two solids gave a substance, m. p. 134—151° (Found : C, 77·4; H, 6·1. $C_{19}H_{18}O_4$ requires C, 77·5; H, 6·2%). When boiled with hydriodic acid, this substance gave a compound, m. p. 122—123°, which did not condense with aromatic aldehydes and was identified as 7-methylflavone.

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