Tetrahedron Vol. 28, pp. 4239 to 4242. Pergamon Press 1972 Printed in Great Britain

ONE STEP CONVERSION OF A STYRENE DERIVATIVE INTO A BENZOYLOLEFIN

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(*Received in the UK* 10 *May* 1972; *Accepted for publication* 30 *May* 1972)

Abstract— Treatment with NBS and DMSO. followed by sodium carbonate, has been shown to be a convenient method for converting the styrene derivative (**5**; R = H) into the benzoylcyclohexene derivative (**6**; R = H) under mild conditions.

IN CONNECTION with another project it recently became necessary for us to devise a convenient method for the conversion of styrenoid compounds of the type **1** into the related aryl αβ-unsaturated ketones (**2**). Reports that the conversion of an olefin into the derived bromohydrin[1] by treatment with N-bromosuccinimide and dimethyl sulphoxide proceeds through the intermediates **3** and **4**[2] suggested that it might be possible to carry out such a reaction under conditions which would result in the elimination of a molecule of dimethyl sulphoxide and a molecule of hydrogen bromide from the latter, so as to give a conjugated ketone in one step. The present paper describes the successful application of this method to the styrene derivative (**5**: R = H).

The acid (**5**: R = H) was prepared by a Wittig condensation between *p*-formylphenoxyacetic acid and the phosphorane derived by treatment of cyclohexyltriphenylphosphonium bromide with sodium hydride. Treatment of the carboxylic acid (**5**: R = H) with N-bromosuccinimide and dimethyl sulphoxide for 5 hr, followed by treatment with sodium carbonate for a further 48 hr gave the enone (**6**: R = H), which was isolated in a yield of 40% by chromatography of the derived methyl ester (**6**: R = Me). Minor products also isolated after treatment of the mixture with diazomethane were assigned structures **7** and **8** on the basis of their spectra. These compounds might reasonably arise from the intermediates **11** and **12** as indicated.

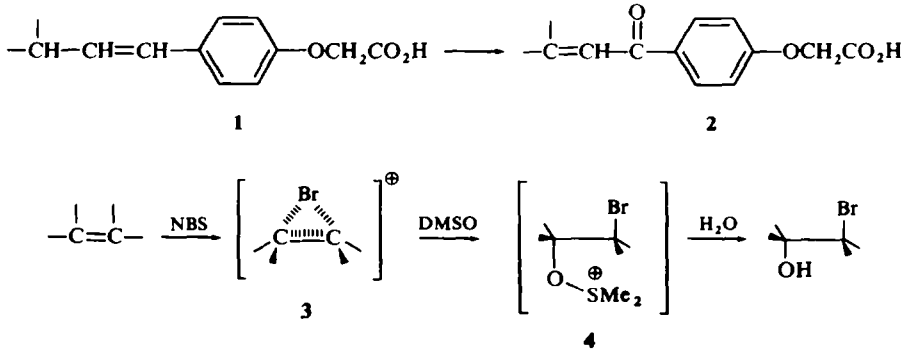
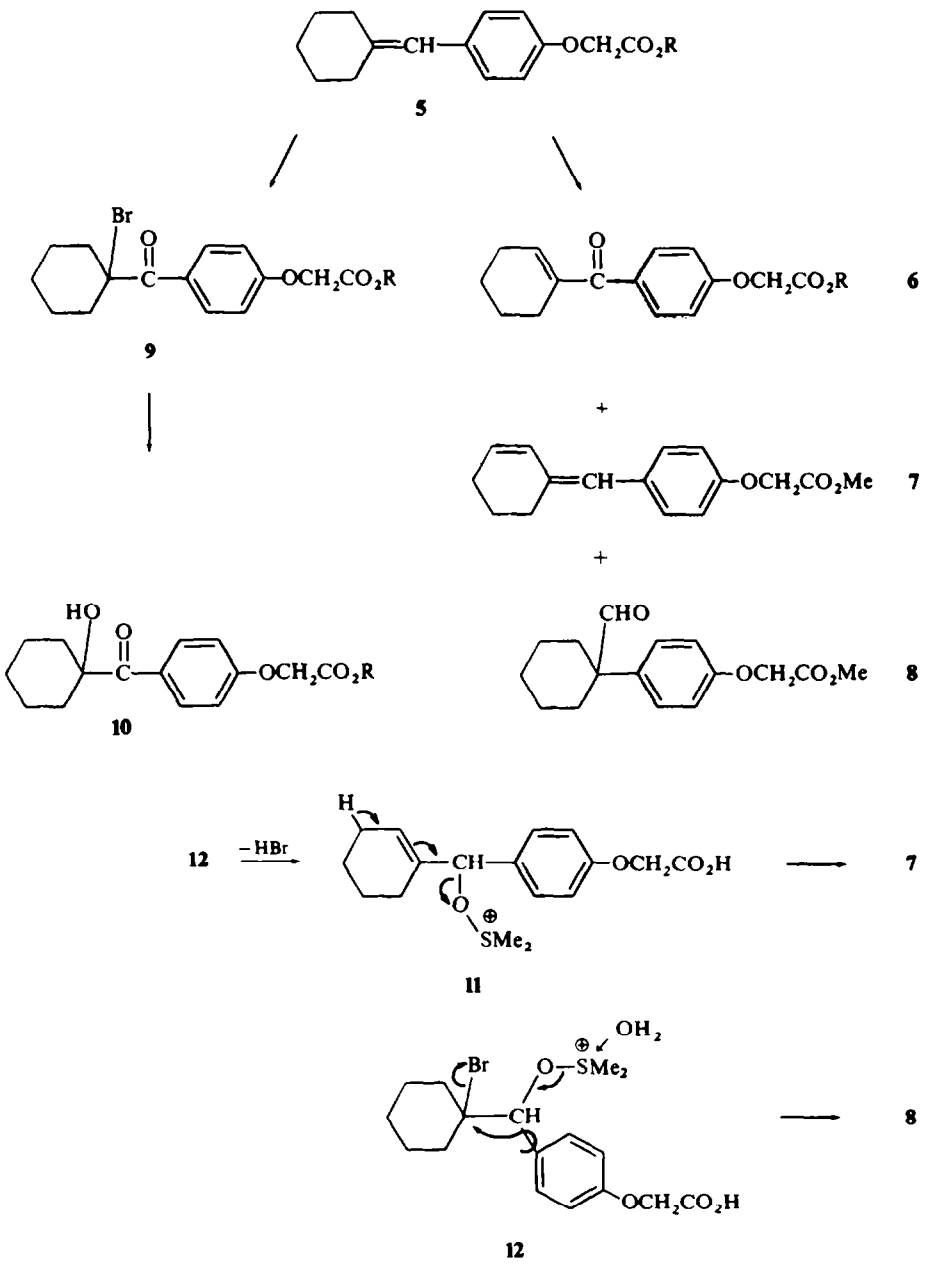


FIG 1



When the carboxylic acid (**5**: R = H) was treated with NBS and DMSO for only 1 hr, followed by treatment with sodium carbonate for a further 5 min the major product (70% yield) was the α-bromoketone (**9**: R = H) which was characterized as the derived methyl ester (**9**: R = Me). Saponification of the methyl ester with sodium hydroxide in aqueous dioxan resulted also in the hydrolysis of the C-Br linkage to give the hydroxyketoacid (**10**: R = H).

EXPERIMENTAL

M.ps were measured on a Kofler block and are uncorrected. IR spectra were recorded on a Unicam SP 1000 spectrophotometer or on a Perkin–Elmer 125 instrument and refer to KCl discs unless stated otherwise. UV spectra were recorded on a Unicam SP 800 spectrophotometer, using 95% EtOH as solvent. NMR spectra were measured on a Varian A60A instrument using $CDCl_3$ as solvent unless specified otherwise. Chemical shifts are given in τ using TMS as internal reference and coupling constants (J) in Hz. Mass spectra were recorded on an A.E.I. MS 902 spectrometer.

p-*Carboxymethoxybenzalcyclohexane* (**5**: R = H). A soln of cyclohexyltriphenylphosphonium bromide (31·9 g) and *p*-formylphenoxyacetic acid (4·5 g) in DMSO (200 ml) and THF (200 ml) was stirred with NaH (3·6 g) under N_2 for 6 hr at 0° and then for a further 20 hr at room temp. Addition of acetone gave a ppt which was collected by filtration and dissolved in boiling water (350 ml). Acidification with dil HCl aq afforded the *carboxylic acid* (**5**: R = H) as a very pale yellow solid (4·05 g, 66%) which crystallized from EtOAc–ligroin, m.p. 144–147°: ν_{max} cm^{-1}: 2400–3200, 1725, 1705, and 840: λ_{max} 253 nm (ε 21,470): NMR (DMSO): 2·88 and 3·15 (each 2H, d, J 9, aromatic protons), 3·84 (1H, broad s, olefinic H), and 5·41 (2H, s, $OC\underline{H}_2CO_2H$). (Found: C, 73·40; H, 7·20: *m/e* 246. $C_{15}H_{18}O_3$ requires: C, 73·15; H, 7·35%; *M*, 246).

The derived *methyl ester* (**5**: R = Me) was obtained as an oil by treatment of **5**(R = H) with ethereal diazomethane at room temp: ν_{max}^{film} cm^{-1}: 1762, 1740, and 848; NMR: 2·86 and 3·18 (each 2H, d, J 9, aromatic protons), 3·85 (1H, broad s, olefinic H), 5·39 (2H, s, $OC\underline{H}_2CO_2Me$): 6·20 (3H, s, CO_2Me), 7·73 (4H, m, allylic CH_2 groups), and 8·40 (6H, m, remaining CH_2 groups). (Found: *m/e*, 260·1419. $C_{16}H_{20}O_3$ requires *M*, 260·1412).

Methyl p-*cyclohex-1-enylcarbonylphenoxyacetate* (**6**: *R = Me*), p-*methoxycarbonylmethoxybenzalcyclohex-2-ene* (**7**), *and* 1-(p-*methoxycarbonylmethoxy*) *phenylformylcyclohexane* (**8**). A soln of **5** (R = H: 1·36 g) in DMSO (30 ml) was stirred at room temp under N_2 for 5 hr with N-bromosuccinimide (2·14 g). After the addition of anhyd Na_2CO_3 (1·27 g), stirring was continued for a further 48 hr and then acetone was added to precipitate Na salts. These were taken up in water (25 ml) and the soln was acidified with dil HCl aq to precipitate the acidic products, which were collected by filtration, dried, dissolved in MeOH (20 ml), and methylated by the addition of excess ethereal diazomethane to afford, after removal of solvent, an oil (960 mg). This was combined with another batch (940 mg) of material obtained in the same way and chromatographed on a column of kieselgel G, using 2% ether—98% benzene as eluant.

Three products were isolated. The material of highest R_f value was p-*methoxycarbonylmethoxybenzalcyclohex-2-ene* (**7**: 162 mg), m.p. 59–61°, after recrystallisation from ligroin: ν_{max}^{KCl} cm^{-1} 1760, and 1600: λ_{max} 283 nm (ε 17,500); NMR: 2·75 and 3·15 (each 2H, d, J 9, aromatic protons), 3·7–4·3 (3H, broad m, olefinic H), 5·37 (2H, s, $-OC\underline{H}_2CO_2Me$), 6·20 (3H, s, CO_2Me), and 7·40, 7·84, 8·30 (each 2H, m, cyclohexanic CH_2). (Found: *m/e*, 258·1266. $C_{16}H_{18}O_3$ requires 258·1256).

Further elution afforded 1-(p-*methoxycarbonylmethoxy*)*phenylformylcyclohexane* (**8**) as an oil: ν_{max}^{film} cm^{-1} 2930, 2850, 2800, 2700, 1760, 1740, 1720, 1600, and 1500; NMR: 0·65 (1H, s, $C\underline{H}O$), 2·75 and 3·11 (each 2H, d, J 9, aromatic protons), 5·39 (2H, s, $OC\underline{H}_2CO_2Me$), 6·20 (3H, s, CO_2Me). (Found: *m/e*, 276·1350. $C_{16}H_{20}O_4$ requires: *M*, 276·1362).

The final fractions from the chromatogram afforded *methyl* p-*cyclohex-1-enylcarbonylphenoxyacetate* (**6**: R = Me; 1·03 g), m.p. 55–60° from ligroin: ν_{max}^{film} cm^{-1} 1760, and 1636: λ_{max} 224 nm (ε 10,300), 253 infl. (10,300), and 274 (12,800): NMR: 2·31 and 3·10 (each 2H, d, J 9, aromatic protons), 3·50 (1H, m, olefinic proton), 5·31 (2H, s, $OC\underline{H}_2CO_2Me$), 6·20 (3H, s, CO_2Me), 7·70 (4H, m, allylic CH_2), and 8·32 (4H, m, remaining CH_2). (Found: C, 70·15; H, 6·7%: *m/e*, 274·1194. $C_{16}H_{18}O_4$ requires: C, 70·05; H, 6·6%: *M*, 274·1205).

p-*Cyclohex-1-enylcarbonylphenoxyacetic acid* (**6**: R = H). To a soln of **6** (R = Me: 110 mg) in dioxan (2 ml) was added NaOH aq (64 mg in 2 ml water). The mixture was left at room temp for 20 hr, diluted with water, and extracted with EtOAc. The extract was washed with water, dried (Na_2SO_4) and evaporated *in vacuo* to afford p-*cyclohex-1-enylcarbonylphenoxyacetic acid* (**6**: R = H), m.p., after recrystallization from chloroform–ligroin, 119–123°: ν_{max}^{KCl} cm^{-1} 2200–3300, 1730, 1704, and 1625: λ_{max} 225 nm (ε 10,600), 253 infl. (ε 9600), and 277 (12,200); NMR (d_6-DMSO): 2·39 and 3·00 (each 2H, d, J 9, aromatic protons), 3·55 (1H, m, olefinic proton), 5·22 (2H, s, $OC\underline{H}_2CO_2H$). (Found: C, 68·7: H, 6·2%: *m/e*, 260·1048. $C_{15}H_{16}O_4$ requires: C, 69·2: H, 6·2%: *m/e*, 260·1049).

Treatment of **6** (R = H) with ethereal diazomethane gave back the ester (**6**: R = Me).

Methyl p-(1-*bromo*)*cyclohexylcarbonylphenoxyacetate* (**9**: R = Me). A soln of **5** (R = H: 490 mg) and N-bromosuccinimide (710 mg) in DMSO (10 ml) was stirred under N_2 for 1 hr at room temp. Anhyd Na_2CO_3 (210 mg) was added and stirring was continued for a further 5 min: addition of acetone then gave

a ppt, which was collected by filtration, dried, and methylated with diazomethane to give the *bromoketone* (**9**; R = Me) which was obtained in a pure state as a colourless oil by preparative TLC (0·1 mm coating of kieselgel G) using 5% ether–95% benzene as eluant: ν_{max}^{film} cm^{-1} 1760, and 1668; λ_{max} 223 nm (ε 6400), and 283 nm (ε 11,760): NMR: 1·86 and 3·10 (each 2H, d, *J* 9, aromatic protons), 5·31 (2H, s, $OC\underline{H}_2CO_2Me$), 6·20 (3H, s, CO_2Me), 7·75 (4H, m, 2- and 6-$C\underline{H}_2$), and 8·40 (6H, m, remaining CH_2 groups). (Found: *m/e*, 356·0435. $C_{16}H_{19}O_4{}^{81}Br$ requires: 356·0447).

p-(1-*Hydroxy*)*cyclohexylcarbonylphenoxyacetic acid* (**10**; R = H). Solns of NaOH (19 mg) in water (1 ml) and **9** (R = Me; 56 mg) in dioxan (1 ml) were mixed and left at room temp for 20 hr. The mixture was then acidified with dilute HCl aq and diluted with water. The *hydroxy-acid* (**10**; R = H) was isolated by extraction with EtOAc as a white solid, m.p., after crystallization from $CHCl_3$–ligroin, 125–27°: ν_{max} cm^{-1}: 3561, 3062, 2300–3200, 1727, 1710, and 1665: λ_{max} 219 nm (ε 10,000), and 273 (13,700): NMR (d_6-DMSO): 1·82 and 3·05 (each 2H, d, *J* 9, aromatic protons), 5·25 (2H, s, $OC\underline{H}_2CO_2H$), and 8·1–9·0 (10H, broad *m*, cyclohexanic CH_2). (Found: C, 64·25; H, 6·5%; *m/e* 278·1152. $C_{15}H_{18}O_5$ requires: C, 64·7; H, 6·5%; *M*, 278·1154).

Acknowledgements—We thank Théramex Ltd. for the award of a Research Fellowship (to M.I.Q.).

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