Tetrahedron, 1958, Vol. 3, pp. 140–143. Pergamon Press Ltd., London

CLAISEN–HAASE REARRANGEMENT OF ENOL ESTERS

F. GOGAN, A. E. O'BRIAIN, E. M. PHILBIN,
N. S. O'CONNOR, R. F. TIMONEY and T. S. WHEELER
College of Pharmacy and University College, Dublin

(*Received* 23 *January* 1958)

Abstract—The Claisen–Haase rearrangement of β-acyloxyacrylates, RC(O·COR') : CH·CO_2Et, into the isomeric diacylacetates, RCO·CH(COR')·CO_2Et, is subject to base and acid catalysis. The reaction is intermolecular when base-catalysed and probably intramolecular when acid-catalysed.

The related transformation of deoxybenzoin enol esters has also been examined.

CLAISEN AND HAASE[1] discovered the conversion by bases of the enol acetate, ethyl *O*-acetylacetoacetate, into ethyl diacetylacetate and suggested that an intermolecular reaction is involved. Subsequent work[2,3] confirmed that the rearrangement was base-catalysed and intermolecular (mixture experiments), and that it could not be effected thermally. Kästner[4] then showed that the reaction is also acid-catalysed (by boron trifluoride) and postulated, without mixture experiments, an intramolecular migration of the Fries type. Anhydrous ferric chloride has now been found to produce transformation, and a number of β-acyloxyacrylates have been transformed by using various catalysts. The results of the mixture experiments described later (see under "Experimental") suggest that the reaction is, as Kästner[4] stated, intramolecular with acid catalysts (absence of crossed products). Michael and Carlson[3] claimed, however, that metallic sodium converts ethyl *O*-benzoylacetoacetate into ethyl sodioacetylbenzoylacetate by intramolecular migration of the benzoyl group.

In an extension of their previous work, Claisen and Haase[5] found that the acetophenone enol ester, 1-phenylvinyl benzoate, on treatment with a base rearranged into benzoylbenzoylmethane. This type of transformation has also been effected thermally[6] and by acid catalysts.[4,6] Hauser and his colleagues[6] produced evidence that the thermal conversion involves an intramolecular rearrangement and the conversion by boron trifluoride an intermolecular acylation. This latter result is contrary to Kästner's view.

The deoxybenzoin enol esters react less readily. Three esters, 1:2-diphenylvinyl acetate,[7] benzoate and *o*-methoxybenzoate, have been examined in conjunction with base and acid catalysts (sodium hydroxide, potassium hydroxide or sodamide in pyridine; sodium ethoxide in pyridine–ethanol; potassium carbonate in ethyl acetate; sodium in benzene or toluene; boron trifluoride; aluminium chloride). The only successful result was obtained with the benzoate, which with aluminium chloride gave benzoylbenzoylphenylmethane.

---

[1] L. Claisen and E. Haase, *Ber. Dtsch. Chem. Ges.* **33**, 3778 (1900).

[2] W. Dieckmann and R. Stein, *Ber. Dtsch. Chem. Ges.* **37**, 3370 (1904).

[3] A. Michael and G. H. Carlson, *J. Amer. Chem. Soc.* **57**, 165 (1935).

[4] D. Kästner, Thesis, pp. 29, 66. Marburg; (1937) and *Newer Methods of Preparative Organic Chemistry* p. 289 Interscience, New York (1948).

[5] L. Claisen and E. Haase, *Ber. Dtsch. Chem. Ges.* **36**, 3674 (1903).

[6] F. G. Young, F. C. Frostick, Jun., J. J. Sanderson and C. H. Hauser, *J. Amer. Chem. Soc.* **72**, 3635 (1950).

[7] R. P. Barnes, S. R. Cooper, V. J. Tulane and H. Delaney, *J. Org. Chem.* **8**, 153 (1943).

EXPERIMENTAL

Crystallisation was from ethanol unless otherwise stated.

Rearrangement by acid catalysts

A mixture of ethyl *O*-acetylacetoacetate[8] (1 g), anhydrous ferric chloride (1·1 g) and dry ether (20 ml) was kept for 24 hr, and then treated with dilute hydrochloric acid. Acidification of the alkaline extract of the ethereal layer gave ethyl diacetylacetate as a yellow oil (0·3 g), b.p. 103–104°/16 mm (cupro derivative,[9] m.p. and mixed m.p. 147–148°).

Boron trifluoride was passed at 0° for 1 hr through ethyl *O*-acetylbenzoylacetate[10] in dry ether. The product was added to 30% aqueous sodium acetate at 5–10°. The ethereal solution yielded on treatment with dilute aqueous sodium hydroxide, ethyl acetylbenzoylacetate (70 per cent yield); cupro derivative, m.p. and mixed m.p. 232–234°. (Michael and Carlson[3] give m.p. 232°).

No rearrangement occurred when ethyl *O*-acetylacetoacetate was heated in a sealed Pyrex-glass tube at 320° for 15 min.

Rearrangement by base catalysts

A mixture of ethyl *O*-benzoylacetoacetate[10] (1·2 g), potassium hydroxide (0·5 g) and pyridine (4 ml) was shaken for 18 hr. The product was diluted with water and extracted with ether, before and after acidification. The second ethereal extract was washed with aqueous sodium hydrogen carbonate and with water. When shaken with saturated aqueous copper acetate, it gave the cupro derivative of ethyl acetylbenzoylacetate (0·7 g)[3] (see above).

This rearrangment was also effected in pyridine by potassium carbonate, sodium hydroxide, sodium peroxide and sodium phenoxide. Potassium hydroxide was the most and sodium phenoxide the least satisfactory reagent.

Potassium hydroxide in pyridine was the reagent most usually employed in the experiments described below, although the utility of the other bases mentioned above was also tested. The *C*-acyl derivatives exhibited a red colour with ethanolic ferric chloride.

Preparation of various esters

Ethyl O-(o-*toluoyl)acetoacetate.* A mixture of *o*-toluoyl chloride (15 g), ethyl acetoacetate (13 g) and pyridine (15 g) was kept for 2 days. Removal of the solvent from the acid- and alkali-washed ethereal extract gave *ethyl* O-(o-*toluoyl)acetoacetate* as a light-yellow oil (14 g), b.p. 148–150°/2 mm (Found: C, 67·8: H, 6·3. $C_{14}H_{16}O_4$ requires C, 67·7; H, 6·5 per cent). The *O*-acyl derivatives described below were similarly prepared. These compounds do not give a colour with ethanolic ferric chloride.

N-*Phenyl*-N′-o-*toluoylhydrazine.* An ethereal solution of ethyl *O*-(*o*-toluoyl)-acetoacetate (1 g) and phenylhydrazine (0·9 g) was kept at −10° for 12 hr. The *hydrazine* crystallised from aqueous ethanol in needles (0·3 g), m.p. 167° (Found: C, 74·5; H, 6·3. $C_{14}H_{14}ON_2$ requires C, 74·3; H, 6·2 per cent).

---

[8] L. Claisen and E. Haase, *Ber. Dtsch. Chem. Ges.* **33**, 1242 (1900).

[9] L. Claisen and W. Zedel, *Liebigs Ann.* **277**, 172 (1893).

[10] A. Bernhard, *Liebigs Ann.* **282**, 164 (1894).

*Ethyl cuproacetyl-*o*-toluoylacetate.* This ester was prepared from the product of the base-catalysed transformation of the above-mentioned *O*-acyl ester. It separated from benzene in blue needles, m.p. 203–204° (Found: C, 60·2; H, 5·6. $C_{14}H_{15}O_4\frac{1}{2}Cu$ requires C, 60·4; H, 5·4 per cent). This cupro derivative was treated with 10% sulphuric acid and the resulting mixture was extracted with ether. Removal of the solvent gave *ethyl acetyl-*o*-toluoylacetate* as an oil, b.p. 130–132°/3 mm (Found: C, 68·0; H, 6·3. $C_{14}H_{16}O_4$ requires C, 67·7; H, 6·5 per cent).

Ethyl O-*(*o*-chlorobenzoyl) acetoacetate.* This ester was obtained as a light-yellow oil, b.p. 160–161°/2·5 mm (Found: C, 58·3; H, 4·8; Cl, 13·5. $C_{13}H_{13}O_4Cl$ requires C, 58·1; H, 4·8; Cl, 13·2 per cent).

*Ethyl acetyl-*o*-chlorobenzoylacetate.* The *cupro derivative* crystallised in dark-blue cubes, m.p. 217–219° (Found: C, 52·0; H, 4·0; Cl, 11·4. $C_{13}H_{12}O_4Cl\frac{1}{2}Cu$ requires C, 52·1; H, 4·0; Cl, 11·9 per cent). The free ester was obtained as an oil, b.p. 139–140/3 mm (Found: C, 58·4; H, 4·6; Cl, 13·1. $C_{13}H_{13}O_4Cl$ requires C, 58·1; H, 4·8; Cl, 13·2 per cent).

Ethyl O-*(*p*-chlorobenzoyl)acetoacetate.* This ester formed a yellow oil, b.p. 156–157°/3 mm, which solidified to a yellow mass, m.p. 27–31°, when kept at −10° for 3 hr (Found: C, 58·2; H, 4·6; Cl 13·5. $C_{13}H_{13}O_4Cl$ requires C, 58·1; H, 4·8; Cl, 13·2 per cent). *Ethyl acetyl-*p*-chlorobenzoylacetate* was obtained as an oil, b.p. 150–152°/3 mm (Found: C, 58·1; H, 4·7; Cl, 12·6. $C_{13}H_{13}O_4Cl$ requires C, 58·1; H, 4·8; Cl, 13·2 per cent).

Ethyl O-*(*p*-anisoyl)acetoacetate.* This ester separated in micro-crystals, m.p. 46–48° (Found: C, 63·3; H, 6·3. $C_{14}H_{16}O_5$ requires C, 63·6; H, 6·1 per cent). *Ethyl acetyl-*p*-anisoylacetate* formed a yellow oil, b.p. 160–162°/4 mm (Found: C, 63·6; H, 5·8. $C_{14}H_{16}O_5$ requires C, 63·6; H, 6·1 per cent).

Ethyl O-*(*p*-nitrobenzoyl)acetoacetate.* This ester separated in micro-crystals, m.p. 83–85° (Found: C, 55·7; H, 4·9; N, 5·0. $C_{13}H_{13}O_6N$ requires C, 55·9; H, 4·7; N, 5·0 per cent). The corresponding *C*-ester crystallised from light petroleum (boiling range 40–60°) in yellow needles, mp. 54–55° (Bülow and Hailer[11] give m.p. 53–55°) (Found: C, 56·2; H, 4·8; N, 4·9. Calc. for $C_{13}H_{13}O_6N$; C, 55·9; H, 4·7; N, 5·0 per cent).

Mixture experiments

(i). Boron trifluoride was passed for 1 hr at 0° through a mixture of ethyl *O*-acetylacetoacetate (2 g) and ethyl benzoylacetate (2·3 g) in dry ether. The product was added to 30% aqueous sodium acetate at 5–10°. The ethereal solution yielded on treatment with dilute aqueous sodium hydroxide an oil (2·2 g), which on fractionation gave:

(*a*) a light-yellow oil (0·4 g), b.p. 94–98°/11 mm (cupro derivative, m.p. and mixed m.p. with ethyl cupro-diacetylacetate,[9] 146–148°);

(*b*) ethyl benzoylacetate, b.p. 146–149°/11mm (cupro derivative, m.p. 180–182°. Wislicenus[12] gives m.p. 182–183°).

Ethyl *O*-acetylacetoacetate (1 g) remained in the ethereal extract of the product.

(ii). When a mixture of ethyl *O*-acetylbenzoylacetate[10] (2·4 g) and ethyl acetoacetate (1·8 g) was treated as described under (*i*), the product consisted mainly

---

[11] C. Bülow and E. Hailer, *Ber. Dtsch. Chem. Ges.* **35**, 930 (1902).

[12] W. Wislicenus, *Ber. Dtsch. Chem. Ges.* **31**, 3157 (1898).

of ethyl acetylbenzoylacetate with some ethyl acetoacetate. The former was characterised by the cupro derivative, m.p. and mixed m.p.[3] 232–234°.

Deoxybenzoin enol esters

1:2-*Diphenylvinyl benzoate* (*Method* 1). A mixture of deoxybenzoin (25 g) and benzoyl chloride (50 ml) was heated in nitrogen for 10 hr at 180°. Excess of the chloride was evaporated at reduced pressure and an ethereal solution of the residue was de-acidified by aqueous sodium carbonate. The *benzoate* that remained in the solvent separated from ligroin in plates (16 g), m.p. 119° (Found: C, 84·5; H, 5·3. $C_{21}H_{16}O_2$ requires C, 84·0; H, 5·4 per cent).

1:2-*Diphenylvinyl benzoate* (*Method* 2). A mixture of deoxybenzoin (5 g), benzoic anhydride (60 g) and sodium benzoate (12 g) was heated at 200° for 4 hr. The product was ground with ice and sodium carbonate and the residue was extracted with boiling water until no more benzoic acid was removed, and was purified in ether as described above. The m.p. of the crystallised product (0·5 g) was not depressed by addition of benzoate prepared by Method 1.

1:2-*Diphenylvinyl* o-*methoxybenzoate*. This was prepared by Method 1. It separated from ethanol in plates, m.p. 88–89° (Found: C, 80·4; H, 5·7; OMe, 10·3. $C_{22}H_{18}O_3$ requires C, 80·0; H, 5·5; OMe, 9·4 per cent).

Benzoylbenzoylphenylmethane

A mixture of 1:2-diphenylvinyl benzoate (1 g), aluminium chloride (0·6 g) and carbon disulphide (20 ml) was heated under reflux for 15 min., and the solvent was evaporated. The residue was kept at 165° for 15 min and then treated with ice and hydrochloric acid. The product was heated under reflux with ethanol for 8 hr. On cooling, the colourless isomer of benzoylbenzoylphenylmethane separated in plates, m.p. and mixed m.p. with an authentic specimen,[13,14] 148° (Found: C, 83·9; H, 5·4. Calc. for $C_{21}H_{16}O_2$: C, 84·0; H, 5·4 per cent).

Acknowledgements—One of us (N. S. O'C) acknowledges the receipt of a grant from the Medical Research Council of Ireland.

---

[13] J. Meisenheimer and K. Weibezahn, *Ber. Dtsch. Chem. Ges* **54**, 3205 (1921).

[14] S. Goldschmidt and F. Nagel, *Ber. Dtsch. Chem. Ges.* **63**, 1214 (1930).