

Thermal Rearrangement of α -Diazo- β -diketones

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From the thermal Wolff rearrangement of diacyldiazomethanes, $\text{ArCO}\cdot\text{CN}_2\cdot\text{COR}$, products arising from the migration of both Ar and R groups have been isolated. Relative migrational aptitudes are mesityl (98), 2,4,6- $\text{Br}_3\text{C}_6\text{H}_2$ - (8), Ph (3), and Me (2), suggesting that, while both steric and electronic effects are important, the steric factor is dominant when the two are in opposition. These results provide a novel route to a number of ketones, β -keto-esters, and *N*-(2-arylacetyl)sulphonamides.

ALTHOUGH α -diazo- β -diketones (II) have long been known, their chemistry has received much less systematic attention than has that of monoacyldiazomethanes. Wolff¹ observed their ready thermal rearrangement; although from acetylbenzoyldiazomethane (II; Ar = Ph, R = Me) he isolated products arising from both phenyl and methyl group migration [(VII) and (VIII); Ar = Ph, R = Me], the relative amounts of the two were not specified. Horner,² using the same diazo-diketone, later reported that irradiation resulted in exclusive methyl group migration, whereas Zeller *et al.*³

showed that the ratio of methyl to phenyl group migration was 25 : 1. Thermal reaction, on the other hand, gave these products in the ratio of 3 : 5. In a kinetic study, during which products were not always isolated, Regitz⁴ showed that diacyldiazomethanes (II) undergo thermal decomposition more readily than do the monoacyl derivatives. Dibenzoyldiazomethane (II; R = Ar = Ph) was shown to be less stable than acetylbenzoyldiazomethane (II; Ar = Ph, R = Me). Wolff rearrangement of a number of 2-diazocyclohexane-1,3-

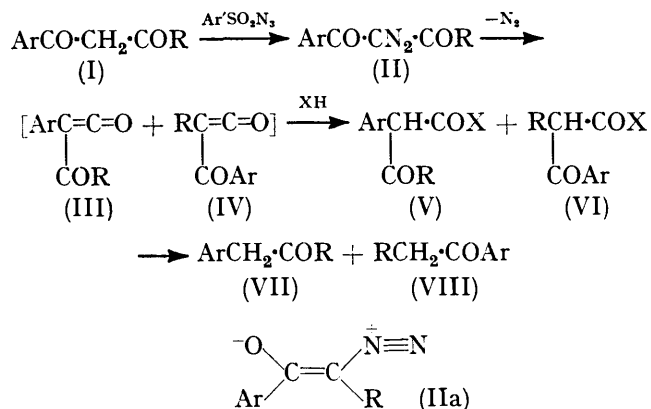
¹ L. Wolff, *Annalen*, 1902, **325**, 129.

² L. Horner and E. Spietschka, *Chem. Ber.*, 1952, **85**, 225.

³ K.-P. Zeller, H. Meier, and E. Muller, *Tetrahedron*, 1972, 5831.

⁴ M. Regitz and W. Bartz, *Chem. Ber.*, 1970, **103**, 1477.

dione derivatives has also been reported but here thermal and photochemical reactions of the unsymmetrically substituted compounds appear to give substantially similar results.⁵ The relatively high incidence of methyl



as opposed to phenyl migration is interesting, since in the Beckmann and related rearrangements which have at least formal analogy to the Wolff rearrangement, phenyl migration takes place almost exclusively.⁶ We therefore investigated the thermal rearrangement of some selected α -diazo- β -diketones. In addition to the mechanistic aspects there appeared to be synthetic possibilities, since diacyldiazomethanes are now available from 1,3-diketones by diazo-group transfer from an arenesulphonyl azide⁷ [(I) \longrightarrow (II)]. Since in the Beckmann rearrangement the mesityl group has been shown⁸ to migrate faster than any other so far studied, investigation of the hitherto unknown diazo-diketones containing mesityl groups seemed particularly worthwhile. Acetylbenzoyldiazomethane (II; Ar = Ph, R = Me), used for the purposes of comparison, decomposed smoothly in boiling propan-1-ol to provide products of phenyl and methyl migration [(V) and (VI); Ar = Ph, R = Me, X = PrⁿO] in the ratio 3 : 2. This result, which is in reasonable agreement with the 5 : 3 ratio claimed by Zeller *et al.*,³ was determined by hydrolysis of the esters and decarboxylation of the resulting acids [(V) and (VI); Ar = Ph, R = Me, X = OH] in high yield to provide a mixture of ketones [(VII) and (VIII); Ar = Ph, R = Me] which was analysed by g.l.c. When a similar procedure was applied to acetyl-2,4,6-trimethylbenzoyldiazomethane (II; Ar = 2,4,6-Me₃C₆H₂, R = Me) the ratio of mesityl to methyl group migration was 98 : 2. Very similar results were obtained with benzoyl-2,4,6-trimethylbenzoyldiazomethane (II; Ar = 2,4,6-Me₃C₆H₂, R = Ph), but in this instance the presence of the minor component was demonstrated by mass spectrometry. Since mixtures of ketones rather than of

esters are convenient for analytical purposes we carried out the rearrangement of the mesityl derivative (II; Ar = 2,4,6-Me₃C₆H₂, R = Me) in dioxan containing a small percentage of water. Under these conditions the keto-acids [(V) and (VI); Ar = 2,4,6-Me₃C₆H₂, R = Me, X = OH] arising from the addition of water to the first formed ketens [(III) and (IV); Ar = 2,4,6-Me₃C₆H₂, R = Me] decomposed spontaneously to provide a mixture of ketones [(VII) and (VIII); Ar = 2,4,6-Me₃C₆H₂, R = Me] in excellent yield. This preponderance of mesityl migration provides an attractive route to the ketones (VII; Ar = 2,4,6-Me₃C₆H₂, R = Me or Ph) and to the propyl esters (V; Ar = 2,4,6-Me₃C₆H₂, R = Me or Ph, X = PrⁿO).

The extreme ease of migration of the mesityl group may be attributed to a combination of steric and electronic factors. In an attempt to throw light on the relative magnitudes of these we prepared and studied the hitherto unknown acetyl-2,4,6-tribromobenzoyldiazomethane (II; Ar = 2,4,6-Br₃C₆H₂, R = Me), since, like the mesityl derivative, this possesses bulky *ortho*-substituents, which, however, have an electronic effect opposite to that of methyl groups. This compound rearranged smoothly but much more slowly than the corresponding mesityl compound in wet dioxan to provide a mixture of ketones (VII) and (VIII) (Ar = 2,4,6-Br₃C₆H₂, R = Me) whose composition indicated that the ratio of 2,4,6-tribromophenyl to methyl migration was 4 : 1. These results indicate migratory aptitudes in the order mesityl > 2,4,6-tribromophenyl > phenyl > methyl (98 : 8 : 3 : 2). Thus while both steric and electronic effects seem to be of importance, the steric factor appears to be dominant when the two are in opposition.

One explanation of these observations is based on Kaplan and Meloy's⁹ suggestion that Wolff rearrangement of α -substituted diazo-ketones takes place through the conformational isomer for which (IIa) is a canonical structure, the diazo-group lying *trans* to the migrating group Ar. If the latter possesses bulky *ortho*-substituents it will be forced out of the plane of the double bond and its associated oxygen atom, and thus be in a particularly favourable situation to present electrons to the diazo-carbon atom. Such an explanation is analogous to that proposed¹⁰ for the influence of *ortho*-substituents on the rearrangement of acetophenone oximes.

Recently we drew attention¹¹ to an example of the comparatively rare reaction between a keten and a sulphonamide. In view of the ease with which the foregoing oxo-ketens react with water it seemed reasonable to expect the corresponding reaction with a sulphonamide. When acetyl or benzoyl-(2,4,6-trimethylbenzoyl)diazomethane was added to boiling chlorobenzene

⁵ H. Veschambre and D. Vocelle, *Canad. J. Chem.*, 1969, **47**, 1981; W. D. Barker, R. Gilbert, J. P. Lapointe, H. Veschambre, and P. Vocelle, *ibid.*, p. 2853.

⁶ L. G. Donaruma and W. Z. Heldt, *Org. Reactions*, 1960, **11**, 1.

⁷ F. Weygand and H. J. Bestmann in 'Newer Methods of Preparative Organic Chemistry,' ed. W. Foerst, Academic Press, New York, 1964, vol. III, p. 451.

⁸ F. Greer and D. E. Pearson, *J. Amer. Chem. Soc.*, 1955, **77**, 6649.

⁹ F. Kaplan and G. K. Meloy, *J. Amer. Chem. Soc.*, 1966, **88**, 950.

¹⁰ D. E. Pearson and W. E. Cole, *J. Org. Chem.*, 1955, **20**, 488.

¹¹ G. Heyes, G. Holt, and A. Lewis, *J.C.S. Perkin I*, 1972, 2351.

containing toluene-*p*-sulphonamide the expected oxo-sulphonamide was obtained in excellent yield. This provides an attractive alternative¹² synthesis of this little studied class of compounds.

EXPERIMENTAL

I.r. spectra were recorded on a Perkin-Elmer 257 instrument, ¹H n.m.r. spectra on Perkin-Elmer R10, Perkin-Elmer-Hitachi R20A, and Varian HA100 spectrometers, and mass spectra on an A.E.I. MS902 spectrometer. G.l.c. was carried out on a Pye Series 104 Chromatograph or on a Perkin-Elmer F21 Chromatograph, both of which were equipped with flame ionisation detectors. The instruments were calibrated with standard mixtures of similar composition to the mixtures under analysis. For products marked with an asterisk, further spectral data are available in Supplementary Publication No. SUP 20672 (8 pp.).†

β-Diketones.—(a) Benzoylacetone,¹³ acetoacetylmesitylene¹³ and 1-mesityl-3-phenylpropane-1,3-dione¹⁴ have been described previously.

(b) **2,4,6-Tribromobenzoylacetone.** (i) 2',4',6'-Tribromoacetophenone (obtained¹⁵ from 2,4,6-tribromobenzoyl chloride¹⁶ in 74% yield) did not react with ethyl acetate under conditions where¹³ acetophenone gave a good yield of benzoylacetone. When the reactants were kept together for 7 days at 18–24°, 2,4,6-tribromobenzoylacetone* (17%) (Found: C, 30.4; H, 1.8. C₁₀H₇Br₃O₂ requires C, 30.1; H, 1.75%), b.p. 153–156° at 1 mmHg, m.p. 37–39° (from methanol), ν_{max.} 1600br (CO) cm⁻¹, m/e 396 (M⁺, 10%), was produced.

(ii) The following alternative synthesis gave erratic results but occasionally was superior to (i). A solution of acetone (1.5 g, 26 mmol) in tetrahydrofuran (THF) (10 ml) was stirred with sodium hydride (1.25 g, 52 mmol) under nitrogen until hydrogen was no longer evolved (ca. 2 h). 2,4,6-Tribromobenzoyl chloride (10.0 g, 26 mmol) in THF was then added during 20 min. After being stirred for 5 h, the THF suspension was concentrated under reduced pressure and water (50 ml) was added. Work-up in the usual way¹³ gave 2,4,6-tribromobenzoylacetone (4.0 g, 39%), identical (m.p.; i.r. and n.m.r. spectra) with that described in (i).

α-Diazo-β-diketones.—These were prepared by diazo-group transfer from an arenosulphonyl azide to the appropriate diketone. Acetylbenzoyldiazomethane¹⁷ has been described previously and acetyl-(2,4,6-trimethylbenzoyl)diazomethane* (84%) was obtained by the same procedure, chromatography of the crude product on silica gel giving, on elution with benzene, material of m.p. 37–40° (Found: C, 68.9; H, 6.6. C₁₃H₁₄N₂O₂ requires C, 67.8; H, 6.0%), ν_{max.} 2108s (diazo) and 1660s (CO) cm⁻¹, τ (CCl₄) 3.15 (2H, s, aromatic) and 7.8br (12H, s, 4 × Me). Benzoyl-(2,4,6-trimethylbenzoyl)diazomethane and acetyl-(2,4,6-tribromobenzoyl)diazomethane were prepared by the general method of Hendrickson and Wolf¹⁸ and because of their lability

were used in subsequent reactions without purification. Indeed although the former showed the expected diazo-band in the i.r. spectrum at 2150 cm⁻¹ it was difficult to obtain it free from products of its Wolff rearrangement. Likewise the tribromo-derivative could not be obtained in a state of high purity even by chromatography. However, its i.r. spectrum showed the expected carbonyl and diazo absorptions at 2110 and 1660 cm⁻¹, respectively, and the n.m.r. spectrum showed τ 2.25 (s, aromatic) and 7.45 (s, Me) and the absence of the methylene group of its progenitor.

Thermal Decomposition of α-Diazo-β-diketones.—(a) *In propan-1-ol.* To refluxing propan-1-ol (100 ml) acetylbenzoyldiazomethane (10.1 g, 0.54 mol) in propan-1-ol (75 ml) was added during 30 min, and heating was continued until the i.r. spectrum showed no diazo-band (1.5 h). Concentration of the solution under reduced pressure and distillation of the resultant oil gave a mixture (5.0 g) of the propyl esters (V) and (VI) (Ar = Ph, R = Me, X = PrⁿO), b.p. 103–106° at 0.6 mmHg, m/e 220.1100 (M⁺; calc. for C₁₃H₁₆O₃: 220.1099), 105 (C₇H₅O⁺, 100%), and 90 (C₇H₆⁺). This material (1.0 g) was refluxed with 5M-hydrochloric acid (25 ml) for 4 h and after cooling and diluting with water was extracted with ether (2 × 25 ml). The dried (MgSO₄) ethereal extract was shown to contain benzyl methyl ketone and propiophenone in the ratio 3 : 2 by analysis on an Apiezon L column (2.5 m) at 137°.

In a similar experiment with acetyl-(2,4,6-trimethylbenzoyl)diazomethane (8.76 g, 38 mmol) decomposition was complete in 15 min and gave propyl 2-mesityl-3-oxobutyrate* (7.0 g, 74%) (Found: C, 72.8; H, 8.2. C₁₆H₂₂O₃ requires C, 73.2; H, 7.4%), b.p. 80° at 0.15 mmHg, m/e 262.1562 (M⁺, 17%; C₁₆H₂₂O₃ requires 262.1568). The mass spectrum indicates only a small amount of the isomeric ester (VI; Ar = 2,4,6-Me₃C₆H₂, R = Me, X = PrⁿO). Analysis of the hydrolysed product, by g.l.c., as before on a 3.5m Apiezon L column at 200° indicated a mixture (98 : 2) of mesitylacetone and 2',4',6'-trimethylpropiophenone (VIII; Ar = 2,4,6-Me₃C₆H₂, R = Me). Recrystallisation of this crude ketone mixture from methanol provided mesitylacetone* (74%), m.p. 55–58° (lit.,¹⁵ 59–60°) (Found: C, 81.6; H, 9.1. Calc. for C₁₂H₁₆O: C, 81.8; H, 9.1%), ν_{max.} 1715s (CO) cm⁻¹. The mass spectrum showed no evidence of the isomeric ketone (VIII; Ar = 2,4,6-Me₃C₆H₂, R = Me).

Decomposition of benzoyl-(2,4,6-trimethylbenzoyl)diazomethane (9.15 g), contaminated with 2',4',6'-trimethylacetophenone (see before), was complete in 5 min. The oily residue obtained on removal of the propanol was stirred with light petroleum (b.p. 60–80°; 25 ml); 2',4',6'-trimethylacetophenone (2.85 g), m.p. 160–164° (from ethanol) (lit.,¹⁹ 164–165°), then separated, and its identity was confirmed by its i.r., n.m.r., and mass spectra. The solution from which the ketone had been separated was concentrated and chromatographed on silica gel (45 × 4 cm) with toluene as eluant to provide a mixture [(V) and (VI); Ar = 2,4,6-Me₃C₆H₂, R = Ph, X = PrⁿO] (4.3 g), m.p. 45–55°, m/e 147 (C₁₀H₁₀⁺, 0.75%), 133 (C₁₀H₁₃, 25%), and 132 (C₁₀H₁₂⁺, 3%).

† For details of Supplementary Publications see *J. Chem. Soc. (A)*, 1970, Issue No. 20 (Notice to Authors No. 7).

¹² E. Haack and R. Heerdt, G.P. 1,091,573 (*Chem. Abs.*, 1961, **55**, 23446e).

¹³ J. M. Sprague, L. J. Beckham, and H. Adkins, *J. Amer. Chem. Soc.*, 1934, **56**, 2665.

¹⁴ E. P. Kohler and C. E. Barnes, *J. Amer. Chem. Soc.*, 1933, **55**, 690.

¹⁵ H. G. Walker and C. R. Hauser, *J. Amer. Chem. Soc.*, 1946, **68**, 1386.

¹⁶ R. C. Fuson, J. H. van Campen, and D. E. Wolff, *J. Amer. Chem. Soc.*, 1938, **60**, 2269.

¹⁷ M. Regitz and A. Liedhegener, *Chem. Ber.*, 1966, **99**, 3128.

¹⁸ J. B. Hendrickson and W. Wolf, *J. Org. Chem.*, 1968, **33**, 3610.

¹⁹ H. H. Weinstock and R. C. Fuson, *J. Amer. Chem. Soc.*, 1936, **58** 1233.

By comparison with the corresponding m/e values for the esters [(V) and (VI); Ar = 2,4,6-Me₃C₆H₂, R = Me, X = PrⁿO] the crude product was shown to contain the esters [(V) and (VI); Ar = 2,4,6-Me₃C₆H₂, R = Ph, X = PrⁿO] in the ratio 49:1. Recrystallisation from propanol provided *propyl 2-mesityl-3-oxo-3-phenylpropionate** (4.2 g, 70%) (Found: C, 77.4; H, 7.4. C₃₁H₂₄O₃ requires C, 77.7; H, 7.4%), m.p. 59–61°. The mass spectrum showed no evidence of the isomeric ester.

(b) *In dioxan-water*. Acetyl-(2,4,6-trimethylbenzoyl)diazomethane (15.0 g, 65 mmol) in dioxan (75 ml) was added during 30 min to a refluxing solution of water (5 ml) in dioxan (75 ml). After 15 min the solution was concentrated under reduced pressure and the resulting orange solid (13.0 g) distilled to give α -mesitylacetone (8.8 g, 80%), b.p. 99–101° at 7 mmHg, m.p. 54–58°, identical (i.r. spectrum and g.l.c.) with that previously described.

Similarly crude acetyl-(2,4,6-tribromobenzoyl)diazomethane (7.0 g) gave after 4 h a brown oil, distillation of which at 0.1 mmHg provided a yellow solid, b.p. 130–160°, m.p. 50–70°, which was chromatographed on silica gel (40 × 4 cm). Elution with light petroleum (b.p. 60–80°)-toluene (4:1) provided *2',4',6'-tribromopropiophenone** (0.4 g) (Found: C, 30.7; H, 2.1. C₉H₇Br₃O requires C, 29.1; H, 1.9%), m.p. 50–56°, ν_{\max} 1782s (CO) cm⁻¹, τ (CCl₄) 1.85 (2H, s, aromatic), 7.23 (2H, q, J 7.5 Hz, CH₂), and 8.77 (3H, t, J 7.5 Hz, Me), m/e 367.8056 (M^+ , 14%, C₉H₇⁷⁹BrO requires 367.8048) and 339 (C₉H₂Br₃O⁺, 100%). Further elution with light petroleum (b.p. 60–80°)-toluene (7:3) gave *2,4,6-tribromophenylacetone** (1.6 g) (Found: C, 29.4; H, 1.8. C₉H₇Br₃O requires C, 29.1; H, 1.9%), m.p. 86–89° (from methanol), ν_{\max} 1720s (CO) cm⁻¹, τ (CCl₄) 2.3 (2H, s, aromatic), 5.95 (2H, s, CH₂), and 7.82 (3H, s, Me),

m/e 368 (M^+ , 5%), 325 (C₇H₄Br₃⁺, 23%), 289 (C₉H₇Br₂O⁺, 51%), 246 (C₇H₄Br₂⁺, 10%), 167 (C₇H₄Br⁺, 19%), 88 (C₇H₄⁺, 11%), and 43 (MeCO⁺, 100%).

(c) *In the presence of toluene-p-sulphonamide*. To a refluxing solution of toluene-*p*-sulphonamide (5.8 g, 34 mmol) in dry chlorobenzene (100 ml), acetyl-(2,4,6-trimethylbenzoyl)diazomethane (7.8 g, 34 mmol) in chlorobenzene (50 ml) was added during 30 min. After heating for a further 15 min, concentration to low bulk provided *N*-(2-mesityl-1,3-dioxobutyl)toluene-*p*-sulphonamide* (10.3 g, 81%) (Found: C, 64.5; H, 6.3; N, 4.0; S, 8.9. C₂₀H₂₃NO₄S requires C, 64.3; H, 6.2; N, 3.7; S, 8.6%), m.p. 153–154° (from ethanol), ν_{\max} 3282s (NH), 1630s, and 1350s and 1155s (SO₂) cm⁻¹, m/e 373.1358 (M^+ , 12.5%; C₂₀H₂₃NO₄S requires 373.1358).

In a similar fashion benzoyl-(2,4,6-trimethylbenzoyl)-diazomethane (4.4 g, 0.015 mol) containing α -mesitylacetophenone was decomposed in the presence of toluene-*p*-sulphonamide (2.56 g, 0.015 mol). The crude product, obtained after removal of the chlorobenzene under reduced pressure, was extracted with hot ethanol (150 ml). The insoluble material proved to be *N*-(2-mesityl-1,3-dioxo-3-phenylpropyl)toluene-*p*-sulphonamide* (3.4 g, 53%) (Found: C, 68.9; H, 5.8; N, 3.3; S, 7.5. C₂₅H₂₅NO₄S requires C, 68.9; H, 5.8; N, 3.2; S, 7.3%), m.p. 179–182° (from benzene-ethanol), ν_{\max} 3250s (NH), 1630s, 1613s, 1375s, and 1170s (SO₂) cm⁻¹, m/e 435.1488 (M^+ ; C₂₅H₂₅NO₄S requires 435.1503).

Concentration of the ethanolic solution provided α -mesitylacetophenone (2.2 g), m.p. 160–164° (from ethanol), identical (i.r. spectrum) with the previously described material.

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