Formation and Fragmentation of 4-Diazo-1,2-diphenyl-3-oxo-butyl Acetate

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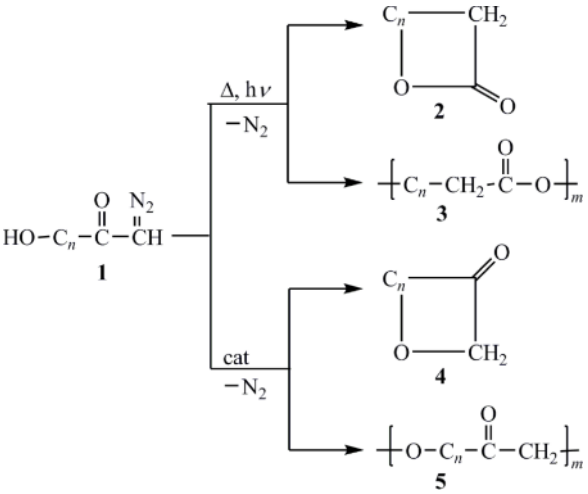
threo-4-Diazo-1,2-diphenyl-3-oxo-butyl acetate (**15**) could be prepared *via* the classical route **6** → **8** → **10** → **12** → **13** → **15**. However, its alkaline hydrolysis to the bifunctional hydroxy compound **17** led to a spontaneous dehydration to the diazoketone (*E*)-**18** and to a fragmentation to acetic acid, benzaldehyde (**8**) and diazoketone **19**.

Key words: Hydroxy-diazoketones, Ester Cleavage, Dehydration, Fragmentation

Introduction

Bifunctional compounds **1** bearing a diazoketone moiety and a hydroxy group are versatile starting materials for synthetic purposes. Scheme 1 summarizes the thermal or photochemical denitrogenation to singlet carbenes which enter a Wolff rearrangement, followed by inter- or intramolecular additions of the hydroxy group, leading to **2** and/or **3**. The rearrangement can be suppressed by applying catalytic denitrogenations to carbenoids which react directly with the hydroxy group to **4** and/or **5**. The competition between intra- and intermolecular processes is determined by the number n of carbon atoms in the chain and by the concentration of **1**. The ring formation is particularly favorable for $n = 2$, 3 and for low concentrations. We have now been mainly interested in compounds **1** with $n = 2$. Newer examples of intramolecular processes leading to **2** are listed in refs. [1 – 3], and those leading to **4** in refs. [4] and [5]. Some years ago we studied the transition metal-catalyzed decomposition of diazoketones **1** with respect to the intermolecular formation of polymers **3** and **5** and found that $Cu(acac)_2$ as a catalyst is superior to $Rh_2(OAc)_4$ for the formation of the polyetherketones **5** [6].



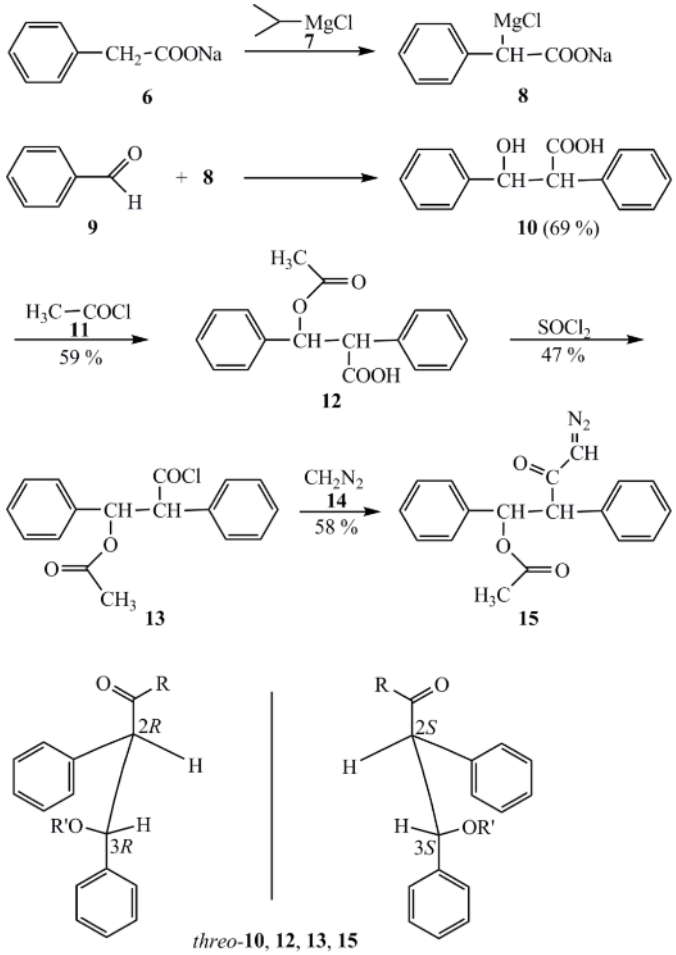
Scheme 1. Intra- and intermolecular reactions of hydroxydiazoketones **1** ($n = 2, 3, \ldots$).

Results and Discussion

The properties of **5** [6] stimulated us now to introduce aromatic substituents at the chain C_n. Scheme 2 shows the preparation of diazoketone **15** which contains a protected hydroxy group. The sodium salt of phenylacetic acid **6** was transformed with the Grignard reagent **7** to the Grignard compound **8**, an original Iwanoff reagent [7]. Our results with sodium salt **6** were much better than with the free acid. The reaction of **8** with benzaldehyde (**9**) yielded 3-acetoxy-2,3-diphenylpropionic acid (**10**), which has mainly the *threo*-configuration. Acetylation of the hydroxy group of **10** with acetyl chloride **11** led then to acetate **12**, which was transformed to the acid chloride **13**. Reaction of **13** with diazomethane (**14**) yielded finally the diazoketone **15**.

According to the Zimmerman-Traxler rule [8], **10**, **12**, **13**, and **15** have predominantly (2*R*, 3*R*)- and the enantiomeric (2*S*, 3*S*)-configurations. The ^{1}H NMR spectrum of the crude addition product **10** showed a *threo* : *erythro* ratio of 4 : 1. Recrystallization from ethyl acetate/petroleum ether (40 – 70 °C) gave the pure *threo*-isomer, which was identified by its NMR spectra.

Surprisingly, the attempt to generate from **15** a polyetherketone **16** failed (Scheme 3). We obtained a complex mixture of products. Therefore, we stud-



Scheme 2. Preparation of acetic acid 4-diazo-3-oxo-1,2-diphenyl-butyl ester (**15**).

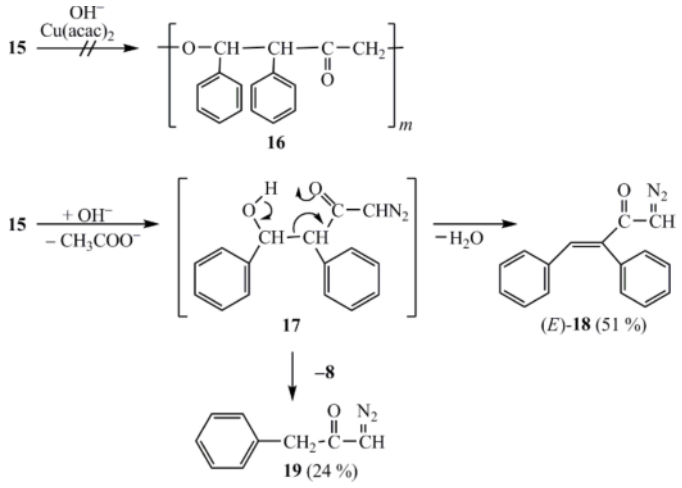
ied the alkaline hydrolysis of **15** in the absence of the Cu^{2+} catalyst and obtained two different diazoketones, namely (*E*)-1-diazo-3,4-diphenyl-but-3-en-2-one (*E*-**18**) as the major product and 1-diazo-3-phenyl-propan-2-one (**19**) as the minor component. The desired hydroxydiazoketone **17** eliminated H_2O to generate the cross-conjugated compound **18**. On the other hand, **17** showed a cleavage to benzaldehyde (**8**) and diazoketone **19** (Scheme 3).

Both reaction routes led to a loss of the bifunctionality. Therefore, the catalytic dinitrogenation can not yield an oligomeric or polymeric etherketone **16**.

Diazoketone **19** is a well-known compound, which can be easily obtained from phenylacetic acid chloride and diazomethane [9]. Diazoketone **18** was obtained before in low yield from an α-diazoester by Padwa *et al.* [10]. Its configuration results here from a *syn*-elimination of H_2O of the intermediate *threo*-**17** [11, 12]. 1-Diazo-4-hydroxy-butan-2-ones are stable, if they have just one [4] or no [5] aryl substituent at C-3 and C-4.

Experimental Section

NMR spectra were recorded on a Bruker AM 400 spectrometer working at 400 MHz for ^1H and 100 MHz for ^{13}C. FD MS (5 kV) and EI MS (70 eV) measurements were made with a Finnigan MAT 95 spectrometer. IR spectra were measured on a Beckman Acculab apparatus. Elemental analyses were performed in the microanalytical laboratory of the Chemistry Department of the University of Mainz. Melting points were taken on a Büchi apparatus and are uncorrected.



Scheme 3. Reactivity of diazoketone **15** in an alkaline medium.

*3-Hydroxy-2,3-diphenylpropionic acid (**10**)*

Magnesium (14.6 g, 0.6 mol) in 100 mL of dry THF was slowly reacted with 2-chloropropane (44.1 g, 0.6 mol) in 100 mL of dry THF. When the reaction at room temperature came to an end, another portion of 600 mL of dry THF was added before powdered sodium phenylacetate (**6**, 47.4 g, 0.3 mol) was added in small portions at 0 °C. The vigorously stirred process was then continued by the slow addition of freshly distilled benzaldehyde (**9**) in 100 mL of THF. After refluxing for 4 h, 150 mL of H_2O and 150 – 200 mL of half-concentrated aqueous HCl were added. The organic layer was separated, and the aqueous layer was three times extracted with the same amount of diethyl ether. The unified organic phases were then extracted with 500 mL of a 10 % aqueous solution of Na_2CO_3. Acidification with half-concentrated aqueous HCl led to the precipitation of a light-yellow solid which was treated with hot benzene to remove impurities. The dry residue melted at 170 – 171 °C and consisted according to the ^{1}H NMR spectrum of about 80 % of *threo*-**10** and 20 % of *erythro*-**10**. Recrystallization from ethyl acetate-petroleum ether (b. p. 40 – 70 °C) 1 : 1 gave 50.2 g (69 %) of a product of almost pure *threo*-configuration, which melted at 178 °C. – ^{1}H NMR (CD_3OD): δ = 3.80 (d, ^3J = 7.4 Hz, 1 H, 2-H), 5.10 (d, ^3J = 7.4 Hz, 1 H, 3-H), 7.15 – 7.26 (m, 10 H, aromat. H). – ^{13}C NMR (CD_3OD): δ = 62.4 (C-2), 78.0 (C-3), 128.0, 128.1, 128.3, 128.9, 129.2, 130.0 (aromat. CH), 138.6, 143.6 (aromat. C_q), 178.1 (C-1). – MS (FD): m/z (%) = 242 (100) $[M]^+$.

*3-Acetoxy-2,3-diphenylpropionic acid (**12**)*

To a refluxing solution of **10** (36.3 g, 0.15 mol) in 16.2 mL of pyridine and 150 mL of dry diethyl ether, acetyl chloride (**11**, 15.7 mL, 17.3 g, 0.2 mol) was added dropwise. The formed pyridine hydrochloride was removed by filtration and excess acetyl chloride and pyridine by distillation at 100 Pa. The remaining solid was recrystallized from ethanol; m. p. 186 °C, yield 25.1 g (59 %). – ^{1}H NMR ($CDCl_3$): δ = 2.05 (s, 3 H, CH_3), 4.05 (d, ^3J = 7.4 Hz, 1 H, 2-H), 6.20 (d, ^3J = 7.4 Hz, 1 H, 3-H), 7.07 – 7.17 (m, 10 H, aromat. H). – ^{13}C NMR ($CDCl_3$): δ = 21.0 (CH_3), 58.2 (C-2), 76.5 (C-3), 127.2, 128.1, 128.2, 128.3, 128.6, 128.8 (aromat. CH), 132.2, 136.8 (aromat. C_q), 169.6 (CO), 177.1 (C-1). – $C_{17}H_{16}O_4$ (284.3): calcd. C 71.82, H 5.67; found C 71.98, H 5.73.

*3-Acetoxy-2,3-diphenylpropionic acid chloride (**13**)*

Thionyl chloride (40 mL, 65.2 g, 0.55 mol) and **12** (22.7 g, 0.08 mol) were stirred for 20 h. Gentle heating accelerated the dissolution of the acid. Evaporation of excess acid chloride yielded a powder (11.3 g, 47 %), which melted at 168 °C. – ^{1}H NMR ($CDCl_3$): δ = 2.10 (s, 3 H, CH_3), 4.50 (d, ^3J = 7.4 Hz, 1 H, 2-H), 6.25 (d, ^3J = 7.4 Hz, 1 H, 3-H), 7.11 – 7.21 (m, 10 H, aromat. H). – ^{13}C NMR ($CDCl_3$): δ = 20.8 (CH_3), 68.2 (C-2), 76.5 (C-3), 127.2, 128.3, 128.5, 128.8, 129.0, 129.1 (aromat. CH), 131.1, 136.4 (aromat. C_q), 169.2 (CO), 172.3 (C-1). – MS (FD): m/z (%) = 302 (Cl isotope pattern, 93 %) $[M]^+$, 242 (100) $[M–CH_3COOH]^+$. – $C_{17}H_{15}ClO_3$ (302.8): calcd. C 67.44, H 4.99; found C 67.51, H 5.08.

*4-Diazo-1,2-diphenyl-3-oxo-butyl acetate (**15**)*

To a freshly prepared solution of diazomethane (**14**) in 250 mL of diethyl ether, prepared from 20.6 g (0.2 mol) *N*-nitroso-*N*-methylurea, **12** (10.6 g, 0.035 mol) was dropped at 0 °C. The stirring was continued at r. t. for 1 h. The solvent was evaporated and the crude product purified by column

filtration (6×40 cm SiO_2, CH_2Cl_2). A light-yellow product was obtained (6.3 g, 58 %) which decomposed on heating at 147 °C. – ^{1}H NMR ($CDCl_3$): $\delta = 2.05$ (s, 3 H, CH_3), 3.90 (d, $^3J = 7.4$ Hz, 1 H, 3-H), 5.30 (s, 1 H, 1-H), 6.35 (d, $^3J = 7.4$ Hz, 1 H, 4-H), 7.07 – 7.22 (m, 10 H, aromat. H). – ^{13}C NMR ($CDCl_3$): $\delta = 21.1$ (CH_3), 55.4 (C-1), 61.9 (C-3), 76.4 (C-4), 127.2, 127.8, 127.9, 128.0, 128.6, 128.9 (aromat. CH), 134.2, 138.0 (aromat. C_q), 169.3 (C-2). – IR (KBr): ν (cm^{-1}) = 2130 (CN_2), 1735 and 1635 (C=O). – MS (FD): m/z (%) = 308 (100) $[M]^+$. – $C_{18}H_{16}N_2O_3$ (308.1): calcd. C 70.12, H 5.23, N 9.09; found C 69.97, H 5.27, N 9.05.

*Alkaline fragmentation of **15***

To a solution of K_2CO_3 (0.83 g, 6.0 mmol) in 40 mL of H_2O, **15** (1.54 g, 5.0 mmol) dissolved in 100 mL of methanol was added dropwise under stirring. The extraction of the mixture with 200 mL of diethyl ether yielded an organic phase whose volatile parts, including benzaldehyde (**8**), were evaporated. The residue was subjected to column chromatography (3×60 cm SiO_2, CH_2Cl_2-H_3CCOCH_3 19 : 1). The first fraction consisted of 190 mg (24 %) of **19** and the second fraction of 635 mg (51 %) of **18**.

*(Z)-1-Diazo-3,4-diphenyl-but-3-en-2-one (**18**)*

Yellowish solid, which decomposes above 105 °C. – ^{1}H NMR ($CDCl_3$): $\delta = 5.00$ (s, 1 H, 1-H), 7.08 – 7.32 (m, 10 H, aromat. H), 7.64 (s, 1 H, 4-H). – ^{13}C NMR ($CDCl_3$): $\delta = 56.0$ (C-1), 128.2, 128.3, 129.0, 129.3, 129.9, 130.9 (aromat. CH), 134.6 (C-3), 135.9 (C-4), 136.6, 138.1 (aromat. C_q), 186.6 (C-2). – IR (KBr): ν (cm^{-1}) = 2110 (CN_2), 1635 (CO). – MS (FD): m/z (%) = 248 (100) $[M]^+$. – $C_{16}H_{12}N_2O$ (248.3): calcd. C 77.40, H 4.87, N 11.28; found C 77.29, H 4.68, N 11.13.

*1-Diazo-3-phenylpropan-2-one (**19**)*

Yellowish, viscous oil. – ^{1}H NMR ($CDCl_3$): $\delta = 3.60$ (s, 2 H, 3-H), 5.15 (s, 1 H, 1-H), 7.25 – 7.35 (m, 5 H, aromat. H). – ^{13}C NMR ($CDCl_3$): $\delta = 48.0$ (C-3), 54.7 (C-1), 127.2, 128.8, 129.3 (aromat. CH), 134.5 (aromat. C_q), 192.6 (C-2). The compound corresponds to an authentic sample [9].

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