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The Conversion of 1,2-Disubstituted 1,2,3-Triazol-5-ones to 2-Substituted 4-Hydroxy-1,2,3-triazoles

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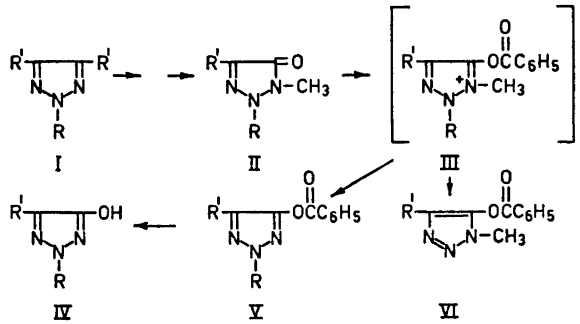
1,2-Disubstituted 1,2,3-triazol-5-ones, when heated with benzoyl chloride, afford 2-substituted 4-benzoyloxy-1,2,3-triazoles (V) which by hydrolysis give 2-substituted 4-hydroxy-1,2,3-triazoles (IV).

Recently, the preparation of 2-alkylsubstituted 4-hydroxy-1,2,3-triazoles (IV) was described.[1] These compounds were prepared in fairly good yields from 4-hydroxy-1,2,3-triazoles which, in succession, were dibenzoylated, selectively *N*-debenzoylated, alkylated, and hydrolyzed. However, the number of reaction steps, including the preparation of the starting material, the 4-hydroxy-1,2,3-triazoles,[2,3] were rather large. Furthermore, 2-aryl-4-hydroxy-1,2,3-triazoles were not available by this method. Until now, only a few 2-aryl-4-hydroxy-1,2,3-triazoles have been described.[4–6] Thus, 2-phenyl-4-



	R	R'
a	CH_3	H
b	CH_3	Br
c	C_6H_5	H

hydroxy-1,2,3-triazole (IVc) was reported to be prepared *via* diazotation and hydrolysis of 2-phenyl-4-amino-1,2,3-triazole.[5] However, this preparation could not be reproduced in our hands.

The synthesis described in the present paper produces 2-alkyl- or 2-aryl-4-hydroxy-1,2,3-triazoles in good yields through few reactions steps. The starting material is the readily available 1,2-disubstituted 1,2,3-triazol-5-ones (II) which are prepared from 2-substituted 1,2,3-triazoles (I) *via* quaternization, bromination, and replacement of bromine with hydroxide.[7] The 1,2-disubstituted 1,2,3-triazol-5-ones (II), when heated with benzoyl chloride, lost the 1-alkyl group and gave 2-substituted 4-benzoyloxy-1,2,3-triazoles (V). In analogy to the corresponding reaction of 1,3-disubstituted 4-(1,2,3-triazolio)-oxides[8] the benzoyl chloride probably attacks the oxygen atom with the formation of a 1,2-disubstituted-4-benzoyloxy-1,2,3-triazolium salt (VI). The latter then looses the *N*-1 methyl group, thereby forming the benzoyloxy-1,2,3-triazole (V). Hydrolysis of (V) subsequently yields the 2-substituted 4-hydroxy-1,2,3-triazoles (IV).

In this way, 2-methyl-1,2,3-triazole (Ia), *via* 1,2-dimethyl-1,2,3-triazol-5-one (IIa), gave 2-methyl-4-hydroxy-1,2,3-triazole (IVa). Similarly, 2-phenyl-1,2,3-triazole (Ic), *via* 1-methyl-2-phenyl-1,2,3-triazol-5-one (IIc), yielded 2-phenyl-4-hydroxy-1,2,3-triazole (IVc); and 2-methyl-4,5-dibromo-1,2,3-triazole (Ib) produced 2-methyl-5-bromo-4-hydroxy-1,2,3-triazole (IVb) *via* the bromo-triazolone (IIb).

Whereas the triazolones (IIa) and (IIc) reacted with benzoyl chloride at 120°C, the bromo-triazolone (IIb) required heating to 180°C. Apparently, the electron withdrawing bromine atom renders the adjacent oxygen atom of IIb less nucleophilic. The addition of pyridine improved the yield considerably. Presumably, the pyridine accelerates the reaction by taking up the alkyl chloride which is cleaved off by the subsequent dealkylation of the intermediate III. A similar effect has been found in the reaction of 4-(1,2,3-triazolio)sulfides with benzoyl chloride.[9] The addition of pyridine was not attempted in the reactions of the 1,2,3-triazol-5-ones (IIa and IIc) with benzoyl chloride since these reactions gave satisfactory yields.

In the reaction of the bromo-1,2,3-triazol-5-one (IIb) with benzoyl chloride 1-methyl-4-bromo-5-benzoyloxy-1,2,3-triazole (VIb) was formed as a byproduct.* The latter may arise if the intermediate benzoyloxy-1,2,3-triazolium salt (IIIb) dealkylates by cleaving off the *N*-2-methyl group. No isomeric byproducts were observed when the 1,2,3-triazol-5-ones (IIa and IIc) were treated with benzoyl chloride. Provided that the reactions are kinetically controlled, the product distribution in the reactions of 1,2,3-triazol-5-ones (IIa and IIb) with benzoyl chloride reflects the relative aptitude for group detachment. Consequently, an alkyl group at position 1 is a better leaving group than an alkyl group at position 2. However, an inductively electron withdrawing bromine atom at position 4 apparently drains the nitrogen atom at position 2 of electrons, thus making this position more attractive to the nucleophilic attack of the chloride ion (or of the pyridine), which most probably initiates the dealkylation.

* The addition of pyridine apparently did not influence the ratio between the two products Vb and VIb.

The infrared spectrum of 2-methyl-4-hydroxy-1,2,3-triazole (IVa) showed that the compound adopts the hydroxy-structure rather than a keto-form or a dipolar form.[1] Similarly, the infrared spectra of 2-phenyl-4-hydroxy-1,2,3-triazole (IVc) and of 2-methyl-5-bromo-4-hydroxy-1,2,3-triazole (IVb), in potassium bromide discs or in chloroform solution, showed no absorptions in the carbonyl region above 1600 cm^{-1}. This indicates that both compounds adopt the hydroxy-structure IV.

EXPERIMENTAL

Column chromatography was carried out as described previously.[10] Preparative thin layer chromatography (TLC) was carried out on 20 × 40 cm plates with a 1 mm layer of silica gel (Merck PF_{254}). NMR-spectra were obtained on a Varian A-60 instrument. Position of signals are given in ppm (δ-values) relative to tetramethylsilane (TMS). Deuteriochloroform was used as a solvent. IR-spectra were obtained in potassium bromide discs. Melting points are uncorrected. All compounds were identified through their melting points, IR-, and NMR-spectra.

2-Phenyl-4-benzoyloxy-1,2,3-triazole (Vc). 1-Methyl-2-phenyl-1,2,3-triazol-5-one [7] (IIc) (1.24 g) and benzoyl chloride (1.75 ml) were heated to 115°C for 3 h. Hexane (17.5 ml) was then added and the mixture was kept at −30°C overnight. The precipitate was filtered off, washed with hexane (2 × 10 ml), dissolved in methylene chloride (50 ml), and extracted 3 times with saturated aqueous sodium hydrogen carbonate. The organic layer was then dried (magnesium sulfate) and the solvent was removed. The residue was washed with hexane (2 × 15 ml) and recrystallized from ethyl acetate-hexane. Yield 1.03 g (55 %) of 2-phenyl-4-benzoyloxy-1,2,3-triazole (Vc), colourless crystals, m.p. 92−93°C. Further recrystallization raised the melting point to 94°C. (Found: C 68.02; H 4.35; N 15.95. Calc. for $C_{15}H_{11}N_3O_2$: C 67.91; H 4.18; N 15.84.) (IR: $\nu_{C=O} = 1745$ cm^{-1}.)

2-Methyl-4-benzoyloxy-1,2,3-triazole (Va). 1,2-dimethyl-1,2,3-triazol-5-one [7] (IIa) (397 mg) and benzoyl chloride (5.20 ml) were heated to 140°C for 115 min, and hexane (52 ml) was added as above. The crude precipitate was recrystallized from hexane giving 224 mg (31 %) of 2-methyl-4-benzoyloxy-1,2,3-triazole (Va), m.p. 61−63°C. IR- and NMR-spectra proved the identity with the material described previously.[1] From the combined mother liquors hexane and benzoyl chloride were distilled off (final bath temperature 120°C, pressure 15 mmHg). The residue was chromatographed on silica gel (50 g) using ether−hexane (1 : 4) as eluent. The first fraction contained benzoyl chloride. The next fraction contained 466 mg of Va. One recrystallization from hexane afforded 420 mg (59 %) of Va, m.p. 55−57°C, bringing the total yield of this compound to 90 %. Further recrystallization raised the melting point to 61−63°C.

2-Methyl-5-bromo-4-benzoyloxy-1,2,3-triazole (Vb). 1,2-Dimethyl-4-bromo-1,2,3-triazol-5-one (IIb) (266 mg), pyridine (0.11 ml), and benzoylchloride (1.90 ml) were heated to 180°C for 90 min. The benzoyl chloride and pyridine were distilled off at 10 mmHg (bath temperature 120°C). The residue was chromatographed on silica gel (50 g) using ether-hexane (1 : 4) as eluent. The first fraction contained benzoyl chloride. Then two close-running fractions left the column. As shown by an NMR-spectrum, the first of these contained 59 mg of a mixture of 2-methyl-5-bromo-4-benzoyloxy-1,2,3-triazole (Vb) and an unidentified compound. Several unsuccessful attempts to separate the two compounds were made, including sublimation and rechromatography with several eluents. The next fraction contained 189 mg (48 %) of pure Vb as colourless crystals, m.p. 83°C. Recrystallization from hexane raised the melting point to 85°C. (Found: C 42.71; H 2.80; N 15.05; Br 28.45. Calc. for $C_{10}H_8N_3O_2Br$: C 42.58; H 2.86; N 14.89; Br 28.33.) (NMR: N-CH_3 $\delta = 4.16$, $J_{^{13}C-H} = 144$ Hz. IR: $\nu_{C=O} = 1753$ cm^{-1}.) The column was then eluted with ether. This gave a fraction which consisted of a mixture of 1-methyl-4-bromo-5-benzoyloxy-1,2,3-triazole (VIb) and benzoic acid. The mixture was dissolved in methylene chloride and extracted with saturated aqueous sodium hydrogen carbonate. The solution was dried (magnesium sulfate) and the solvent was removed giving 37 mg (10 %) of (VIb) as colourless crystals, m.p. 80−81°C. Recrystallization from ether-hexane raised the melting point to 90−91°C. (Found: C 42.69; H 3.03; N 14.92; Br 28.24.) The compound

was identified through its NMR-spectrum (N-CH_3 $\delta = 3.97$, $J_{^{13}C-H} = 144$ Hz. IR: $\nu_{C-O} = 1753$ cm^{-1}). Melting point, IR-, and NMR-spectra were different from those of 1-methyl-5-bromo-4-benzoyloxy-1,2,3-triazole.[8]

2- Phenyl-4-hydroxy-1,2,3-triazole (IVc). 2-Phenyl-4-benzoyloxy-*1,2,3*-triazole (Vc) (1.03 g) and 1 N sodium hydroxide (8.00 ml) were heated to reflux for 90 min. Acidification with 1 N hydrochloric acid and cooling to 0°C gave colourless crystals which were dried and extracted with ether (3 × 10 ml). Removal of the ether left a mixture of benzoic acid and 2-phenyl-4-hydroxy-1,2,3-triazole (IVc) which was recrystallized 3 times from hexane yielding 525 mg (84 %) of pure IVc as colourless crystals, m.p. 123 – 124°C. (Reported m.p., 124°C[5].) (Found: C 59.47; H 4.54; N 26.15. Calc. for $C_8H_7N_3O$: C 59.62; H 4.38; N 26.07.) The IR-spectrum was devoid of absorption in the 1600 – 1800 cm^{-1} range, in a potassium bromide disc as well as in chloroform solution.

2-Methyl-5-bromo-4-hydroxy-1,2,3-triazole (IVb). 2-Methyl-5-bromo-4-benzoyloxy-1,2,-3-triazole (Vb) (188 mg) and 1 N sodium hydroxide were heated with stirring to reflux for 3 h. 4 N Hydrochloric acid (0.52 ml) was then added, the water was removed *in vacuo*, and the residue was extracted with methylene chloride (5 × 10 ml). Removal of the methylene chloride gave a residue which was purified by preparative TLC eluting three times with ether-hexane (1 : 4). The first fraction contained benzoic acid; the second fraction contained 117 mg (98 %) of 2-methyl-5-bromo-4-hydroxy-1,2,3-triazole (IVb) as colourless crystals, m.p. 132 – 137°C. Recrystallization from ether-hexane raised the melting point to 142 – 146°C. (Found: C 20.37; H 2.28; N 23.47; Br 44.74. Calc. for $C_3H_4N_3OBr$: C 20.24; H 2.27; N 23.61; Br 44.90.)

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