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Mendeleev Commun., 1995, **5(6)**, 234–235

Mendeleev
Communications

A Novel Synthesis of 1,2-Dihydroquinoline Derivatives

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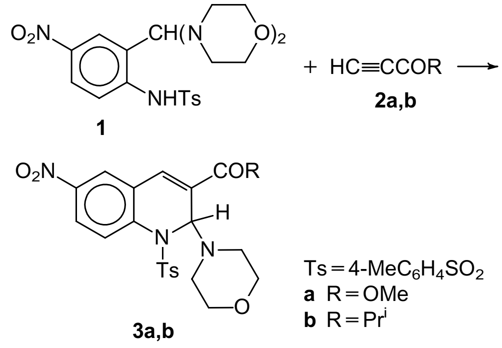
2-Tosylamino-5-nitrobenzaldehyde di(morpholin-4-yl)aminal reacts with substituted acetylenes to yield novel 1,2-dihydroquinoline derivatives.

A number of methods for the preparation of 1,2-dihydroquinoline derivatives are known. Reissert bases were obtained by interaction of quinolines with chloroanhydrides of carboxylic acids and HCN or KCN.[1] Their acetylenic analogues have also been described.[2] Anilino magnesium halides react with aldehydes of general formula RCH_2CHO to give 1,2,3-trisubstituted 1,2-dihydroquinolines.[3] 2-Methyl-2,4-diphenyl-1,2-dihydroquinolines were obtained by treatment of lithium anilides with tin(IV) chloride in boiling toluene and then with phenylacetylene.[4] Quinoline oxide reacts with acetoacetic or cyanoacetic esters in the presence of acetic anhydride forming 1*H*-2-vinylidene-1,2-dihydroquinoline derivatives.[5]

Aromatic *o*-aminoaldehydes and their aminals are efficient precursors in the synthesis of different heterocyclic compounds.[6–11]

Recently, we described the synthesis of 2*H*-6-nitro-1,2-dihydrochromene derivatives from aminals of nitrosalicylic aldehydes.[12] In the present communication we report a new method for the synthesis of 2*H*-1,2-dihydroquinoline derivatives.

We have found that 2-tosylamino-5-nitrobenzaldehyde di(morpholin-4-yl)aminal **1** [or an adduct **1a** of **1** with CCl_4 (1:1)] reacts with methyl propynoate or 4-methylprop-1-yn-3-one **2a,b**, rapidly and exothermically in the absence of solvent, to give 2*H*-1-tosyl-2-morpholino-3-alkoxycarbonyl-6-nitro-1,2-dihydroquinolines **3**, Scheme 1.



Scheme 1

We propose that the first step of this reaction involves formation of *Z*-isomers of **4**, as has recently been found for the reactions of 2-tosylaminobenzaldehyde aminals with acetylenes.[11] In that case, compounds **4** underwent regrouping to yield compounds **3** with expansion of the ring and transfer of two functional groups, Scheme 2.

Compounds **3a,b** were characterized by IR (Specord IR-75, Nujol) and ^{1}H NMR spectra (UNITY 300) and elemental analysis data.[†]

Aminal **1** was prepared in a similar manner to the aminal of 5-nitrosalicylaldehyde.[10] Adduct **1a** was obtained by treatment of a solution of **1** in isopropyl alcohol with excess CCl_4. The structure of compound **1a** was confirmed by an X-ray structural study which will be published elsewhere.

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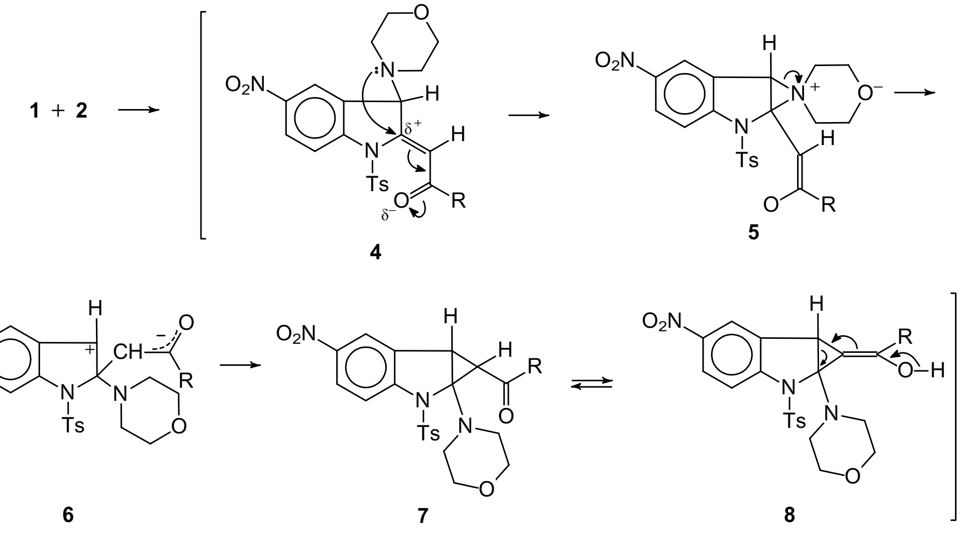
Received: Moscow, 10th April 1995
Cambridge, 7th June 1995; Com. 5/02535D



Scheme 2

[†] 2*H*-1-tosyl-2-morpholino-3-methoxycarbonyl-6-nitro-1,2-dihydroquinoline **3a**. Compound **2a** (0.18 ml) was added to the crystalline adduct **1a** (0.48 g, 0.6 mmol). After a self-initiated exothermic reaction 3 ml ethanol was added to the reaction mixture. The mixture was cooled by an ice bath and rubbed with a glass stick. The resulting precipitate was filtered off, washed with cooled ethanol and dried, yield 0.3 g (83%); colourless crystals, m.p. 161–162 °C (from EtOH). IR ν/cm^{-1}: 1713 (C=O), 1641, 1621, 1601, 1581 (C=C, aromatic), 1527, 1361 (NO_2), 1347, 1167 (SO_2), 1127 (C–O–C); ^{1}H NMR ($CDCl_3$) δ: 2.31 (s, 3H, Me), 2.36 (m, 2H, CH_2N), 2.57 (m, 2H, CH_2N), 3.54 (m, 4H, CH_2O, $J = 3$ Hz), 3.87 (s, 3H, OMe), 6.28 (s, 1H, CH), 7.08 (d, 2H, H_{arom}, $J = 8$ Hz), 7.30 (d, 2H, H_{arom}, $J = 8$ Hz), 7.44 (s, 1H, ^{5}CH), 8.07 (d, 1H, ^{5}CH, $^4J = 2.6$ Hz), 8.12 (d, 1H, ^{8}CH, $J = 9$ Hz), 8.22 (dd, 1H, ^{7}CH, $^3J = 9$ Hz, $^4J = 2.6$ Hz). (Found: C 55.73, H 5.32, N 8.50, S 7.09. Calc. for $C_{22}H_{23}N_3O_7S$: C 55.81, H 4.86, N 8.88, S 6.77%).

2*H*-1-Tosyl-2-morpholino-3-(prop-2-yl)carbonyl-6-nitro-1,2-dihydroquinoline **3b**. This was obtained under similar conditions as above from **1a** (0.48 g, 0.6 mmol) and **2b** (0.2 ml). Ethanol (3 ml) and pentane (2 ml) were then added to the reaction mixture. The mixture was cooled by an ice bath and rubbed with a glass stick. The resulting precipitate was filtered off, washed with cooled ethanol and pentane and dried, yield 0.2 g (56%); colourless crystals, m.p. 150–151 °C (from EtOH). IR ν/cm^{-1} 1661 (C=O), 1634, 1614, 1581 (C=C, aromatic), 1527, 1367 (NO_2), 1354, 1167 (SO_2), 1114 (C–O–C); ^{1}H NMR ($CDCl_3$) δ: 1.06 (d, 3H, Me, $J = 6.7$ Hz), 1.15 (d, 3H, Me, $J = 6.7$ Hz), 2.29 (s, 3H, Me), 2.36 (m, 2H, CH_2N), 2.55 (m, 2H, CH_2N), 3.19 (m, 1H, CH, $J = 6.7$ Hz), 3.51 (t, 4H, CH_2O, $J = 4.7$ Hz), 6.33 (s, 1H, CH), 7.05 (d, 2H, H_{arom}, $J = 7.9$ Hz), 7.24 (d, 2H, H_{arom}, $J = 7.9$ Hz), 7.28 (s, 1H, ^{4}CH), 8.10 (d, 1H, ^{5}CH, $^4J = 2.4$ Hz), 8.14 (d, 1H, ^{8}CH, $J = 9$ Hz), 8.24 (dd, 1H, ^{7}CH, $^3J = 9$ Hz, $^4J = 2.6$ Hz). (Found: C 57.44, H 5.17, N 8.23, S 6.09. Calc. for $C_{24}H_{24}N_3O_6S$: C 57.37, H 4.78, N 8.37, S 6.37%).