
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.

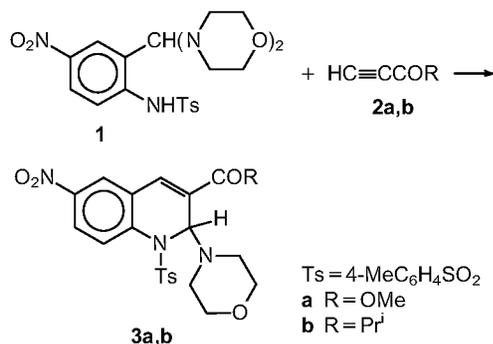
A number of methods for the preparation of 1,2-dihydroquinoline derivatives are known. Reissert bases were obtained by interaction of quinolines with chloroanhydrides of carboxylic acids and HCN or KCN.¹ Their acetylenic analogues have also been described.² Anilino magnesium halides react with aldehydes of general formula RCH₂CHO 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 amins 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 amins 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 CCl₄ (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.

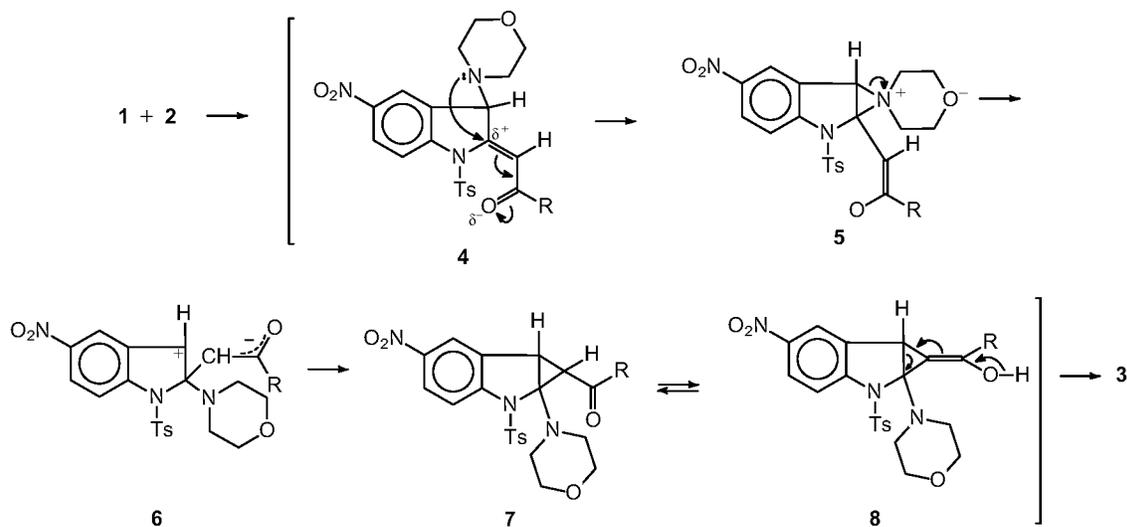


Scheme 1

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 amins 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 ¹H 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 CCl₄. The structure of compound **1a** was confirmed by an X-ray structural study which will be published elsewhere.



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 (NO₂), 1347, 1167 (SO₂), 1127 (C–O–C); ¹H NMR (CDCl₃) δ : 2.31 (s, 3H, Me), 2.36 (m, 2H, CH₂N), 2.57 (m, 2H, CH₂N), 3.54 (m, 4H, CH₂O, *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, ⁵CH), 8.07 (d, 1H, ⁵CH, ⁴*J* = 2.6 Hz), 8.12 (d, 1H, ⁸CH, *J* = 9 Hz), 8.22 (dd, 1H, ⁷CH, ³*J* = 9 Hz, ⁴*J* = 2.6 Hz). (Found: C 55.73, H 5.32, N 8.50, S 7.09. Calc. for C₂₂H₂₃N₃O₇S: C 55.81, H 4.86, N 8.88, S 6.77%).

References

- 1 K. V. Vatsuro and T. L. Mishchenko, *Imennye reaktsii v organicheskoi khimii (Named reactions in organic chemistry)*, Khimiya, Moscow, 1976 (in Russian).
- 2 T. Agawa and S. I. Miller, *J. Am. Chem. Soc.*, 1961, **83**, 449.
- 3 Y. Sato, H. Kojima and H. Shirai, *Tetrahedron*, 1974, **30**, 2695.
- 4 A. Arduini, F. Bigi, G. Casiraghi, G. Casnati and G. Sartori, *Synthesis*, 1981, 975.
- 5 M. Iwao and T. Kuraishi, *J. Heterocycl. Chem.*, 1978, **15**, 1425.
- 6 P. Caluwe, *Tetrahedron*, 1980, **36**, 2359.
- 7 L. Yu. Ukhin, V. N. Komissarov, I. A. Litvinov, V. A. Piven and N. A. Litvinova, *Dokl. Akad. Nauk SSSR*, 1988, **303**, 646 [*Dokl. Chem. (Engl. Transl.)*, 1988, 344].
- 8 L. Yu. Ukhin, V. N. Komissarov, M. S. Korobov and L. E. Nivorozhkin, *Mendeleev Commun.*, 1991, 71.
- 9 L. Yu. Ukhin, V. N. Komissarov, M. S. Korobov and L. E. Nivorozhkin, *Zh. Org. Khim.*, 1992, **28**, 408 (*Russ. J. Org. Chem.*, 1992, 331).
- 10 L. Yu. Ukhin, V. N. Komissarov, S. V. Lindeman, V. N. Khrustalev and Yu. T. Struchkov, *Izv. Akad. Nauk, Ser. Khim.*, 1994, 455 (*Russ. Chem. Bull.*, 1994, **43**, 413).
- 11 L. Yu. Ukhin, V. N. Komissarov, Zh. I. Orlova, G. S. Borodkin, S. V. Lindeman, V. N. Khrustalev and Yu. T. Struchkov, *Izv. Akad. Nauk, Ser. Khim.* (in press).
- 12 L. Yu. Ukhin, Zh. I. Orlova, O. V. Shishkin and Yu. T. Struchkov, *Izv. Akad. Nauk, Ser. Khim.* (in press).
- 13 G. Kalischer, H. Ritter and E. Honold, *US Patent 1.876.955 (Chem. Abstr.*, 1933, **27**, P993²).

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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 (NO₂), 1354, 1167 (SO₂), 1114 (C–O–C); ¹H NMR (CDCl₃) 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, CH₂N), 2.55 (m, 2H, CH₂N), 3.19 (m, 1H, CH, *J* = 6.7 Hz), 3.51 (t, 4H, CH₂O, *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, ⁴CH), 8.10 (d, 1H, ⁵CH, ⁴*J* = 2.4 Hz), 8.14 (d, 1H, ⁸CH, *J* = 9 Hz), 8.24 (dd, 1H, ⁷CH, ³*J* = 9 Hz, ⁴*J* = 2.6 Hz). (Found: C 57.44, H 5.17, N 8.23, S 6.09. Calc. for C₂₄H₂₄N₃O₆S: C 57.37, H 4.78, N 8.37, S 6.37%).