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UNEXPECTED TRANSFORMATION OF SPIRO-3-CYANOMETHYL-3-METHYL-1,2,3,4,5,6-HEXAHYDROBENZO[*f*]ISOQUINOLINIUM-1,2'-(1',2',3',4'-TETRAHYDRONAPHTHALEN-1'-ONE) CHLORIDE TO SPIRO-3,4,5,6-TETRAHYDRO-2H-BENZO[*h*]CHROMENE-2,2'-(TETRAHYDRONAPHTHALEN-1'-ONE)

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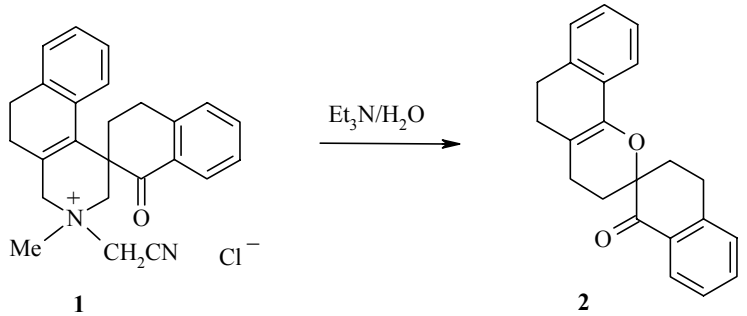
Keywords: spiro-3-cyanomethyl-3-methyl-1,2,3,4,5,6-hexahydrobenzo[*f*]isoquinolinium-1,2'-(1',2',3',4'-tetrahydronaphthalen-1'-one) chloride, spiro-3,4,5,6-tetrahydro-2H-benzo[*h*]chromene-2,2'-(tetrahydronaphthalen-1'-one), hydration, deamination.

In a study of sigmatropic transformations of quaternary salts of various tetrahydropyridinium derivatives, we have discovered an unexpected cascade transformation of spirohexahydrobenzo[*f*]isoquinolinium-1,2'-(tetrahydronaphthalen-1'-ne) chloride (**1**) into spirotetrahydro-2H-benzo[*h*]chromene-2,2'-(tetrahydronaphthalen-1'-one) (**2**). This reaction proceeds in the presence of moist triethylamine upon heating salt **1** in moist dioxane at reflux for 20 h. The structure of compound **2** isolated chromatographically in 40% yield was established unequivocally by GC/MS and ^{1}H NMR spectroscopy as well as by comparison with the data of Quail et al. [4].



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The reaction cascade leading to the final spiro compound **2** probably begins with hydration of quaternary salt **1** and formation of the 10*b*-hydroxy derivative, which then undergoes the retroaldol condensation to give a double Mannich base. Then, this double Mannich base undergoes deamination to give an intermediate 2-methylene-α-tetralone. This intermediate tetralone readily dimerizes through a [4+2] cycloaddition (Diels-Alder reaction). A literature search showed that dimer **2** was obtained by various workers by the action of base on 2-(N,N-dimethylaminomethyl)-α-tetralone hydrochloride [1-3]. Quail et al. [4] unequivocally established the structure of this compound by X-ray diffraction structural analysis and also found that dimer **2** has cytotoxic and antitumor effects on murine and human cells.

The IR spectra were taken on an Infralum FT-801 spectrometer for KBr pellets. The ^{1}H NMR spectra were taken on a Bruker WP-400 spectrometer at 400 MHz in $CDCl_3$ with the residual protons of the deuterated solvent as the internal standard. An Agilent 1100 liquid chromatograph with DAD and Sedex 75 detectors combined with an Agilent LC/MSD VL mass spectrometer with electrospray ionization was used for analyzing the reaction mixture and purity of isolated product **2**.

A sample of starting quaternary salt **1** was obtained in 68% yield by quaternization of spiro-N-methyl-hexahydrobenzo[*f*]isoquinoline-1,2'-(tetrahydronaphthalen-1'-one) by chloroacetonitrile upon heating in dichloromethane at reflux for 5 h; mp 174-175°C. Mass spectrum, *m/z* (HPLC/MS, proton ionization): 369 $[M\text{-}Cl]^+$. Found, %: Cl 8.97; N 6.52. $C_{25}H_{25}ClN_2O$. Calculated, %: Cl 8.77; N 6.92. M 404.5.

Spiro-3,4,5,6-tetrahydro-2H-benzo[*h*]chromene-2,2'-(1',2',3',4'-tetrahydronaphthalen-1'-one) (2). Moist triethylamine (0.32 ml, 3.7 mmol) was added to a suspension of salt **1** (0.5 g, 1.2 mmol) in moist dioxane and the solution obtained was heated at reflux for 20 h. The precipitate was separated and the filtrate was evaporated. The residue was subjected to chromatography on a silica gel column with gradient elution proceeding from 1:0 to 1:10 hexane–ethyl acetate to give 0.16 g (40%) compound **2** as colorless crystals, mp 103-105°C (mp 103-105°C [4]). IR spectrum, ν, cm^{-1}: 1677 (C=O), 1622 (C=C). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.89 and 2.40 (1H each, both m, CH_2); 2.17-2.27 (6H, m, CH_2); 2.76 (2H, t, *J* = 8.0, CH_2); 3.09 and 3.22 (1H each, both m, CH_2); 7.07 (3H, m, H arom); 7.20 (1H, m, H arom); 7.37 (2H, m, H arom); 7.55 (1H, t, *J* = 7.2, H-6'); 7.88 (1H, d, *J* = 7.6, H-8'). Mass spectrum, *m/z*: 317 $[M+H]^+$ (proton ionization). Calculated: M 316.

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