Communications

Novel Reaction of *o*-Phenolic Mannich Bases with α-Chloroacrylonitrile

Summary: In an attempt to use phenolic Mannich bases in syntheses of 3-chromanones, a novel transformation leading to a convenient and simple synthesis of naphthonaphthopyranopyrans was encountered.

Sir: *o*-Phenolic Mannich bases are versatile synthons which are widely employed in diverse types of organic transformations. The phenolic Mannich bases were prepared from phenols by known methods.[1-4] In the area of cycloaddition reactions of α,β-unsaturated carbonyls,[5] *o*-quinone methides generated from phenolic Mannich bases have proven very valuable as intermediates,[6] especially for the construction of condensed benzopyran ring systems. In an attempt to extend this approach for a one-pot synthesis of 3-chromanones involving the reaction of phenolic Mannich bases and α-chloroacrylonitrile, a ketene equivalent,[7] we have encountered a novel transformation leading to a convenient and simple synthesis of 7a,15a-dihydro-7a-amino-15*H*,16*H*-naphtho[2,1-*b*]-naphtho[1′,2′:5,6]pyrano[3,2-*e*]pyrans[8] as outlined in Scheme I.

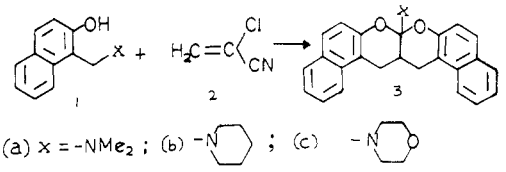
The reaction of 1-[(dimethylamino)methyl]-2-naphthol (**1a**) and α-chloroacrylonitrile (**2**) in dry dioxane under reflux conditions yielded a white solid. Elemental analysis and spectral data clearly indicated it to be neither the expected cycloadduct, viz., 3-chloro-3-cyano-2*H*-naphtho-[3,2-*e*]pyran, nor the corresponding 3-chromanone. On the basis of its analytical and IR, mass, ^{1}H NMR, and ^{13}C NMR spectral data, structure **3a** is assigned to this product.

Other Mannich bases of β-naphthol also reacted similarly with α-chloroacrylonitrile and afforded the respective chromanochromans listed in Table I. Attempts to extend this reaction to the Mannich bases of simple and substituted phenols, however, failed to furnish the expected products. The reason for the failure may be due to the relatively greater thermal stability of these phenolic Mannich bases compared to that of the β-naphthol Mannich base and consequent difficulty in generating the quinone methides under the conditions mentioned in this paper.

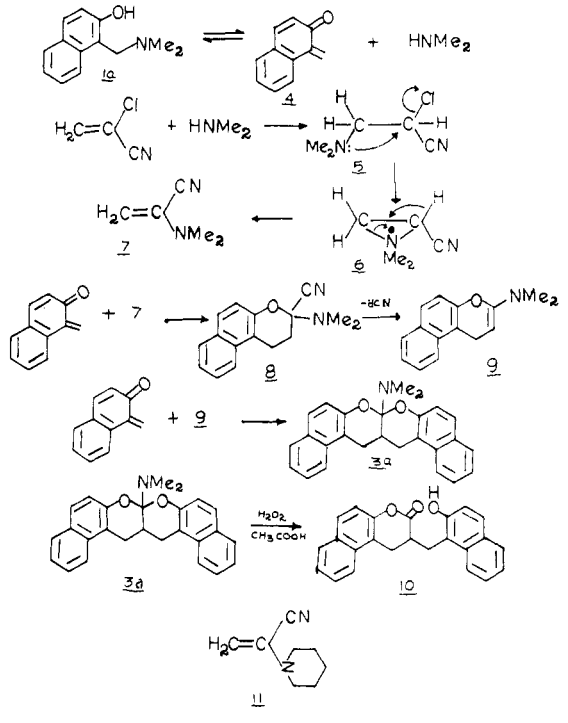
The mechanism of this transformation has been rationalized as depicted in Scheme II.

Mannich bases of phenols are thermally unstable and decompose to the respective secondary amine and *o*-quinone methide. It is conceivable that in the presence of α-chloroacrylonitrile the liberated secondary amine leads

Scheme I



Scheme II



to the formation of α-cyano enamine **7** through a Michael addition followed by neighboring-group participation. In fact, thiols have been known to furnish analogous α-(arylthio)acrylonitriles[9,10] when treated with α-chloroacrylonitrile. A [4 + 2] cycloaddition between the in situ liberated *o*-quinone methide and the α-cyano enamine **7** and a subsequent elimination of HCN from the cycloadduct would lead to the 2-aminonaphthopyran **9** which by way of one more [4 + 2] cycloaddition with *o*-quinone methide would lead to the final product (**3a**). The proposed mechanism is supported by the observation that α-chloroacrylonitrile has been found to furnish the α-cyano enamine when heated with secondary amines in the absence of the Mannich bases. Further, when the α-cyano enamines were treated with the Mannich base of β-naphthol under identical conditions, they afforded the chromanochromans **3** in 75% yield. It was also observed that when the Mannich bases of β-naphthol and α-chloroacrylonitrile were reacted in the presence of *p*-toluene sulfonic acid, the above-described transformation did not occur.[17] Similarly, when the quaternary methiodide was employed in the place of the free base, the chromanochroman **3a** was not formed. The regiochemistry of the

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Table I. Physical and Spectral Data of 3a-c[a]

compd	yield, %	mp, °C	^{1}H NMR,[b] δ	^{13}C NMR,[b] ppm
3a	55	221	2.6 (s, 6 H), 2.9-3.4 (m, 5 H), 7.0-7.8 (m, 12 H)	152.34 (s), 135.67 (s), 132.46 (s), 131.48 (d), 131.11 (d), 129.36 (d), 126.56 (d), 125.10 (d), 121.54 (d), 116.19 (s), 110.60 (s), 39.58 (q), 31.50 (d), 29.50 (t)
3b	72	225-226	1.4 (s, 6 H), 2.8-3.4 (m, 9 H), 7.0-7.8 (m, 12 H)	152.50 (s), 135.60 (s), 132.33 (s), 131.40 (d), 126.38 (d), 125.02 (d), 121.57 (d), 116.22 (s), 110.50 (s), 47.90 (t), 31.08 (s), 29.43 (t), 29.20 (t), 27.94 (t), 130.87 (d), 129.21 (d)
3c	60	222-224	2.9-3.35 (m, 9 H), 3.7 (t, 4 H, J = 8 Hz), 7.0-7.8 (m, 12 H)	

[a] Satisfactory analytical data (±4%) for C and H were reported for 3a-c. [b] $CDCl_3$ with Me_4Si as the standard was used as the solvent for ^{1}H and ^{13}C NMR spectra.

two [4 + 2] cycloadditions, viz., the formation of the intermediate **8** and the final product **3** envisaged in the mechanistic proposal, is also in accordance with the literature reports.[11-14]

With a view to obtaining additional proof for the proposed structure, we made an attempt to prepare the *N*-oxide of **3a** and pyrolyze it to the Cope elimination product. Reaction of the adduct **3a** with 30% H_2O_2 in acetic acid yielded the lactone **10** [mp 219 °C (lit.[15] mp 220 °C)] instead of the expected *N*-oxide.

All melting points were uncorrected. IR spectra were recorded on a Perkin-Elmer 257 grating spectrometer as potassium bromide disks (KBr). ^{1}H and ^{13}C NMR spectra were recorded on a Varian XL-100 spectrometer. Mass spectra were obtained with a Varian MAT CH-7 spectrometer. The samples were prepared for NMR analysis by using $CDCl_3$ with Me_4Si as internal standard.

General Procedure for the Reaction α-Chloroacrylonitrile with Mannich Bases of β-Naphthol. A mixture of the Mannich base of β-naphthol (0.02 mol) and α-chloroacrylonitrile (0.01 mol) was refluxed for 10 h in dry dioxane (15 mL). After the completion of the reaction, the mixture was poured into water and extracted with ether (100 mL). The ether layer was washed with water and cold, dilute sodium hydroxide solution and finally dried over Na_2SO_4. After evaporation of the ether, the product was isolated. The crude product was recrystallized from benzene–ethanol.

Preparation of α-Piperidinoacrylonitrile (11). To a solution of α-chloroacrylonitrile (0.87 g, 0.01 mol) in 10 mL of dry benzene was added piperidine (0.02 mol, 1.72 g) drop by drop for 45 min. The reaction mixture was stirred for 4 h and then heated under reflux conditions for another 4 h. A solid separated out of the reaction mixture. This solid was filtered, the filtrate was washed with water, and the organic layer was dried over Na_2SO_4. After evaporation of the benzene solvent, a crude sample of **11** was obtained. It was purified by distillation at 100 °C (2 mm). The distilled product was further purified by column chromatography using neutral alumina and benzene–hexane (1:1) as the eluent: yield 80%; IR 2200, 1630, 1250, 1120 cm^{-1}; ^{1}H NMR δ 1.6 (s, 6 H), 3.0 (m, 4 H), 4.55 (d, 1 H, J = 2 Hz), 4.75 (d, 1 H, J = 2 Hz).

Reaction of 1-(Piperidinomethyl)-2-naphthol (1b) with α-Piperidinoacrylonitrile (11). A mixture of 1-(piperidinomethyl)-2-naphthol (2.4 g, 0.01 mol) and α-piperidinoacrylonitrile (0.68 g, 0.005 mol) in dry dioxane (10 mL) was refluxed for 5 h. The reaction mixture was poured into water, this was extracted with ether, and the extract was dried over Na_2SO_4. After evaporation of the ether, 1.5 g of the product (**3b**) was obtained in 75% yield, and the crude product was recrystallized from benzene–ethanol.

Reaction of 3a with H_2O_2 in an Acetic Acid Mixture. Formation of 3-[(2-Hydroxynaphth-1-yl)]-methyl]-3,4-dihydro-5,6-benzocoumarin (10). Compound **3a**; (0.01 mol, 3.81 g) was dissolved in acetic acid (10 mL), and 30% H_2O_2 (5 mL) was added. The reaction mixture was kept overnight. The precipitated white solid was filtered and dried. The crude solid product was recrystallized from chloroform to afford 3 g of **11**: 80% yield; mp 219 °C (lit. mp 220 °C); IR 3300, 1730, 1615, 1500, 1210, 1150 cm^{-1}; ^{1}H NMR δ 3.2–3.4 (m, 5 H), 7.2–8.0 (m, 12 H).

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Registry No. **1a**, 16413-71-1; **1b**, 5342-95-0; **1c**, 27438-39-7; **2**, 920-37-6; **3a**, 49633-17-2; **3b**, 74262-48-9; **3c**, 49633-18-3; **10**, 49672-82-4; **11**, 74262-49-0; piperidine, 110-89-4.

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