Reactions of secondary amines with derivatives of 5-(2-methyl-3-furyl)cyclopent-2-en-1-one

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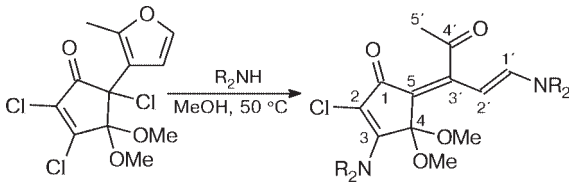
The reactions of 2,3,5-trichloro- and 2,5-dichloro-3-furfuryloxy-5-(2-methyl-3-furyl)-4,4-dimethoxycyclopent-2-en-1-ones with diethylamine or morpholine result in the decyclization of the 2-methylfuran substituent, giving the corresponding products in good yields.

Key words: di- and trichloro-5-furylcyclopentenones, amines, decyclization, dioxo dienamines.

While continuing to study the reactions of 5-furylcyclopentenones **1** and **2** with secondary amines,[1,2] we discovered an unusual decyclization of their methylfuran fragments. Thus heating trichloro-5-furylcyclopentenone **1** with Et_2NH or morpholine in MeOH afforded the corresponding dioxo dienamines **3** and **4** in good yields (Scheme 1). An analogous reaction of the difuryl derivative **2** with morpholine gave dioxo dienamine **5**. The structure of compound **4** was confirmed by an NOE effect (~7%) observed on the OMe protons upon irradiation of the proton at the C(2′) atom.

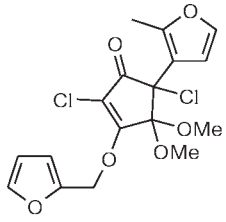
Such transformations of substituted furans have already been reported in the literature. For example, it is known that derivatives of furfural and 2-acylfuran react with ammonia or ammonium salts to give 3-hydroxypyridines.[3,4] Analogous products are obtained from furan-2-carboxylic acids and their esters. Ethyl benzofuran-3-carboxylate **6** easily undergoes decyclization[5] resulting in enamino ketone **7** (Scheme 2).

Scheme 1

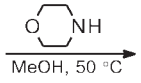


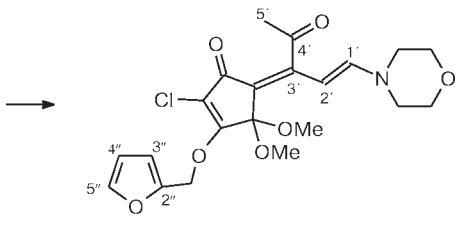
1 **3, 4**

R_2 = —$(CH_2)_2$—O—$(CH_2)_2$— (**3**), R = Et (**4**)



2





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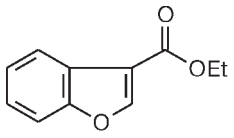
Scheme 2



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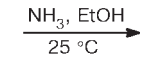

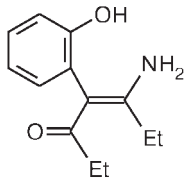

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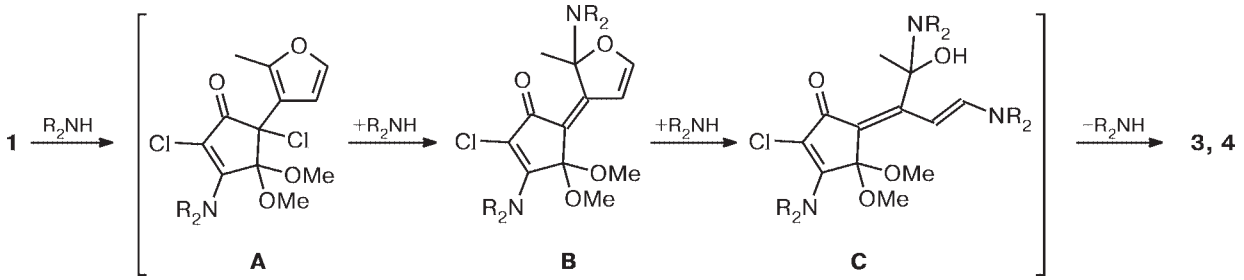
Scheme 3



In general, the literature data suggest that the reactions with amines are possible only for furan derivatives containing electron-acceptor groups. Insofar as compounds **1** and **2** do not belong to this type, it appears evident that the observed decyclization is due to a mobile Cl atom at C(5) atom, which is in an allylic position relative to the double bond of the methylfuryl fragment. A possible mechanism of the observed transformations can be visualized as follows (Scheme 3). Apparently, the reactions of 5-furylcyclopentenone **1** with amines initially give intermediates **B** *via* the smooth Ad_NE-replacement of the vinylic Cl atom at the C(3) atom (*cf.* Refs. 6, 7) followed by the S_N2'-replacement of the Cl atom at the C(5) atom. Then intermediates **B** undergo aminolysis to give, through intermediates **C**, products **3** and **4**.

Experimental

IR spectra were recorded on UR-20 and Specord M-80 spectrophotometers (Vaseline oil). UV spectra were recorded on a Specord M-400 spectrophotometer in EtOH. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AM-300 spectrometer (300.13 and 75.47 MHz, respectively) in $CDCl_3$. The mass spectrum was obtained on a Varian MAT CH-5 instrument (EI, 70 eV). TLC analysis was performed on Silufol UV 254:366 plates (Czech Republic); the spots were developed in the iodine vapor or by heating the plates with an applied solution of anisaldehyde and sulfuric acid in EtOH (1 : 0.5 : 10) at 120—150 °C. The reaction products were isolated by column chromatography on L 100/160 silica gel (Chemapol, Czech Republic) (30—60 g per 1 g of a product) in freshly distilled solvents as eluents. Before use, amines were dried over powdered KOH and distilled.

2-Chloro-4,4-dimethoxy-3-morpholino-5-(1-morpholino-4-oxopent-1(*E*)-en-3(*Z*)-ylidene)cyclopent-2-en-1-one (3). A solution of morpholine (0.40 g, 4.4 mmol) in 5 mL of MeOH was added dropwise to a stirred solution of compound **1** (0.20 g, 0.6 mmol) in 5 mL of MeOH. The reaction mixture was stirred at ~20 °C for 3 h until the starting compound was completely consumed (TLC; AcOEt—light petroleum, 1 : 9, as the eluent). The solvent was evaporated, water (10 mL) was added, and the organic material was extracted with $CHCl_3$ (4×20 mL). The combined extracts were washed with brine, dried with $MgSO_4$, and concentrated. The residue was purified by column chromatography on silica gel in AcOEt—light petroleum (1 : 9) to give compound **3** (0.15 g, 58%) as bright yellow crystals, m.p. 198—201 °C (decomp.; from AcOEt—light petroleum, 1 : 10). Found (%): C, 55.80; H, 6.20; Cl, 8.62; N, 6.50. $C_{20}H_{27}ClN_2O_6$. Calculated (%): C, 56.27; H, 6.37; Cl, 8.30; N, 6.57. IR, ν/cm^{-1}: 956 (CH=CH$_{trans}$); 1376 (Me); 1608 (C=C); 1664, 1704 (C=O). UV, λ_{max}/nm (ε): 251.5 (5080), 310.5 (10430), 415.5 (20710). ^{1}H NMR, δ: 2.44 (s, 3 H, Me); 3.20 (br.s, 10 H, 2 OMe, 2 NCH_2); 3.66 (t, 4 H, 2 NCH_2, J = 4.5 Hz); 3.74, 4.02 (both t, 4 H each, 4 CH_2O, J = 4.5 Hz); 5.54 (d, 1 H, H(2′), J = 13.90 Hz); 6.36 (d, 1 H, H(1′), J = 13.90 Hz). ^{13}C NMR, δ: 31.9 (Me); 48.0 (NCH_2); 51.8 (OMe); 65.9 (OCH_2); 67.3 (OCH_2); 90.72 (C(2′)); 106.5 (C(4)); 107.9 (C(5)); 109.5 (C(2)); 147.8 (C(1′)); 147.8 (C(3′)); 154.5 (C(3)); 181.9 (C(1)); 205.8 (C(4′)). MS, m/z: 428, 426 [M$^+$], 397, 395 [M − OMe]$^+$, 385, 383 [M − MeCO]$^+$.

2-Chloro-3-diethylamino-5-(1-diethylamino-4-oxopent-1(*E*)-en-3(*Z*)-ylidene)-4,4-dimethoxycyclopent-2-en-1-one (4) was obtained analogously from compound **1** (0.20 g, 0.6 mmol) and diethylamine (0.61 g, 8.3 mmol). The yield of compound **4** was 0.16 g (66%), yellowish brown crystals, m.p. 149.5—151 °C (from AcOEt—light petroleum, 1 : 10). Found (%): C, 59.80; H, 7.50; Cl, 9.22; N, 6.81. $C_{20}H_{31}ClN_2O_4$. Calculated (%): C, 60.23; H, 7.83; Cl, 8.89; N, 7.02. IR, ν/cm^{-1}: 952, 980 (HC=CH$_{trans}$); 1376 (Me); 1604, 1616 (C=C); 1656, 1704 (C=O). UV, λ_{max}/nm (ε): 251.0 (5700), 311.0 (11350), 424.5 (24100). ^{1}H NMR, δ: 1.11, 1.19 (both t, 6 H each, 2 Me, J = 7.0 Hz); 2.45 (s, 3 H, C(5′)H$_3$); 3.16 (s, 6 H, OMe); 3.17, 3.78 (both q, 4 H each, NCH_2, J = 7.0 Hz); 5.43 (d, 1 H, H(2′), J = 14.0 Hz); 6.41 (d, 1 H, H(1′), J = 14.0 Hz). ^{13}C NMR, δ: 14.5 (Me), 32.1 (C(5′)H$_3$); 44.2 (NCH_2); 51.5 (OMe); 89.5 (C(2′)); 104.9 (C(4)); 107.4 (C(5)); 108.1 (C(2)); 146.6 (C(1′)); 147.9 (C(3′)); 155.0 (C(3)); 182.1 (C(1)); 206.5 (C(4′)).

2-Chloro-3-furfuryloxy-4,4-dimethoxy-5-(1-morpholino-4-oxopent-1(*E*)-en-3(*Z*)-ylidene)cyclopent-2-en-1-one (5) was obtained analogously from ketone **2** as a semicrystalline yellowish brown mass. The yield of compound **5** was 50%. Found (%): C, 57.98; H, 5.65; Cl, 8.56; N, 3.38. $C_{21}H_{24}ClNO_7$. Calculated (%): C, 57.60; H, 5.52; Cl, 8.10; N, 3.20. IR, ν/cm^{-1}: 985 (HC=CH$_{trans}$); 1375 (Me); 1620 (C=C); 1690 (C=O). ^{1}H NMR, δ: 2.44 (s, 3 H, C(5′)H$_3$); 3.01 (s, 6 H, OMe); 3.28 (t, 4 H, NCH_2, J = 4.8 Hz); 3.67 (t, 4 H, OCH_2 morpholine, J = 4.8 Hz); 5.49 (s, OCH_2); 5.65 (d, 1 H, H (2′), J = 13.8 Hz); 6.26 (d, J = 1.9 Hz) and 6.27 (d, 1 H, H (4″), J = 1.8 Hz); 6.36 (d, 1 H, H(3″), J = 3.2 Hz); 6.52 (d, 1 H, H(1′), J = 13.8 Hz); 7.36 (d, 1 H(5″), J = 1.2 Hz). ^{13}C NMR, δ: 31.7 (Me); 50.7

(NCH_2); 51.0 (OMe); 63.8 (OCH_2); 66.8 (OCH_2 morpholine); 91.4 (C(2′)); 104.4 (C(4)); 110.1 (C(5)); 110.3 (C(4″)); 111.1 (C(3″)); 131.0 (C(2)); 143.5 (C(5″)); 149.6 (C(3′)); 149.7 (C(1′)); 152.1 (C(2″)); 153.7 (C(3)); 183.2 (C(1)); 205.5 (C(4′)).

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