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Reactions of 5-aryl-3-arylmethylene substituted 3*H*-furan-2-ones and 3*H*-pyrrol-2-ones with acetoacetic ester

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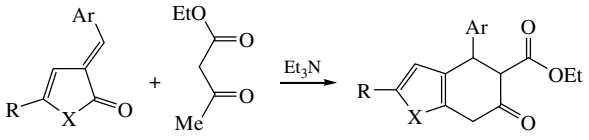
The title reactions afforded ethyl 4-(arylmethylene)-6-oxo-2-aryl-4,5,6,7-tetrahydrobenzofuran-5-carboxylates and ethyl 4-(arylmethylene)-6-oxo-2-aryl-4,5,6,7-tetrahydro-1*H*-indole-5-carboxylates the structures of which were confirmed by IR and ^{1}H NMR spectroscopy.

The synthetic capabilities of 3-arylmethylene-3*H*-furan(pyrrol)-2-ones are due to the presence of two electrophilic centres in their structures. In view of the enonic fragment being fixed in its *S-cis* configuration, the above compounds can be used as acceptors in Michael reaction.

Earlier, Michael condensation has been studied in the arylmethylene-3*H*-furan-2-one series with the use of cyclohexanone[1] and acetylacetone.[2] We used acetoacetic ester as a C-nucleophile in this interplay. The interaction of 5-aryl-3-arylmethylene-3*H*-furan-2-ones with acetoacetic ester was studied under conditions of basic catalysis (triethylamine) and with the use of microwave heating (Scheme1).



1a–d
2a,**b**

3a–d
4a,**b**

1a, **3a** Ar = 2-ClC_6H_4, R = *p*-Tol, X = O
1b, **3b** Ar = 2-O_2NC_6H_4, R = *p*-Tol, X = O
1c, **3c** Ar = 3-MeOC_6H_4, R = *p*-Tol, X = O
1d, **3d** Ar = 3-HO-4-MeOC_6H_3, R = *p*-Tol, X = O

2a, **4a** Ar = 3-HO-4-MeOC_6H_3, R = Ph, X = NH
2b, **4b** Ar = 2-ClC_6H_4, R = *p*-Tol, X = NH

Scheme 1

Ethyl-4-(arylmethylene)-6-oxo-2-aryl-4,5,6,7-tetrahydrobenzofuran-5-carboxylates **3a–d** and ethyl-4-(arylmethylene)-6-oxo-2-aryl-4,5,6,7-tetrahydro-1*H*-indole-5-carboxylates **4a**,**b** were isolated in ~50% yields; their structures were confirmed by IR and ^{1}H NMR spectroscopy.†

The IR spectra of compounds **3a–d** and **4a**,**b** show a wide absorption band at 1750–1735 cm^{-1} caused by the absorption of ester groups and an absorption band characteristic of a C=O group at 1730–1715 cm^{-1}.

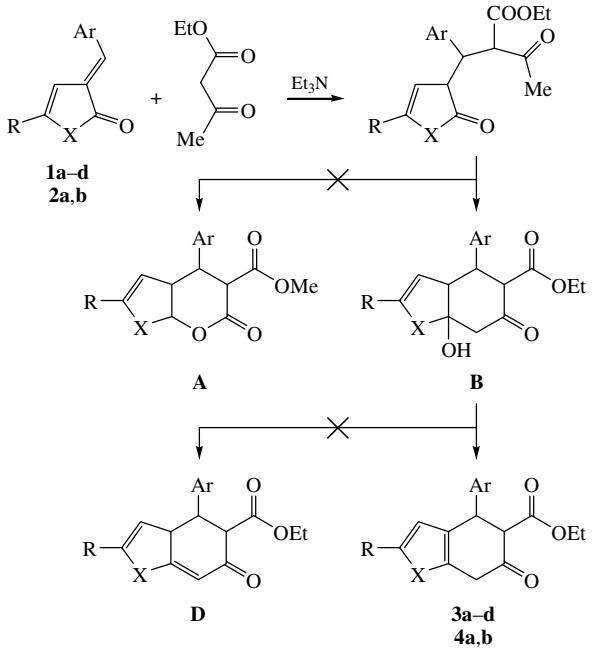
The ^{1}H NMR spectra provide more information; they contain a set of signals to completely confirm the structures of compounds **3a–d** and **4a**,**b**.

A singlet of methylene protons is detected at 3.80–3.90 ppm (2H); the signal at 4.83–4.88 ppm corresponds to a proton at the aromatic substituent (d, 1H, C*H*Ar); the signal of ester group protons is detected at 3.95–3.99 ppm (d, 1H, C*H*COOEt); the signal of a furan ring proton (compounds **3a–d**) is observed at 5.60–5.66 ppm; the signal of a pyrrole ring (compounds **4a**,**b**) is at 5.80–5.82 ppm; a proton at the N atom manifests itself by a signal at 8.48–8.50 ppm.

According to the spin–spin coupling constants of methinic hydrogens ^{45}J 3.53–4.04 Hz (compounds **1a–d**, **2a**,**b**), the dihedral angle γ between these hydrogen atoms varied from 48 to 56°.

When acetoacetic ester is used as a reagent, one could expect an ambiguous course of the reaction. Under basic catalysis conditions, the reaction did not stop at the formation of 1,5-dicarbonyl compounds, it produced intramolecular carbocyclization products; as a result of the dehydration of intermediate **B**, the formation of products like **D** or compounds **3a–d** and **4a**,**b** is possible (Scheme 2). However, according to the above spectral data, products **A** and **D** do not form.

The synthesis under microwave activation can be performed without a solvent.† In this case, the temperature of the reaction mixture is not limited by the boiling point of the solvent and the reaction proceeds much faster. Compounds **1c**,**d** and **2b** with an



1a–d
2a,**b**

A

B

D

3a–d
4a,**b**

Scheme 2

excess of acetoacetic ester were introduced into microwave synthesis.

† A Daewoo-KOR 6167 microwave oven (800 W, 2450 MHz) was employed for microwave syntheses. The IR spectra were measured on a Specord instrument at 400–4000 cm^{-1} (in a KBr tablet). The ^1H NMR spectra were recorded on a Bruker-MSL 400 spectrometer (400 MHz) in [$^2H_6$]DMSO; TMS was an internal standard.

5-R-3-arylmethylene-3*H*-furan-2-ones and 5-R-3-arylmethylene-3*H*-pyrrol-2-ones were obtained according to published procedures.[3,4]

Synthesis of compounds **3a–d** *and* **4a,b**.

Procedure A. A mixture of 10 mmol of **1a–d** or **2a,b**, 10 mmol of acetoacetic ester and 10 mmol of triethylamine was heated in 25 ml of ethanol for 5 h. Then, the resulting mixture was extracted with a 1:1 mixture of diisopentyl ether and isopropanol. After evaporation, the crystals obtained were filtered off and recrystallised from isopropanol.

Procedure B. 0.01 mol of **1a–d** or **2a,b** and 0.03 mol of acetoacetic ester were thoroughly mixed in a heat-resistant glass. The reaction mixture was placed in a microwave oven for 10 min at 800 W. The product was resrystallised from isopropanol.

For **3a**: yield 53%, mp 175–177 °C (Pr^iOH). ^1H NMR, δ: 5.60 (s, 1H), 3.85 (s, 2H, CH_2), 4.83 (d, 1H, C*H*-Ar), 3.95 (d, 1H, C*H*COOEt, ^{45}J 3.73 Hz), 1.30 (t, 3H, OCH_2*Me*), 4.12 (m, 2H, OCH_2), 6.57–7.48 (m, 8H, Ar), 2.33 (s, 3H, *Me*-C_6H_4). Found (%): C, 70.15; H, 5.00. Calc. for $C_{24}H_{21}O_4Cl$ (%): C, 70.50; H, 5.14.

For **3b**: yield 65%, mp 183–185 °C (Pr^iOH). ^1H NMR, δ: 5.63 (s, 1H), 3.80 (s, 2H, CH_2), 4.84 (d, 1H, C*H*-Ar), 3.95 (d, 1H, C*H*COOEt, ^{45}J 3.90 Hz), 1.31 (t, 3H, OCH_2*Me*), 4.14 (m, 2H, OCH_2), 6.53–7.50 (m, 8H, Ar), 2.35 (s, 3H, *Me*-C_6H_4). Found (%): C, 68.71; H, 5.09; N, 3.94. Calc. for $C_{24}H_{21}NO_6$ (%): C, 68.73; H, 5.01; N, 3.34.

For **3c**: yield 48%, mp 165–168 °C (Pr^iOH). ^1H NMR, δ: 5.64 (s, 1H), 3.82 (s, 2H, CH_2), 4.86 (d, 1H, C*H*-Ar), 3.96 (d, 1H, C*H*COOEt, ^{45}J 3.73 Hz), 1.33 (t, 3H, OCH_2*Me*), 4.15 (m, 2H, OCH_2), 6.50–7.45 (m, 8H, Ar), 2.37 (s, 3H, *Me*-C_6H_4), 3.73 (s, 3H, OMe). Found (%): C, 74.08, H, 5.92. Calc. for $C_{25}H_{24}O_5$ (%): C, 74.25; H, 5.94.

For **3d**: yield 69%, mp 170–173 °C (Pr^iOH). ^1H NMR, δ: 5.66 (s, 1H), 3.83 (s, 2H, CH_2), 4.88 (d, 1H, C*H*-Ar), 3.99 (d, 1H, C*H*COOEt, ^{45}J 3.53 Hz), 1.28 (t, 3H, OCH_2*Me*), 4.10 (m, 2H, OCH_2), 6.57–7.45 (m, 7H, Ar), 2.31 (s, 3H, *Me*-C_6H_4), 3.71 (s, 3H, OMe), 5.05 (s, 1H, OH). Found (%): C, 71.53; H, 6.02. Calc. for $C_{25}H_{24}O_6$ (%): C, 71.43; H, 5.72.

For **4a**: yield 45%, mp 200–203 °C (Pr^iOH). ^1H NMR, δ: 5.80 (s, 1H), 3.90 (s, 2H, CH_2), 4.85 (d, 1H, C*H*-Ar), 8.48 (s, 1H, NH), 3.97 (d, 1H, C*H*COOEt, ^{45}J 3.90 Hz), 1.31 (t, 3H, OCH_2*Me*), 4.13 (m, 2H, OCH_2), 6.59–7.52 (m, 8H, Ar). Found (%): C, 71.47; H, 5.59; N, 3.57. Calc. for $C_{24}H_{23}NO_5$ (%): C, 71.11; H, 5.68; N, 3.46.

For **4b**: yield 49%, mp 198–200 °C (Pr^iOH). ^1H NMR, δ: 5.82 (s, 1H), 3.86 (s, 2H, CH_2), 4.83 (d, 1H, C*H*-Ar), 8.50 (s, 1H, NH), 3.97 (d, 1H, C*H*COOEt, ^{45}J 4.04 Hz), 1.30 (t, 3H, OCH_2*Me*), 4.15 (m, 2H, OCH_2), 6.52–7.43 (m, 8H, Ar), 2.40 (s, 3H, *Me*-C_6H_4). Found (%): C, 70.75; H, 5.04; N, 3.16. Calc. for $C_{24}H_{22}NO_3Cl$ (%): C, 70.70; H, 5.39; N, 3.44.

The synthesis in a microwave oven allowed us to shorten the duration of the process by 15 times in comparison with the usual technique (in an alcohol solution), and the yield of the final products increased considerably (up to 90%).

The physico-chemical characteristics of the compounds obtained under classical conditions and on microwave heating were the same.

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