Chemistry of Heterocyclic Compounds, Vol. 41, No. 9, 2005

LETTERS TO THE EDITOR

2-CARBOXYARYLDIFURYLMETHANES IN SYNTHESIS OF KETONES IN THE ISOCOUMARIN SERIES

A. S. Dmitriev[1], S. A. Podelyakin[1], V. T. Abaev[2], and A. V. Butin[1]

Keywords: isocoumarin, *ortho*-carboxybenzylfuran, protolytic opening of furan, recyclization.

In contrast to chromones and coumarins, which are abundant in nature and rather popular as objects of investigation, researchers have focused much less attention on their structural isomers (isocoumarin or isochromone). Nevertheless, a broad spectrum of biological activity has been found for substances in the isocoumarin series [1-4], which is the main reason for interest in synthesis of novel structures containing an isocoumarin moiety.

Popular methods for synthesis of the isocoumarin ring include methods based on cyclization of *ortho*-(2-oxoethyl)benzoic acids or benzoic acids with a functional group in the *ortho*-position which is a latent analog of the 2-oxoethyl group [5]. We propose a general procedure for synthesis of benzannelated heterocycles based on *ortho*-substituted benzylfurans [6] in which the furan ring acts as a latent 1,4-dicarbonyl compound. The presence of a second furan ring in the original benzylfuran may cause a secondary reaction of intramolecular cyclization to form tetracyclic compounds [6].

Thus we have shown that recyclization of 2-carboxyaryldifurylmethanes containing methyl or ethyl substituents in the 5 position of the furan ring, when boiled in a saturated solution of hydrogen chloride in ethanol, does not stop in the step of formation of the corresponding ketones but rather leads to tetracyclic derivatives of isocoumarin [7].

We have observed that in the case of 2-carboxyaryldifurylmethanes **1a-c**, with a *tert*-butyl substituent in the 5 position of the furan ring, under analogous reaction conditions stops in the step of isocoumarins ketones **2a-c**, which are obtained in high yields. Even prolonged boiling does not make it possible to obtain tetracyclic compounds **3a-c**, but rather leads to considerable resin formation. We associate this fact with steric hindrances created by the bulky *tert*-butyl substituent at the carbonyl group of the 3-oxopropyl moiety, which makes subsequent intramolecular cyclization impossible.

Compounds **1a-c** were obtained by the method as in [7].

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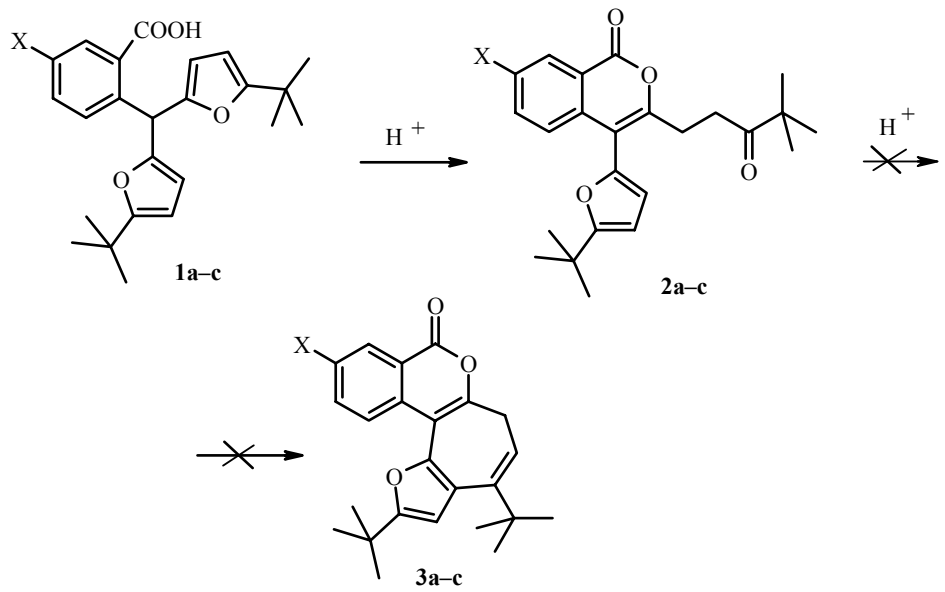
[1] Scientific Research Institute of Heterocyclic Chemistry, Kuban State University of Technology, Krasnodar 350072, Russia; e-mail: alexander_butin@mail.ru. [2] North-Ossetian State University, Vladikavkaz 362025, Russia. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 9, pp. 1400-1402, September, 2005. Original article submitted June 1, 2005.



1-3 a X = H, **b** X = NO_2, **c** X = Cl

4-(5-*tert*-Butylfuran-2-yl)-3-(4,4-dimethyl-3-oxopentyl)isochromen-1-one (2a). Compound **1a** (1.0 g, 2.63 mmol) in a 30% solution of hydrogen chloride in ethanol was boiled for 5 min. The reaction mass obtained was poured into water and extracted with methylene chloride. The extract was dried with Na_2SO_4, petroleum ether was added, and the mixture was passed through a thin layer of silica gel. The solution was evaporated down and the oil obtained was dried under vacuum. Yield 0.85 g (85%), oil. IR spectrum (nujol), ν, cm^{-1}: 1702 (C=O), 1741 (OC=O). ^{1}H NMR spectrum (250 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 1.16 (9H, s, *t*-Bu); 1.33 (9H, s, *t*-Bu); 2.76-2.85 (2H, m, CH_2); 2.92-3.00 (2H, m, CH_2); 6.12 (1H, d, *J* = 3.2, 4-H_{Fur}); 6.37 (1H, d, *J* = 3.2, 3-H_{Fur}); 7.31-7.35 (1H, m, H_{Ar}); 7.46-7.53 (1H, m, H_{Ar}); 7.65-7.72 (1H, m, H_{Ar}); 8.29-8.33 (1H, m, H_{Ar}). Found, %: C 75.87; H 7.50. $C_{24}H_{28}O_4$. Calculated, %: C 75.76; H 7.42.

Compounds 2b,c were obtained by a similar method as for **2a**.

4-(5-*tert*-Butylfuran-2-yl)-3-(4,4-dimethyl-3-oxopentyl)-7-nitroisochromen-1-one (2b). Yield 84%, yellow crystals; mp 115-116°C (petroleum ether). IR spectrum (nujol), ν, cm^{-1}: 1709 (C=O), 1749 (OC=O). ^{1}H NMR spectrum (250 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 1.17 (9H, s, *t*-Bu); 1.33 (9H, s, *t*-Bu); 2.81-2.89 (2H, m, CH_2); 2.93-3.01 (2H, m, CH_2); 6.16 (1H, d, *J* = 3.2, 4-H_{Fur}); 6.44 (1H, d, *J* = 3.2, 3-H_{Fur}); 7.48 (1H, d, *J* = 8.9, H_{Ar}); 8.45 (1H, dd, *J* = 2.4, *J* = 8.9, H_{Ar}); 9.13 (1H, d, *J* = 2.4, H_{Ar}). Found, %: C 67.59; H 6.53. $C_{24}H_{27}NO_6$. Calculated, %: C 67.75; H 6.40.

4-(5-*tert*-Butylfuran-2-yl)-7-chloro-3-(4,4-dimethyl-3-oxopentyl)isochromen-1-one (2c). Yield 84%, colorless crystals; mp 94-95°C (petroleum ether). IR spectrum (nujol), ν, cm^{-1}: 1703 (C=O), 1745 (OC=O). ^{1}H NMR spectrum (250 MHz, $CDCl_3$), δ, ppm (*J*, Hz): 1.15 (9H, s, *t*-Bu); 1.32 (9H, s, *t*-Bu); 2.72-2.84 (2H, m, CH_2); 2.90-3.02 (2H, m, CH_2); 6.11 (1H, d, *J* = 3.2, 4-H_{Fur}); 6.37 (1H, d, *J* = 3.2, 3-H_{Fur}); 7.28 (1H, d, *J* = 8.6, H_{Ar}); 7.61 (1H, dd, *J* = 2.2, *J* = 8.6, H_{Ar}); 8.26 (1H, d, *J* = 2.2, H_{Ar}). Found, %: C 69.56; H 6.41. $C_{24}H_{27}ClO_4$. Calculated, %: C 69.47; H 6.56.

This work was done with the financial support of the Russian Fund for Fundamental Research (grant No. 03-03-32759) and Bayer HealthCare AG.

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