Chemistry of Heterocyclic Compounds, Vol. 38, No. 4, 2002

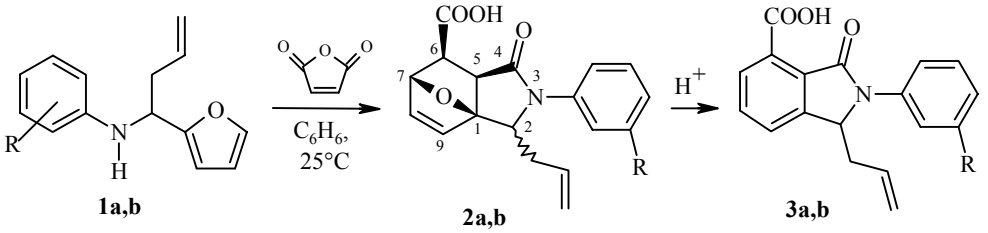
LETTERS TO THE EDITOR

SYNTHESIS OF 2-ARYL-SUBSTITUTED 3-ALLYL-7-CARBOXYPHTHALAMIDINES – NEW SYNTHONES FOR THE CONSTRUCTION OF ISOINDOLO[2,1-*a*]QUINOLINES

A. V. Varlamov, N. V. Sidorenko, F. I. Zubkov, and A. I. Chernyshev

Keywords: homoallylamines, isoindolinones, furfurylamines, intramolecular [4+2] cycloaddition.

The major synthones for the construction of isoindolo[2,1-*a*]quinolines are 1-hydroxy- and 1-carboxymethyl-2,3-dihydro-2-aryl-3-oxoisoindoles obtained from N-arylphthalimides [1, 2]. We have developed an original method for the synthesis of 3-allyl-2-aryl-7-carboxy-1-isoindolinones, which are new synthones for the construction of this heterocyclic system, by means of transformations of furan homoallylamines. Homoallylamines **1a**,**b** were obtained by the reaction of the corresponding Schiff bases with allylmagnesium bromides [3].



a R = H; **b** R = Me

The reaction of allylamines **1a**,**b** with maleic anhydride was carried out in benzene at 25°C and gave 3a,6-epoxyisoindolinones **2a**,**b**, in 88 and 95% yield, respectively. Adducts **2a**,**b** are the products of the acylation and subsequent *exo*-[4+2] cycloaddition of the amide fragment to the furan ring [4]. ^{1}H NMR spectroscopy showed that adducts **2a**,**b** are obtained as 1:1 mixtures of isomers differing in the position of allyl substituent relative to the epoxide bridge. Aromatization of these compounds to the desired dihydroisoindolones **3a**,**b** was carried out by the action of excess phosphoric acid.

2-Allyl-3-aryl-4-oxo-10-oxa-3-azatricyclo[5.2.1.01,5]dec-8-ene-6-carboxylic Acids (2a,b). A mixture of maleic anhydride (0.1 mol) and homoallylamine **1a** or **1b** (0.1 mol) in benzene (100 ml) was stirred for 24 h at 25°C. The crystalline precipitate was filtered off, washed with benzene, and dried at 90°C to constant mass.

Russian People's Friendship University, 117198 Moscow, e-mail: avarlamov@sci.pfu.edu.ru. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 4, pp. 556-557, April, 2002. Original article submitted November 23, 2001.

 0009-3122/02/3804-0490$27.00©2002 Plenum Publishing Corporation

Adduct 2a (mixture of isomers) was obtained in 88% yield as white crystals with mp 149-152°C. ^{1}H NMR spectrum ($CDCl_3$, 200 MHz), δ, ppm, *J* (Hz): isomer *A*: 10.06 (1H, br. s CO_2H); 7.45-7.20 (5H, m, H-Ph); 6.62 (1H, d, J_{98} = 5.8, 9-H); 6.49 (1H, dd, J_{89} = 5.8, J_{78} = 1.8, 8-H); 5.77 (1H, m, ^3J = 9.3, ^3J = 18.0, 2-H); 5.33 (1H, d, J_{78} = 1.8, 7-H); 5.19 (1H, dd, ^3J = 9.3, ^3J = 1.3, 1'-H-*cis*); 5.17 (1H, dd, ^3J = 18.0, ^3J = 1.3, 1'-H-*trans*); 4.63 (1H, t, $J_{23'A}$ = $J_{23'B}$ = 4.8, 2-H); 3.10 (1H, d, J_{56} = 9.2, 5-H); 2.86 (1H, d, J_{56} = 9.2, 6-H); 2.62 (2H, m, 3'A-H and 3'B-H). Isomer *B*: 10.06 (1H, br. s, CO_2H); 7.45-7.20 (5H, m, H-Ph); 6.47 (1H, d, J_{89} = 5.8, 9-H); 6.39 (1H, dd, J_{89} = 5.8, J_{78} = 1.8, 8-H); 5.71 (1H, m, ^3J = 10.4, ^3J = 18.5, 2'-H); 5.27 (1H, d, J_{78} = 1.8, 7-H); 5.09 (1H, dd, ^3J = 10.4, ^3J = 1.3, 1'-H-*cis*); 5.07 (1H, dd, ^3J = 18.5, ^3J = 1.3, 1'-H-*trans*); 4.59 (1H, dd, $J_{23'A}$ = 5.2, $J_{23'B}$ = 9.8, 2-H); 3.02 (1H, d, J_{56} = 9.2, 5-H); 2.84 (1H, d, J_{56} = 9.2, 6-H); 2.41 (2H, m, 3'A-H and 3'B-H). IR spectrum (KBr), ν, cm^{-1}: 1689, 1756 (C=O), 2610, 3390 (OH). Found, %: C 69.55; H 5.74; N 4.53; M^+ 311. $C_{18}H_{17}NO_4$. Calculated, %: C 69.45; H 5.47; N 4.50; M 311.

Adduct 2b (mixture of isomers) was obtained in 95% yield as white crystals; mp 139-141°C. ^{1}H NMR spectrum (DMSO-d_6, 200 MHz), δ, ppm, *J* (Hz): Isomer *A*: 7.45-7.20 and 7.15-6.95 (4H, m, H-Ar); 6.73 (1H, d, J_{89} = 6.1, 9-H); 6.52 (1H, dd, J_{89} = 6.1, J_{78} = 1.8, 8-H); 5.77 (1H, m, ^3J = 10.1, ^3J = 18.0, 2'-H); 5.15 (1H, m, ^3J = 18.0, 1'-H-*trans*); 5.13 (1H, m, ^3J = 10.1, 1'-H-*cis*); 5.02 (1H, d, J_{78} = 1.8, 7-H); 4.66 (1H, dd, $J_{23'A}$ = 6.4, $J_{23'B}$ = 4.3, 2-H); 3.04 (1H, d, J_{56} = 9.2, 5-H); 2.58 (1H, d, J_{56} = 9.2, 6-H); 2.65-2.57 (2H, m, 3'-H); 2.32 (3H, s, CH_3-Ar). Isomer *B*: 7.45-7.20 and 7.15-6.95 (4H, m, H-Ar); 6.56 (1H, d, J_{89} = 5.8, 9-H); 6.42 (1H, dd, J_{89} = 5.8, J_{78} = 1.8, 8-H); 5.77 (1H, m, ^3J = 10.1, ^3J = 18.0, 2'-H); 5.09 (1H, d, J_{78} = 1.8, 7-H); 5.10-5.00 (2H, m, 1'-H); 4.81 (1H, dd, $J_{23'A}$ = 10.1, $J_{23'B}$ = 4.6, 2-H); 2.95 (1H, d, J_{56} = 9.2, 5-H); 2.59 (1H, d, J_{56} = 9.2, 6-H); 2.32 (2H, s, CH_3-Ar); 2.65-2.55 (2H, m, 3'-H). IR spectrum (KBr), ν, cm^{-1}: 1660, 1700, 1743 (C=O), 2600, 3400 (OH). Found, %: C 69.89; H 5.80; N 4.39; M^+ 325. $C_{19}H_{19}NO_4$. Calculated, %: C 70.15; H 5.85; N 4.31; M 325.

3-Allyl-2-aryl-7-carboxy-1-isoindolinones (3a,b). A sample of epoxyisoindolinone **2** (16.6 mmol) in 85% phosphoric acid (40 ml) was heated at 60°C for 1 h with monitoring by thin-layer chromatography. The mixture was cooled and poured into water. The crystalline precipitate was filtered off, washed with water until the wash water was neutral, dried, and recrystallized from ethyl acetate.

Dihydroisoindolone 3a was obtained in 80% yield as white crystals; mp 132-134°C. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz), δ, ppm, *J* (Hz): 8.47 (1H, dd, 6-H); 7.80-7.75 (2H, m, 5-H and 4-H); 7.53-7.37 (5H, m, H-Ph); 5.41 (1H, dd, $J_{33'A}$ = 3.7, $J_{33'B}$ = 6.1, 3-H); 5.26 (1H, m, ^3J = 10.4, ^3J = 17.1, 2'-H); 5.00 (1H, dd, ^3J = 10.4, $J_{11'}$ = 1.2, 1'-H-*cis*); 4.86 (1H, dd, ^3J = 17.1, $J_{11'}$ = 1.2, 1'-H-*trans*); 2.80 (1H, m, $J_{3'A3}$ = 3.7, 3'A-H); 2.62 (1H, m, $J_{3'B3}$ = 6.1, 3'B-H). IR spectrum (KBr), ν, cm^{-1}: 1652, 1728, 1745 (C=O), 2580 (OH). Found, %: C 73.51; H 5.48; N 4.41; M^+ 293. $C_{18}H_{15}NO_3$. Calculated, %: C 73.78; H 5.12; N 4.79; M 293.

Dihydroisoindolone 3b was obtained in 81% yield as colorless crystals; mp 122-125°C. ^{1}H NMR spectrum ($CDCl_3$, 400 MHz), δ, ppm, *J* (Hz): 15.75 (1H, br. s, CO_2H); 8.47 (1H, dd, 6-H); 7.83-7.76 (2H, m, 5-H and 4-H); 7.41 (1H, t, ^3J = 7.3, 5''-H); 7.35 (1H, br. s, 2''-H); 7.28 (1H, br. d, ^3J = 7.3, 4''-H); 7.20 (1H, br. d, ^3J = 7.3, 6''-H); 5.37 (1H, dd, $J_{33'A}$ = 3.5, $J_{33'B}$ = 5.6, 3-H); 5.30 (1H, m, ^3J = 9.7, ^3J = 16.2, $J_{3'B2'}$ = 6.2, 2'-H); 5.01 (1H, br. d, 3*J* = 9.7, 1'-H-*cis*) 4.87 (1H, br. d, ^3J = 16.2, 1'-H-*trans*); 2.80 (1H, m, $J_{3'A3}$ = 3.5, $J_{3'3'}$ = 13.7, 3'A-H); 2.63 (1H, m, $J_{3'B3}$ = 5.6, $J_{3'3'}$ = 13.7, $J_{3'2'}$ = 6.2, 3'B-H), IR spectrum (KBr), ν, cm^{-1}: 1610, 1713 (C=O), 2290, 3430 (OH). Found, %: C 74.31; H 5.73; N 4.72; M^+ 307. $C_{19}H_{17}NO_3$. Calculated, %: C 74.27; H 5.54; N 4.56; M 307.

This work was carried out with the financial support of the Russian Basic Research Fund (Grant No. 01-03-32844).

REFERENCES

1. J. Abe, A. Ohsawa, and H. Igeta, *Heterocycles*, **19**, 49 (1982).
2. C. Lorincz, K. Szasz, and L. Kistaludy, *Arzneim-Forsch.*, **26**, 1907 (1976).
3. P. Brun, J. Zylber, G. Pepe, and J.-P. Reboul, *Heterocycl. Commun.*, **1**, 13 (1994).
4. V. V. Kuznetsov, A. E. Aliev, and N. S. Prostakov, *Khim. Geterotsikl. Soedin.*, 73 (1994).