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LETTERS TO THE EDITOR

UNUSUAL ACID-CATALYZED TRANSFORMATION OF 2-[DI(2-FURYL)METHYL]BENZHYDROLS

A. V. Butin[1]*, A. V. Fin'ko[1], E. V. Sudarkin[1], and F. A. Tsiunchik[1]

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In previous work [1, 2], we showed that 2-[di(2-furyl)methyl]benzoic acids may be converted in the presence of an acid catalyst into various compounds of different structures. Thus, the treatment of these acids by ethanolic hydrogen chloride leads to recyclization of one of the furan rings to give isocoumarins [1]. In this case, the carboxylic acid group reacts as an O-nucleophile. 2-[Di(2-furyl)methyl]benzoic acids in a mixture of acetic acid and acetic anhydride in the presence of anhydrous zinc chloride are converted into 9-furylnaphtho[2,3-*b*]furans [2]. This reaction proceeds through electrophilic cyclization, while the carboxylic acid function acts as a C-electrophile.

On one hand, derivatives of 2-[di(2-furyl)methyl]benzyl alcohol in ethanolic hydrogen chloride are known to convert to isochromenes [3]. The hydroxymethyl group in this reaction displays properties of an O-nucleophile. On the other hand, under acid conditions, benzyl alcohols may undergo protonation to give the corresponding carbocations, which are C-electrophiles. Thus, we set out to find the conditions for this reaction, under which derivatives of 2-[di(2-furyl)methyl]benzyl alcohol would convert to 4,9-dihydronaphtho[2,3-*b*]furans. However, all our attempts to carry out this reaction were unsuccessful, apparently due to the instability of the benzyl cation formed.

In order to increase the stability of the carbocation formed in this reaction, we synthesized benzhydrol **2** by the reaction of aldehyde **1** [2] with *p*-tolylmagnesium bromide. However, treating aryldifurylmethane **2** with stannic chloride led to dihydronaphthofuran **4** instead of the expected chloride **3**. Furan **4** was obtained as a 2:1 mixture of diastereomers. The structure of these diastereomers was supported by two-dimensional NMR spectroscopy (^{1}H, ^{13}C–HSQC, ^{1}H, ^{13}C–HMBC, ^{1}H, ^{1}H–NOESY) but the available data do not permit assignment of their relative configuration.

*To whom correspondence should be addressed, e-mail: alexander_butin@mail.ru.

[1] Research Institute of Heterocyclic Compounds Chemistry, Kuban State Technological University, 2 Moskovskaya Str., Krasnodar 350072, Russia.

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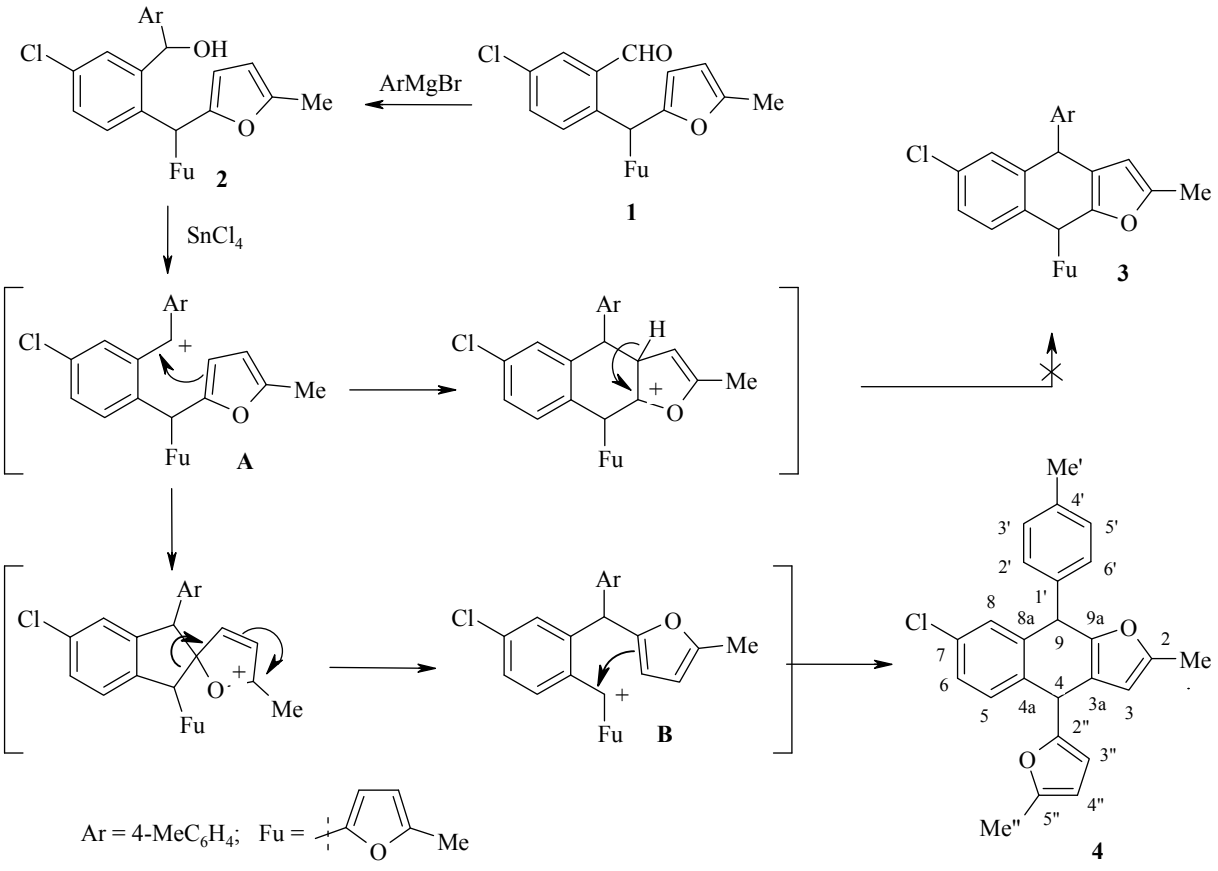

We assume that the reaction starts with formation of carbocation **A**, which isomerizes to cation **B** as the result of electrophilic attack of the cationic site at the α-position of one of the furan rings with subsequent migration of this ring [4, 5]. Further electrophilic cyclization leads to the formation of furan **4**.

The ^{1}H and ^{13}C NMR spectra were taken on a Bruker DPX 300 spectrometer at 300 and 75 MHz, respectively. The two-dimensional spectra were taken on a Bruker Avance 600 spectrometer in $CDCl_3$ with signals of the residual solvent protons as the standard (7.25 ppm for $CDCl_3$ for the ^{1}H NMR spectrum and 77.0 ppm for the ^{13}C NMR spectrum). The electron impact mass spectra were taken on a Kratos MS-30 spectrometer. The ionizing voltage was 70 eV. The ionization chamber temperature was 200°C. The reaction mixtures were purified using KSK silica gel (5–40 μm fraction) from Sorbpolimer.

[5-Chloro-2-di(5-methyl-2-furyl)methylphenyl](4-methylphenyl)methanol (2). A solution of compound **1** (4.7 g, 15 mmol) in absolute ether (50 ml) was added dropwise with stirring to tolylmagnesium bromide prepared from magnesium (0.8 g, 33 mmol) and 4-bromotoluene (4.3 g, 25 mmol) in absolute ether (500 ml) with the prevention of vigorous reflux. The reaction mixture was then stirred at reflux for an additional 2 h. At the end of the reaction (monitored by thin-layer chromatography), the reaction mixture was carefully poured into 500 ml cold water with stirring and left overnight. The reaction mixture was then filtered. The organic layer was separated and the aqueous layer was extracted with three 100 ml ethyl acetate portions. The combined organic fractions were dried over anhydrous sodium sulfate, purified with activated carbon, and evaporated to dryness in vacuum to give 4.63 g (76%) compound **2** as a light-yellow oil, which was used without further purification.

7-Chloro-2-methyl-4-(5-methyl-2-furyl)-9-(4-methylphenyl)-4,9-dihydronaphtho[2,3-*b*]furan (4). $SnCl_4$ (3 ml) was added dropwise with vigorous stirring to a solution of compound **2** (4.1 g, 10 mmol) in absolute benzene (100 ml). The reaction mixture was stirred for 5–10 min at room temperature. At the end of the reaction (monitored by thin-layer chromatography), the reaction mixture was poured into 250 ml water and brought to pH 7 by the addition of sodium bicarbonate. The organic layer was separated and the aqueous layer

was extracted with four 50-ml ethyl acetate portions. The combined organic phases were dried over anhydrous sodium sulfate and evaporated to dryness in vacuum. The residue was initially purified by passing through a silica gel column using 1:10 methylene chloride–petroleum ether as the eluent. The yellow oily residue was separated by chromatography on a silica gel column (5/40 μ fraction) using petroleum ether as the eluent.

The major diastereomer of compound 4 was obtained as a white powder; mp 169–170°C (petroleum ether). The yield was 1.39 g (36%). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.19 (3H, s, CH_3); 2.24 (3H, s, CH_3"); 2.32 (3H, s, CH_3'); 5.18 (1H, d, *J* = 4.2, H-9); 5.26 (1H, d, *J* = 4.2, H-4); 5.87 (1H, d, *J* = 3.0, H-4"); 5.88 (1H, s, H-3); 5.94 (1H, d, *J* = 3.0, H-3"); 7.02 (2H, m, AA'BB' system, H-2', H-6'); 7.08 (1H, d, *J* = 2.3, H-8); 7.11 (2H, m, AA'BB' system, H-3', H-5'); 7.12 (1H, dd, *J* = 2.3, *J* = 8.4, H-6); 7.29 (1H, d, *J* = 8.4, H-5). ^{13}C NMR spectrum, δ, ppm: 13.6 (CH_3"); 13.7 (CH_3); 21.1 (CH_3'); 38.1 (C-4); 44.2 (C-9); 105.4 (C-3); 106.0 (C-4"); 107.2 (C-3"); 117.2 (C-3a); 126.7 (C-6); 128.4 (C-2', C-6'); 129.5 (C-3', C-5'); 130.0 (C-8); 130.7 (C-5); 132.4 (C-7); 133.6 (C-4a); 136.5 (C-4'); 139.5 (C-8a); 140.1 (C-1'); 147.9 (C-9a); 151.5 (C-5"); 151.9 (C-2); 154.9 (C-2"). Mass spectrum, *m/z* (I_{rel}, %): 390/388 $[M]^+$ (23/62), 347/345 (21/60), 308/306 (35/100), 296 (34), 253 (16), 219 (15), 101 (15), 59 (45), 43 (53). Found, %: C 77.35; H 5.49. $C_{25}H_{21}ClO_2$. Calculated, %: C 77.21; H 5.44.

The minor diastereomer of compound 4 was obtained as a white powder; mp 146–147°C (petroleum ether). The yield was 0.74 g (19%). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.22 (3H, s, CH_3); 2.27 (3H, s, CH_3"); 2.32 (3H, s, CH_3'); 5.11 (1H, d, *J* = 4.0, H-9); 5.16 (1H, d, *J* = 3.0, H-4); 5.87 (1H, d, *J* = 3.0, H-4"); 5.90 (1H, d, *J* = 3.0, H-3"); 5.95 (1H, s, H-3); 7.10 (2H, m, AA'BB' system, H-3', H-5'); 7.14 (1H, d, *J* = 2.3, H-8); 7.16 (1H, dd, *J* = 2.3, *J* = 8.3, H-6); 7.17 (2H, m, AA'BB' system, H-2', H-6'); 7.40 (1H, d, *J* = 8.3, H-5). ^{13}C NMR spectrum, δ, ppm: 13.6 (CH_3"); 13.7 (CH_3); 21.0 (CH_3'); 38.3 (C-4); 44.4 (C-9); 105.5 (C-3); 106.0 (C-4"); 106.6 (C-3"); 116.7 (C-3a); 126.7 (C-6); 128.5 (C-2', C-6'); 129.3 (C-3', C-5'); 130.0 (C-8); 131.2 (C-5); 132.4 (C-7); 133.4 (C-4a); 136.4 (C-4'); 139.5 (C-8a); 140.2 (C-1'); 148.2 (C-9a); 151.4 (C-5"); 152.0 (C-2); 155.3 (C-2"). Mass spectrum, *m/z* (I_{rel}, %): 390/388 $[M]^+$ (36/100), 347/345 (28/83), 308 (44), 253 (37), 218 (23), 119 (15), 59 (27), 43 (72). Found, %: C 77.13; H 5.47. $C_{25}H_{21}ClO_2$. Calculated, %: C 77.21; H 5.44.

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