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LETTERS TO THE EDITOR

One-Pot Synthesis of Tetrahydrobenzofuran-3-carboxylates

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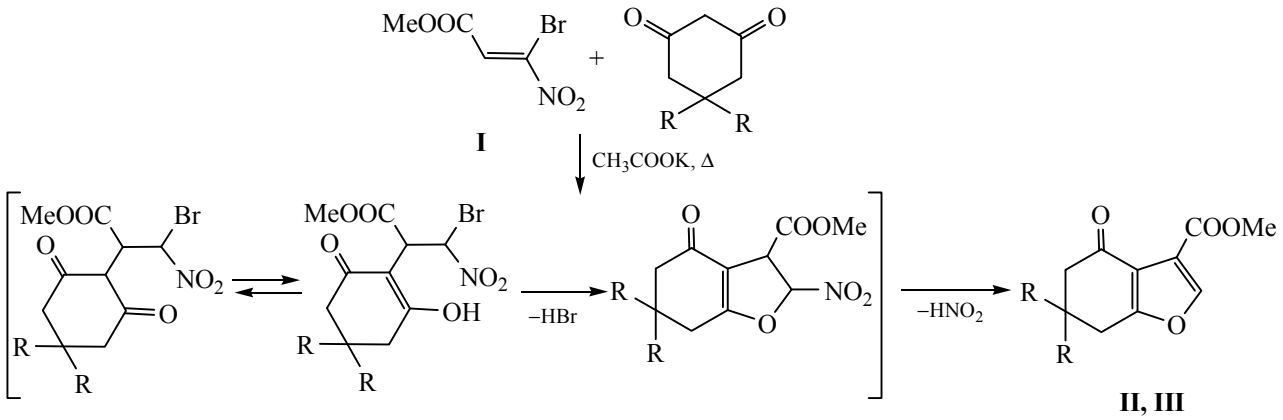
Benzofuran cycle is constituent of some natural compounds and drugs [1–3]. In particular, tetrahydrobenzofuran fragment contributes to the composition of sesquiterpenoids ligularone and isoligularone [4], and benzodihydrofuran system is present in the molecules of such antifungal antibiotics as griseofulvin and sodium usninate [5].

We developed a convenient one-pot approach to tetrahydrobenzofuran series representatives **II** and **III** on the basis of condensation of methyl-3-bromo-3-nitroacrylate **I** with cyclic β-diketones: dihydroresorcin and dimedone. Reaction proceeds at reflux of equimolar amounts of reagents in methanol in the presense of potassium acetate.



R = H (**II**), Me (**III**).

Heterocycles formation is a result of some sequential processes: nucleophilic addition of β-diketone at bthe C=C double bond of methyl-3-bromo-3-nitroacrylate **I**, intramolecular *O*-alkylation of intermediate accompanied with dehydrobromination and then denitration of the formed hexahydrobenzofuran to give aromatic furan system. Tetrahydrobenzofuran-3-carboxylates **II** and **III**, obtained in high yields (60–84%), are colorless crystalline substances. Their structure was proved by spectral methods. Thus, the ^{1}H NMR spectrum of compound **III** contains a signal of the furan ring proton at 7.89 ppm and methylene protons of tetrahydrobenzofuran fragment at 2.42 and 2.75 ppm. In the IR spectrum of this compound there are intensive absorption band of conjugated carbonyl (1680 cm^{-1}) and of ester fragment (1735 cm^{-1}). Also was observed an absorption band at 1550 cm^{-1} belonging to skeleton vibrations of furan cycle [6]. The electron spectrum of compound **III** contains absorption band at λ_{max} 257 nm (ε 6700) originating from system of conjugated bonds C=C and C=O [7].

It should be noted that compounds **II** and **III** were reported in [8], but they were obtained by other method in low yields (12–15%) and characterized as oily substances.

Methyl-3-bromo-3-nitroacrylate **I** was prepared by procedure developed by us earlier [9].

Methyl-4,5,6,7-tetrahydro-4-oxobenzofuran-3-carboxylate (II). A mixture of 0.99 g of methyl-3-bromo-3-nitroacrylate **I**, 0.53 g of dihydroresorcin, 0.46 g of potassium acetate in 20 ml of absolute methanol was refluxed for 6 h and poured into crushed ice. The formed suspension was extracted with chloroform (2×50 ml). The solution was dried with calcium chloride and concentrated. Yield 0.53 g (60%), mp 93–94°C (hexane). IR spectrum, ν, cm^{-1}: 1550 (C=C), 1670 (C=O), 1735 (C=O ester function). ^1H NMR spectrum, δ, ppm: 2.14–2.20 m (2H, CH_2), 2.35–2.57 t (2H, CH_2), 2.89–2.92 t (2H, CH_2), 3.86 s (3H, OCH_3), 7.88 s (1H, =CH). ^{13}C NMR spectrum, δ, ppm: 22.05, 23.50, 38.58 (CH_2); 51.91 (CH_3O); 116.98, 118.60, 147.88, 162.26 (furan cycle); 168.30 (*C*$OOCH_3$); 191.92 (C=O). UV spectrum, λ_{max}, nm (ε): 256 (6000). Found, %: C 62.20; H 5.08. $C_{10}H_{10}O_4$. Calculated, %: C 61.85; H 5.19.

Methyl-6,6-dimethyl-4,5,6,7-tetrahydro-4-oxobenzofuran-3-carboxylate (III) was prepared similarly from 0.86 g of methyl-3-bromo-3-nitroacrylate **I**, 0.57 g of dimedone and 0.40 g of potassium acetate. Crude oily product (0.8 g) was crystallized on working with diethyl ether. Yield 0.76 g (84%), mp 55–57°C (hexane). IR spectrum, ν, cm^{-1}: 1550 (C=C), 1680 (C=O), 1735 (C=O ester function). ^1H NMR spectrum, δ, ppm: 1.12 s (6H, $2CH_3$), 2.42 s (2H, CH_2), 2.75 s (2H, CH_2), 3.84 s (3H, OCH_3), 7.89 s (1H, =CH). ^{13}C NMR spectrum, δ, ppm: 28.27 ($2CH_3$); 34.81, 37.43 ($2CH_2$); 51.89 (CH_3O); 53.01 [*C*$(CH_3)_2$]; 116.85, 117.52, 148.43, 162.26 (furan cycle); 167.48 (*C*$OOCH_3$); 191.48 (C=O). UV spectrum, λ_{max}, nm (ε): 257 (6700). Found, %: C 64.87; H 6.19. $C_{12}H_{14}O_4$. Calculated, %: C 64.85; H 6.35.

The IR spectra were recorded on a SHIMADZU Fourier spectrometer IRPrestige-21 in KBr pellets. The ^1H and ^{13}C NMR spectra were taken on a Bruker spectrometer WM-400 (400 MHz) in $CDCl_3$ using residual signal of nondeuterated solvent as an internal reference. The UV spectra were registered on a Shimadzu spectrophotometer UV-2401PC in chloroform using quartz cuvettes (*l* 1 mm, *c* 3.8–4.3× 10^{-4} mol l^{-1}). Elemental analysis was performed on a Eurovector EA3028 analyzer. Compound individuality and reaction progress were monitored by TLC method on a Silufol UV-254 plates eluting with acetone-hexane mixture (1:2) and detecting by chromatoscope and iodine vapor.

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