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On the 100th anniversary of V.V. Perekalin

Geminally Activated β-Nitrostyrenes in Reactions with Cyclic β-Diketones

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Abstract—The interaction of *gem*-benzoylnitroethenes and *gem*-alkoxycarbonylnitroethenes with cyclic β-diketones (dihydroresorcinol and dimedone) occurs as a one-pot process via sequential Ad_N and S_N steps followed by denitration to give functionally substituted hexahydrobenzofurans. The intermediate products of the nucleophilic addition have been isolated in the reactions of *gem*-acetylnitroethenes with dihydroresorcinol. The structures of the synthesized compounds have been confirmed by IR, ^1H, and $^{13}C–\{^1H\}$ spectroscopy including the heteronuclear correlation experiments ($^1H–^{13}C$ HMQC and $^1H–^{13}C$ HMBC).

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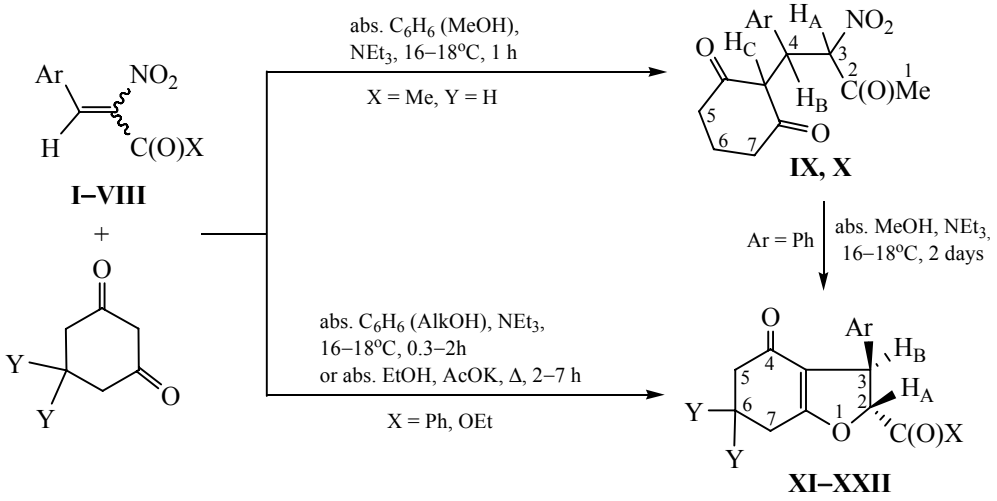
Geminally activated nitroethenes containing both nitro and acyl (acetyl, benzoyl) or ester groups at the same sp^2 carbon atom are preparatively available, highly reactive substances. These compounds are of special interest as numerous linear and cyclic structures with the important utilitarian properties may be designed on their basis: α-aminoketones, α- and γ-aminoacids, pyrrole(indole)-containing nitroketones and nitroesters, isoxazole derivatives, pyrazoles, benzothiazepine, etc. [1–8].

Since cyclic β-dicarbonyl compounds exist predominantly in the enol form in solutions [9, 10], their interaction with *gem*-acyl and *gem*-ethoxycarbonylnitroethenes leads, in addition to the Michael adducts, to heterocyclic structures –the products of the Michael adducts further transformations. Indeed, some *gem*-functionalized nitroethenes react with cyclohexane-1,3-diones to form the linear Michael adducts or substituted hexahydrobenzofurans (*gem*-dinitro- and *gem*-bromonitrostyrenes [11–14]) and tetrahydrochromenes (*gem*-cyanonitrostyrenes [15, 16]).

It was found that the reaction of *gem*-acylnitroethenes and α-nitroacrylates **I**–**VIII** with dihydroresorcinol and dimedone proceeded smoothly in anhydrous benzene or methanol in the presence of triethylamine excess (16–18°C, 0.3–2 h) or in anhydrous ethanol or methanol in the presence of potassium acetate (refluxing, 2–7 h) to give in most cases the substituted hexahydrobenzofurans **XI**–**XXII** with yields up to 82%. Their formation was a result of a one-pot process including nucleophilic addition of β-diketones at the C=C bond of activated *gem*-nitroethenes followed by intramolecular O-alkylation of the initially formed enol adducts; the process was accompanied by elimination of nitrous acid.

Only in the cases of β-acetyl-β-nitrostyrenes **I** and **II** reaction with dihydroresorcinol (anhydrous benzene, triethylamine, 16–18°C, 1 h), the process could be stopped at the stage of β-diketone addition at the C=C bond to form **IX** and **X**, respectively; the linear adducts were isolated from the solution as precipitates with yields of 90% (**IX**) and 68% (**X**). **IX** was obtained with yield of 69% in the reaction of **I** with dihydroresorcinol in methanol as well; even though in that medium the content of the enol form of 1,3-cyclohexanedione was considerably higher compared to that in nonpolar benzene [17].

The possibility of the adducts heterocyclization was demonstrated by the transformation of **IX** into the corresponding substituted hexahydrobenzofuran **XI**



X = Me: Ar = Ph (**I**), 4-$MeOC_6H_4$ (**II**); X = Ph: Ar = Ph (**III**), 4-$MeOC_6H_4$ (**IV**); X = OEt: Ar = Ph (**V**), 4-$MeOC_6H_4$ (**VI**), 4-$Me_2NC_6H_4$ (**VII**), 4-$O_2NC_6H_4$ (**VIII**); Ar = Ph (**IX**), 4-$MeOC_6H_4$ (**X**); X = Me, Ar = Ph: Y = H (**XI**); X = Ph, Ar = Ph: Y = H (**XII**), Me (**XIII**); X = Ph, Ar = 4-$MeOC_6H_4$: Y = H (**XIV**), Me (**XV**); X = OEt, Ar = Ph: Y = H (**XVI**), Me (**XVII**); X = OEt, Ar = $MeOC_6H_4$: Y = Me (**XVIII**); X = OEt, Ar = 4-$Me_2NC_6H_4$: Y = H (**XIX**), Me (**XX**); X = OEt, Ar = 4-$O_2NC_6H_4$: Y = H (**XXI**), Me (**XXII**).

after continuous incubation (for 2 days) in methanol in the presence of triethylamine.

When the reaction of ethyl α-nitroacrylates with β-diketones was performed in anhydrous methanol (instead of ethanol), partial transesterification of the products was observed. The latter process significantly complicated the isolation of individual products.

Composition and structure of the prepared linear and cyclic compounds were confirmed by results of elemental analysis, IR, ^{1}H, and ^{13}C–{^{1}H} NMR spectroscopy, including heteronuclear correlation experiments.

The IR spectra (KBr) of linear adducts **IX** and **X** contained absorption bands of non-conjugated nitro group stretching vibrations at 1560 and 1370 cm^{-1} and broad absorption bands in the range of 1580–1660 cm^{-1}, assigned to the carbonyl groups of dimedone fragment and acetyl group. The unusual shape of the carbonyl bands was probably due the ability of 1,3-cyclohexanediones enol form, predominant in the solid state, to form hydrogen bonds, including those of the intermolecular associates [18, 19]. In the IR spectrum of dimedone (KBr), a broad absorption band with maxima at 1616 and 1575 cm^{-1} was attributed to the dimer of its enol form [20].

According to the ^{1}H NMR spectra of **IX** (DMSO-d_6) and **X** ($CDCl_3$), those adducts were individual diastereomers. The signals of three methyne protons appeared as doublets at 4.74–5.25 (H_A) and 4.39–4.50 ppm (H_C) and the doublet of doublets at 3.82–3.94 ppm (H_B) with $^3J(H_AH_B)$ of 9.00–15.00 Hz and $^3J(H_BH_C)$ of 5.00–10.00 Hz. The protons of methyl groups [$C(O)CH_3$] were assigned to the singlets at 2.14–2.18 ppm.

The prepared hexahydrobenzofuranes **XI**–**XXII** were individual diastereomers as well. In particular, in the ^{1}H NMR spectrum of **XX** in $CDCl_3$ (Fig. 1), the signals of methyne protons H_A and H_B appeared at 4.93 and 4.35 ppm. The corresponding spin–spin coupling constant [$^3J(H_AH_B)$ of 4.58 Hz] and the respective values throughout the whole hexahydrobenzofurans series [$^3J(H_AH_B)$ of 4.00–5.50 Hz] indicated that **XI**–**XXII** were *trans*-isomers [21].

From ^{1}H–^{13}C HMQC spectrum of **XX**, the downfield H_A signal (4.93 ppm) correlated with the signal of carbon atom at 88.56 ppm, whereas the H_B signal (4.35 ppm) correlated with the carbon atom signal at 49.16 ppm; thus the downfield signal could be assigned to C^2 and the upfield one corresponded to C^3. The methyl groups signals of dimedone fragment (1.14 and 1.16 ppm) and of dimethylamine moiety (2.90 ppm) revealed cross-peaks with the signals of C^{21} (28.57 ppm), C^{22} (29.09 ppm), and $C^{19,20}$ (40.73 ppm), respectively. The signals of ethoxycarbonyl group protons appearing as a triplet at 1.24 ppm ($C^{12}H_3$) and two doublets of quartets (due to the magnetic non-equivalence of

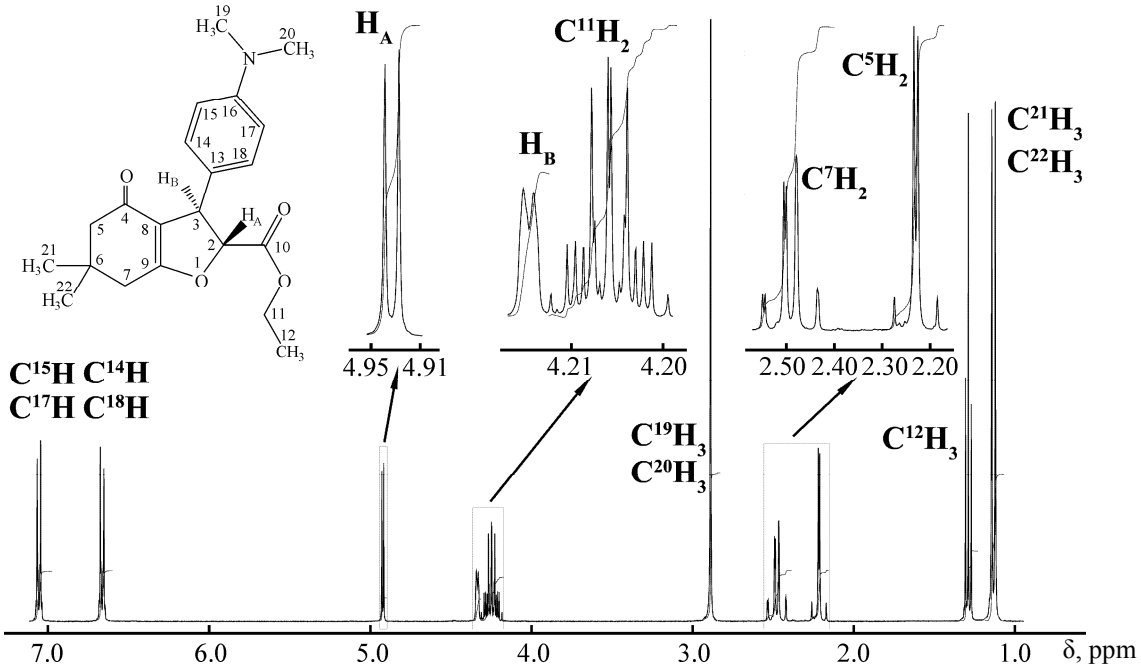
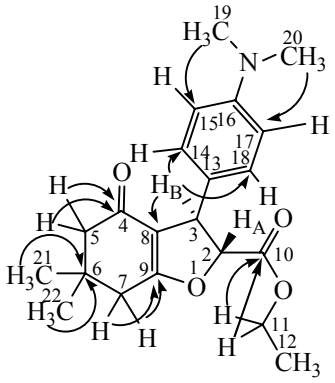


Fig. 1. ^{1}H NMR spectrum of compound **XX** in $CDCl_3$.

diastereotopic methylene protons) at 4.24 and 4.28 ppm (^{2}J 10.75 and ^{3}J 7.15 Hz) ($C^{11}H_2$) correlated with the signals of C^{12} (14.27 ppm) and C^{11} (61.87 ppm), respectively. The methylene protons of dimedone rings appeared as two strongly coupled AB systems at 2.21, 2.25 (^{2}J 16.17 Hz) and 2.46, 2.53 ppm (^{2}J 16.17 Hz) in the ^{1}H NMR spectra, those signals were correlated with the respective carbons C^5 (51.33 ppm) and C^7 (37.77 ppm). It should be noted that the proton signal at 2.53 ppm was observed as a doublet of doublets, the spin–spin coupling constant with the H_B being of 2.14 Hz, the latter appeared as a broad doublet for this reason; the interaction between those protons through 5 bonds was confirmed by the presence of the cross-peak in the COSY experiment. The protons of *para*-substituted benzene ring at 6.67 ($C^{15}H$, $C^{17}H$) and 7.07 ppm ($C^{14}H$, $C^{18}H$) showed cross-peaks with $C^{15,17}$ (113.02 ppm) and $C^{14,18}$ (127.66 ppm), respectively. The described assignments were additionally confirmed by the ^{1}H–^{13}C HMBC spectral data (Fig. 2), namely by the cross-peaks of: 2.21, 2.25 ppm (C^5H_2) with 193.92 ppm (C^4), 2.46, 2.53 ppm (C^7H_2) with 176.08 ppm (C^9), 4.35 ppm (H_B) with 114.90 ppm (C^8), 4.24, 4.28 ppm ($C^{11}H_2$) with 169.86 ppm (C^{10}), 1.14, 1.16 ppm ($C^{21}H_3$, $C^{22}H_3$) with 34.34 ppm (C^6), 2.90 ppm (C^{19} H_3, $C^{20}H_3$) with 113.02 ppm ($C^{15,17}$), and 4.35 ppm (H_B) with 127.66 ppm ($C^{14,18}$). The above listed interpretation of the ^{1}H and ^{13}C NMR spectra were in accordance with the similar assignments made for the structural analog of **XX** containing *p*-tolyl and *p*-chlorophenyl substituents at positions 2 and 3 instead of ethoxycarbonyl and *p*-*N,N*- dimethylaminophenyl groups, respectively [22]. At the same time, in [23] the H_B proton was assigned to the signal in a weaker field than that of H_A, however, no arguments supporting that assumption were given.



The melting points and spectroscopic data of **XII**–**XVIII** were close to those of the samples prepared by other methods in [22–29]. For example, compounds **XII** and **XIII** were obtained by microwave or convection heating of α-sulfonyl chalcone derivative with cyclohexane-1,3-dione in ethanol in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene [22], and compounds **XVI**–**XVIII** were synthesized via the three-

component interaction of aromatic aldehydes, haloacetates, and cyclic β-diketones upon refluxing in acetonitrile in the presence of pyridine and catalytic amounts of 1,4-diazabicyclo[2.2.1]octane for 10–12 h [24].

After the experiment presented in this work had been finished, the Chinese authors reported [30] on the reaction of α-nitrocinnamic esters with cyclic β-diketones (1:2 ratio). The reaction was performed in water in the presence of triethylamine and tetrabutylammonium bromide at 70°C (6 h). The resulting cyclic products, compounds **XVI** and **XVII** (prepared in this work starting from α-nitrocinnamic acid ester **V**) being among them, were isolated by silica gel chromatography. However, the melting point (106–109°C) of **XVII** given in [30] significantly differed from that of the reference sample prepared in [22] (82–84°C) and the sample synthesized in this work (80–82°C).

Thus, the studied reactions illustrated the use of *gem*-acylnitroethenes and *gem*-alkoxycarbonylnitroethenes as synthons for preparation of the substituted 2,3,4,5,6,7-hexahydrobenzofurans, being of interest in many application areas. For example, hydrobenzofuran and benzofuran rings are key moieties in many natural substances, drugs and dietary supplements [31–33]. The widely used examples of such products are benzofurocainum (local analgesic), fenicaberanum (antispasmodic agent and vasodilator), griseofulvin (antifungal antibiotic), etc. According to [22], compounds of hexahydrobenzofuran type can be successfully applied for the treatment of traumatic and ischemic diseases, arteriosclerosis, hepatopathy, cerebrovascular accidents, etc.

EXPERIMENTAL

The ^{1}H, ^{13}C–{^{1}H}, ^{1}H–^{13}C HMQC, HMBC, and COSY NMR spectra were recorded with Jeol ECX400A spectrometer [399.78 (^{1}H), 100.53 (^{13}C) MHz] in $CDCl_3$ or DMSO-d_6; the residual non-deuterated solvent signals were used as internal standard. IR spectra were registered with Shimadzu

Table 1. The IR and ^{1}H NMR spectra of compounds **IX**–**XXII**

Comp. no.	IR spectra ($CHCl_3$), ν, cm^{-1}[a]	^{1}H, ^{13}C NMR ($CDCl_3$), δ, ppm (J, Hz)[b]								
	C=O (NO_2)	H_A	H_B	H_C	OCH_2CH_3 [$C(O)CH_3$]	OCH_3 [$N(CH_3)_2$]	C^5H_2	C^7H_2	C^6H_2 [CH_3]	Ar
IX	1580–1660 (1560, 1370)	5.25 d	3.82 d.d	4.50 d	[2.14 s]	–	2.41 m, 2.68 m			7.30–7.50 m
		$J(H_AH_B)$ 15.00	$J(H_BH_C)$ 10.00							
X	1580–1660 (1560, 1370)	4.79 d	3.94 d.d	4.39 d	[2.18 s]	3.69 s	1.96 m, 2.34 m			6.75 d, 7.25 d
		$J(H_AH_B)$ 9.00 0	$J(H_BH_C)$ 5.0							
XI	1730, 1645	4.97 d	4.47 d	–	[2.24 s]	–	2.15 m, 2.40 m			7.20–7.35 m
		$J(H_AH_B)$ 5.50								
XII	1700, 1640	5.75 d	4.35 d	–	–	–	2.19 m, 2.62 m			7.21–7.71 m
		$J(H_AH_B)$ 4.00								
XIII	1700, 1635	5.79 d	4.30 d	–	–	–	2.12 m	2.49 m	[1.09 s]	7.17–7.70 m
		$J(H_AH_B)$ 4.00								
XIV	1695, 1625–1650	5.83 d	4.34 d	–	–	3.79 s	2.12 m, 2.31 m, 2.71 m			6.87 d, 7.14 d, 7.44 t, 7.60 d, 7.80 d
		$J(H_AH_B)$ 4.58								
XV	1700, 1640	5.85 d	4.33 br.d	–	–	3.80 s	2.16 d, 2.24 d (^{2}J 16.17)	2.52 d, 2.62 d.d [^{2}J 17.70, $^{5}J(C^7HH_B)$ 1.83]	[1.15 s]	6.88 d, 7.15 d, 7.45 t, 7.61 d, 7.81 d
		$J(H_AH_B)$ 4.58								
XVI	1750, 1640	4.95 d	4.45 d	–	1.33 t, 4.26 d.q, 4.31 d.q (^{2}J 10.75, ^{3}J 7.15)	–	2.13 m, 2.37 m, 2.66 m			7.21–7.31 m
		$J(H_AH_B)$ 4.88								

Table 1. (Contd.)

Comp. no.	IR spectra ($CHCl_3$), ν, cm^{-1}[a]	^1H, ^{13}C NMR ($CDCl_3$), δ, ppm (*J*, Hz)[b]								
	C=O (NO_2)	H_A	H_B	H_C	OCH_2CH_3 [$C(O)CH_3$]	OCH_3 [$N(CH_3)_2$]	C^5H_2	C^7H_2	C^6H_2 [CH_3]	Ar
XVII	1750, 1640	4.98 d	4.44 br.d	–	1.33 t, 4.26 d.q, 4.30 d.q (^2J 10.80, ^3J 7.15)	–	2.22 d, 2.27 d (^2J 16.37)	2.48 d, 2.55 d.d [^2J 17.81, $^5J(C^7HH_B)$ 1.75]	[1.15 s, 1.17 s]	7.21–7.31 m
		$J(H_AH_B)$ 4.43								
XVIII	1755, 1640	4.95 d	4.40 br.d	–	1.32 t, 4.25 d.q, 4.30 d.q (^2J 10.80, ^3J 7.20)	3.77 s	2.21 d, 2.26 d (^2J 16.44)	2.47 d, 2.54 d.d [^2J 17.83, $^5J(C^7HH_B)$ 1.90]	[1.14 s, 1.16 s]	6.84 d, 7.12 d
		$J(H_AH_B)$ 4.68								
XIX	1750, 1640	4.92 d	4.37 d	–	1.31 t, 4.24 d.q, 4.30 d.q (^2J 10.75, ^3J 7.15)	[2.91 s]	2.11 m, 2.34 m, 2.64 m			6.68 d, 7.07 d
		$J(H_AH_B)$ 4.88								
XX	1750, 1640	4.93 d	4.35 br.d	–	1.30 t, 4.24 d.q, 4.28 d.q (^2J 10.75, ^3J 7.15)	[2.90 s]	2.21d, 2.25d (^2J 16.17)	2.46 d, 2.53 d.d [^2J 17.70, $^5J(C^7HH_B)$ 2.14]	[1.14 s, 1.16 s]	6.67 d, 7.07 d
		$J(H_AH_B)$ 4.58								
XXI	1755, 1640 (1525, 1350)	4.93 d	4.56 d	–	1.33 t, 4.28 d.q, 4.33 d.q (^2J 10.80, ^3J 7.15)	–	2.14 m, 2.37 m, 2.68 m			7.39 d, 8.18 d
		$J(H_AH_B)$ 5.34								
XXII	1755, 1640 (1525, 1350)	4.96 d	4.54 br.d	–	1.35 t, 4.28 d.q, 4.32 d.q (^2J 10.75, ^3J 7.15)	–	2.22 d, 2.28 d (^2J 16.35)	2.50 d, 2.57 d.d [^2J 17.60, $^5J(C^7HH_B)$ 1.94]	[1.158 s, 1.161 s]	7.39 d, 8.19 d
		$J(H_AH_B)$ 5.19								

[a] IR spectra of compounds **IX**, **X** were registered in KBr pellets. [b] ^1H NMR spectrum of compound **IX** was recorded in DMSO-d_6.

Table 2. The $^{13}C–\{^1H\}$ NMR spectral data of hexahydrobenzofurans **XIV**, **XV**, **XX** in $CDCl_3$ (δ, ppm)

Comp. no.	C^2	C^3	C^4	C^5	C^6	C^7	C^8	C^9	$\underline{C}OC_6H_5$ ($COOCH_2CH_3$)	CH_3 (OCH_3) [$N(CH_3)_2$]	Ar
XIV	91.81	48.47	194.41	21.81, 23.97, 36.88			116.65	177.21	193.09	(55.39)	114.48, 128.44, 128.99, 129.03, 133.29, 133.33, 134.24, 159.06
XV	92.05	48.51	193.71	51.24	34.40	37.74	115.31	176.23	193.00	28.45, 29.18 (55.38)	114.53, 128.41, 128.99, 129.00, 133.28, 133.41, 134.23, 159.08
XX	88.56	49.16	193.92	51.33	34.34	37.77	114.90	176.08	(169.86, 61.87, 14.27)	28.57, 29.09 [40.73]	113.02, 127.66, 129.19, 150.02

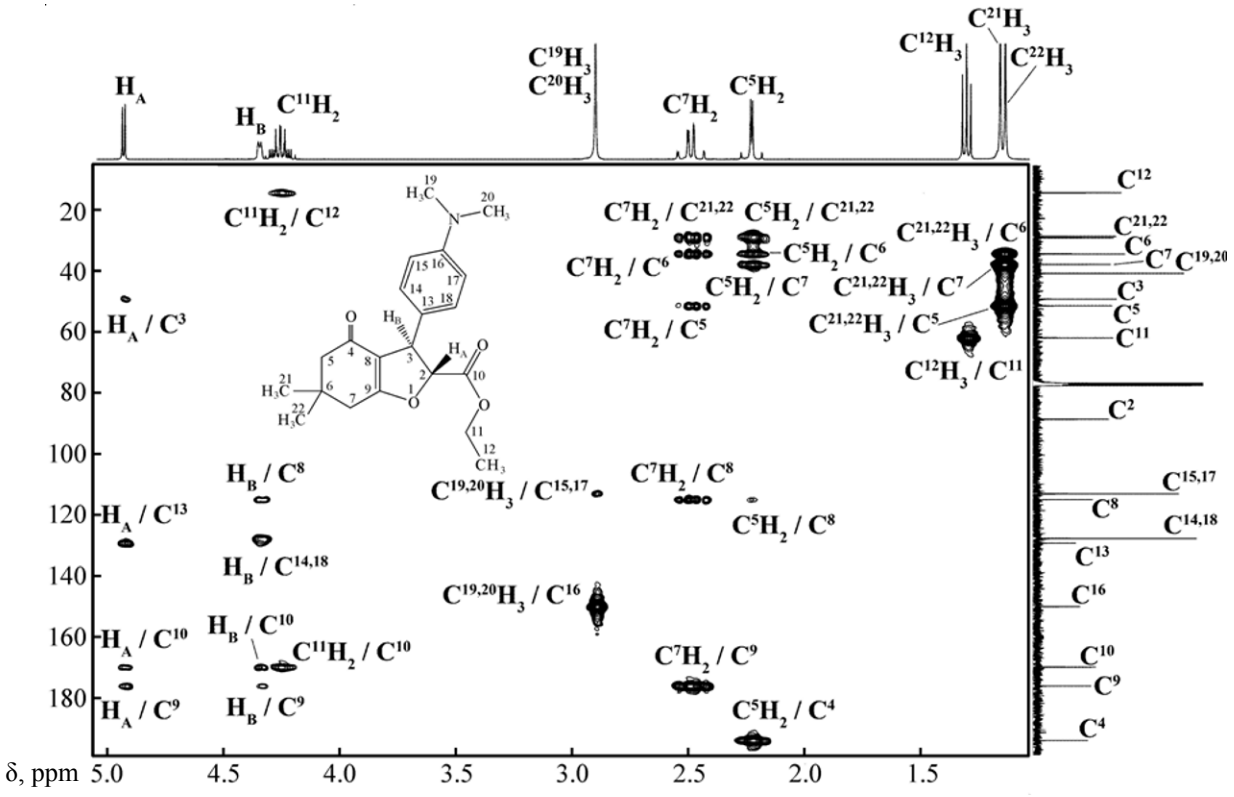


Fig. 2. Fragment of ^1H–^{13}C HMBC spectrum of compound **XX** in $CDCl_3$.

IRPrestige-21 Fourier spectrometer in $CHCl_3$ (*c* = 40 mg ml^{-1}) or in KBr pellets. Elemental analysis was performed with Eurovector EA 3000 (CHN Dual mode) analyzer. The ^1H NMR spectra of **IX**–**XIII** were recorded with Tesla BS-487S spectrometer (80 MHz).

Starting *gem*-acyl nitrostyrenes **I**–**IV** were prepared as described in [3, 34, and 35]. Synthesis of α-nitrocinnamic ester **V**–**VII** was performed similarly to [2], and **VIII** was obtained according to [36].

3-Nitro-4-phenyl-4-(cyclohexane-1,3-dione-2-yl)-butan-2-one (IX). *a*. 0.2 g (2 mmol) of triethylamine was added to a suspension of 0.29 g (1.5 mmol) of 3-nitro-4-phenyl-3-buten-2-one **I** and 0.17 g (1.5 mmol) of dihydroresorcinol in 4 ml of anhydrous benzene at 16–18°C. The reaction mixture was kept at this temperature for 1 h. The formed solid was filtered off and dried. Yield 0.41 g (90%), colorless crystals, mp 178–180°C (ethanol). Found, %: C 63.25, 63.25; H 5.71, 5.72; N 4.52, 4.51. $C_{16}H_{17}NO_5$. Calculated, %: C 63.37; H 5.61; N 4.62.

b. 0.15 g (1.5 mmol) of triethylamine was added to a suspension of 0.19 g (1 mmol) of 3-nitro-4-phenyl-3-buten-2-one **I** and 0.11 g (1 mmol) of dihydroresorcinol in 5 ml of anhydrous methanol at 16–18°C. The reaction mixture was kept at this temperature for 1 h. The formed crystalline product was filtered off and dried. Yield 0.21 g (69%), mp 176–178°C (ethanol). Melting point of the mixture of samples ob-tained by the both methods was not depressed.

4-(4-Methoxyphenyl)-3-nitro-4-(cyclohexane-1,3-dione-2-yl)butan-2-one (X). 0.15 g (1.5 mmol) of triethylamine was added to a suspension of 0.22 g (1 mmol) of 4-(4-methoxyphenyl)-3-nitro-3-buten-2-one **II** and 0.11 g (1 mmol) of dihydroresorcinol in 4 ml of anhydrous benzene at 16–18°C. The reaction mixture was kept at this temperature for 1 h. The formed crystalline product was filtered off and dried. Yield 0.23 g (68%), mp 152–154°C (chloroform). Found, %: C 61.28, 61.32; H 5.74, 5.74; N 4.37, 4.36. $C_{17}H_{19}NO_6$. Calculated, %: C 61.26; H 5.71; N 4.20.

2-Acetyl-4-oxo-3-phenyl-2,3,4,5,6,7-hexahydro-benzofuran (XI). 0.10 g (1 mmol) of triethylamine was added to a suspension of 0.30 g (1 mmol) of 3-nitro-4-phenyl-4-(cyclohexane-1,3-dione-2-yl)butan-2-one **XI** in 10 ml of anhydrous methanol at a 16–18°C. The reaction mixture was kept at this temperature for

2 days. After evaporation of the solvent, the residue was treated with a small amount of ethanol and filtered off. Yield 0.17 g (67%), colorless crystals, mp 118–120°C (ethanol). Found, %: C 74.92, 74.95; H 6.31, 6.32. $C_{16}H_{16}O_3$. Calculated, %: C 75.00; H 6.25.

2-Benzoyl-4-oxo-3-phenyl-2,3,4,5,6,7-hexahydrobenzofuran (XII). 0.20 g (2 mmol) of triethylamine was added to a suspension of 0.25 g (1 mmol) of 1,3-diphenyl-2-nitro-2-propen-1-one **III** and 0.11 g (1 mmol) of dihydroresorcinol in 10 ml of anhydrous benzene at 16–18°C. The reaction mixture was kept at this temperature for 2 h. After evaporation of the solvent, the residue was treated with a small amount of ethanol and filtered off. Yield 0.26 g (81%), colorless crystals, mp 118–120°C (ethanol) {mp 124–126°C [22]}. Found, %: C 79.33, 79.27; H 5.70, 5.58. $C_{21}H_{18}O_3$. Calculated, %: C 79.25; H 5.66.

2-Benzoyl-6,6-dimethyl-4-oxo-3-phenyl-2,3,4,5,6,7-hexahydrobenzofuran (XIII). 0.30 g (3 mmol) of triethylamine was added to a suspension of 0.51 g (2 mmol) of 1,3-diphenyl-2-nitro-2-propen-1-one **III** and 0.28 g (2 mmol) of dimedone in 15 ml of anhydrous benzene at 16–18°C. The reaction mixture was kept at this temperature for 1 h. After evaporation of the solvent, the residue was treated with a small amount of ethanol and filtered off. Yield 0.28 g (41%), colorless crystals, mp 97–99°C (ethanol) {mp 98°C [25]}. Found, %: C 79.79, 79.74; H 6.74, 6.38. $C_{23}H_{22}O_3$. Calculated, %: C 79.77; H 6.36.

2-Benzoyl-3-(4-methoxyphenyl)-4-oxo-2,3,4,5,6,7-hexahydrobenzofuran (XIV). 0.15 g (1.5 mol) of triethylamine was added to a suspension of 0.28 g (1 mmol) of 3-(4-methoxyphenyl)-2-nitro-1-phenyl-2-propen-1-one **IV** and 0.11 g (1 mmol) of dihydroresorcinol in 9 ml of anhydrous benzene at 16–18°C. The reaction mixture was kept at this temperature for 20 min. After evaporation of the solvent, the residue was treated with a small amount of ethanol and filtered off. Yield 0.2 g (56%), colorless crystals, mp 118–120°C (ethanol) {mp 118°C (ethanol) [26]}. Found, %: C 75.92, 75.94; H 5.58, 5.61. $C_{22}H_{20}O_4$. Calculated, %: C 75.86; H 5.75.

2-Benzoyl-6,6-dimethyl-3-(4-methoxyphenyl)-4-oxo-2,3,4,5,6,7-hexahydrobenzofuran (XV). 0.20 g (2 mmol) of triethylamine was added to a suspension of 0.43 g (1.5 mmol) of 3-(4-methoxyphenyl)-2-nitro-1-phenyl-2-propen-1-one **IV** and 0.21 g (1.5 mmol) of dimedone in 15 ml of anhydrous benzene at 16–18°C. The reaction mixture was kept at this temperature for 2 h. After evaporation of the solvent, the residue was treated with a small amount of ethanol and filtered off. Yield 0.34 g (60%), colorless crystals, mp 143–146°C (ethanol) {mp 143–146°C (ethanol) [23]}. Found, %: C 76.69, 76.61; H, 6.42, 6.39. $C_{24}H_{24}O_4$. Calculated, %: C 76.60; H 6.38.

Ethyl-4-oxo-3-phenyl-2,3,4,5,6,7-hexahydrobenzofuran-2-carboxylate (XVI). A mixture of 0.22 g (1 mmol) of ethyl 2-nitro-3-phenylpropenoate **V**, 0.11 g (1 mmol) of dihydroresorcinol, and 0.10 g of potassium acetate in 7 ml of anhydrous ethanol was refluxed for 2 h. After cooling, the formed precipitate was filtered off. Yield 0.16 g (56%), colorless crystals, mp 78–80°C (hexane) {mp 80–82°C [24]}. Found, %: C 71.49; H 6.64. $C_{17}H_{18}O_4$. Calculated, %: C 71.33; H 6.29.

Ethyl 6,6-dimethyl-4-oxo-3-phenyl-2,3,4,5,6,7-hexahydrobenzofuran-2-carboxylate (XVII). A mixture of 1.52 g (6.9 mmol) of ethyl 2-nitro-3-phenylpropenoate **V**, 0.97 g (6.9 mmol) of dimedone, and 0.67 g of potassium acetate in 30 ml of anhydrous methanol was refluxed for 6 h. Then the resulting solution was poured into crushed ice. The oily product was extracted with ether, dried over $MgSO_4$, and the solvent was evaporated to give 1.04 g (48%) of crude product, transparent oil. The latter was separated on silica gel by eluting with chloroform and diethyl ether. Yield 0.79 g (36%), colorless crystals, mp 80–82°C (hexane) {mp 82–84°C (ethanol) [24]}. Found, %: C 72.67; H 7.06. $C_{19}H_{22}O_4$. Calculated, %: C 72.61; H 7.01.

Ethyl 6,6-dimethyl-3-(4-methoxyphenyl)-4-oxo-2,3,4,5,6,7-hexahydrobenzofuran-2-carboxylate (XVIII). A mixture of 1.06 g (4.2 mmol) of ethyl 3-(4-methoxyphenyl)-2-nitropropenoate **VI**, 0.59 g (4.2 mmol) of dimedone, and 0.41 g of potassium acetate in 20 ml of anhydrous methanol was refluxed for 6 h. Then the resulting solution was poured into crushed ice. The oily product was extracted with ether, dried over $MgSO_4$, and the solvent was evaporated to give 1.04 g (72%) of crude product, oil. The latter was separated on silica gel by eluting with chloroform and diethyl ether. Yield 0.19 g (13%), colorless crystals, mp 110–112°C (ethanol) {mp 110–112°C (ethanol) [24]}. Found, %: C 69.44; H 7.22. $C_{20}H_{24}O_5$. Calculated, %: C 69.77; H 6.98.

Ethyl 3-(4-*N*,*N*-dimethylaminophenyl)-4-oxo-2,3,4,5,6,7-hexahydrobenzofuran-2-carboxylate (XIX). A mixture of 1.19 g (4.5 mmol) of ethyl 3-(4-*N*,*N*-dimethylaminophenyl)-2-nitropropenoate **VII**, 0.50 g

(4.5 mmol) dihydroresorcinol, and 0.44 g of potassium acetate in 20 ml of anhydrous methanol was refluxed for 6 h. Then the resulting solution was poured into crushed ice. The oily product was extracted with ether, dried over $MgSO_4$, and the solvent was evaporated to give 0.82 g (55%) of crude product, dark oil. The latter was separated on silica gel by eluting with chloroform and benzene. Yield 0.36 g (24%), mp 76–78°C. Found, %: N 4.28. $C_{19}H_{23}NO_4$. Calculated, %: N 4.26.

Ethyl 6,6-dimethyl-3-(4-*N*,*N*-dimethylaminophenyl)-4-oxo-2,3,4,5,6,7-hexahydrobenzofuran-2-carboxylate (XX). A mixture of 0.4 g (1.5 mmol) of ethyl 3-(4-*N*,*N*-dimethylaminophenyl)-2-nitropropenoate **VII**, 0.21 g (1.5 mmol) of dimedone, and 0.15 g of potassium acetate in 7 ml of anhydrous ethanol was refluxed for 7 h. The resulting solution was poured into crushed ice. The formed solid was filtered off. Yield 0.41 g (76%), colorless crystals, mp 113–115°C (hexane). Found, %: C 70.38; H 8.05; N 3.94. $C_{21}H_{27}NO_4$. Calculated, %: C 70.59; H 7.56; N 3.92.

Ethyl 3-(4-nitrophenyl)-4-oxo-2,3,4,5,6,7-hexahydrobenzofuran-2-carboxylate (XXI). *a*. A mixture of 0.27 g (1 mmol) of ethyl 2-nitro-3-(4-nitrophenyl)-propenoate **VIII**, 0.11 g (1 mmol) dihydroresorcinol, and 0.10 g of potassium acetate in 7 ml of anhydrous ethanol was refluxed for 2 h. Then the resulting solution was poured into crushed ice. The oily product was extracted with ether, dried over $MgSO_4$, and the solvent was evaporated. After treatment of the residue with ethanol, the formed solid was filtered off. Yield 0.27 g (82%), pale yellow crystals, mp 101–103°C (carbon tetrachloride–hexane, 1:1). Found, %: C 61.57; H 5.17; N 4.28. $C_{17}H_{17}NO_6$. Calculated, %: C 61.63; H 5.14; N 4.23.

b. A mixture of 0.27 g (1 mmol) of ethyl 2-nitro-3-(4-nitrophenyl)propenoate **VIII**, 0.11 g (1 mmol) dihydroresorcinol, and 0.15 g (1.5 mmol) of triethylamine in 5 ml of anhydrous ethanol was kept at 16–18°C for 2 h. After evaporation of the solvent and treatment of the residue with ethanol, the formed solid was filtered off. Yield 0.22 g (68%), pale yellow crystals, mp 98–100°C (carbon tetrachloride–hexane, 1:1). The melting point of the mixture of samples obtained by the both methods was not depressed.

Ethyl 6,6-dimethyl-3-(4-nitrophenyl)-4-oxo-2,3,4,5,6,7-hexahydrobenzofuran-2-carboxylate (XXII). *a*. A mixture of 0.27 g (1 mmol) of ethyl 2-nitro-3-(4-nitrophenyl)propenoate **VIII**, 0.14 g (1 mmol) of dimedone, and 0.1 g of potassium acetate in 7 ml of anhydrous ethanol was refluxed for 2 h. Then the solution was poured into crushed ice, and the formed solid was filtered off. Yield 0.29 g (81%), colorless crystals, mp 81–83°C (ethanol). Found, %: C 63.31; H 6.10. $C_{19}H_{21}NO_6$. Calculated, %: C 63.51; H 5.85.

b. 0.15 g (1.5 mmol) of triethylamine was added to a suspension of 0.27 g (1 mmol) of ethyl 2-nitro-3-(4-nitrophenyl)propenoate **VIII** and 0.14 g (1 mmol) of dimedone in 5 ml of anhydrous ethanol at a 16–18°C. The reaction mixture was kept at this temperature for 2 h. After evaporation of the solvent and treatment of the residue with ethanol, the formed solid was filtered off. Yield 0.21 g (57%), colorless crystals, mp 80–81°C (ethanol). Melting point of the mixture of samples obtained by the both methods was not depressed.

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