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Synthesis and Structure of Geminally Activated Nitroethenes of the Indole Series[1]

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Abstract—A series of 2-(indol-3-yl)-1-nitroethenes containing an ester, acetyl, benzoyl, or cyano group in the geminal position with respect to the nitro group have been synthesized, and their structure has been studied by ^{1}H, ^{13}C–{^{1}H} NMR, IR, and UV spectroscopy.

Keywords: indole, *gem*-ethoxycarbonylnitroethene, *gem*-acetylnitroethene, *gem*-benzoylnitroethene, *gem*-cyanonitroethene

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β-Nitrostyrenes and their furan and thiophene analogs containing an ester, acyl, or cyano group in the geminal position with respect to the nitro group are reactive compounds and convenient intermediate products for the synthesis of various linear and cyclic structures [1–4], many of which (α-amino acids, α-amino ketones, 1,2,3-triazoles, dihydrofurans, dihydro-1,5-benzothiazepines, etc.) possess practically useful properties.

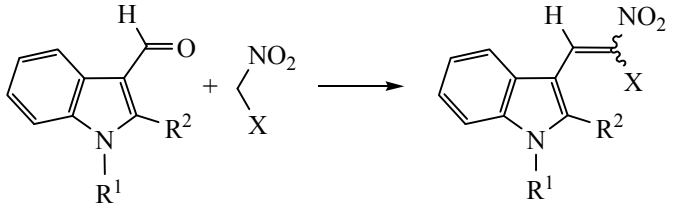
On the other hand, an important position among biologically active compounds is occupied by those containing a pharmacophoric indole ring [5–9]. For example, medicines of the indole series, such as vinprocetine, indometacin, α-methyltryptamine, bopindolol, umifenovir, etc., are widely used in medical practice [10, 11]. Preparatively accessible indole compounds are widely used in organic synthesis [12]. Interest in 3-(2-nitrovinyl)indoles has increased in recent years [13–17]. However, published data on geminally functionalized nitroethenes containing an indole fragment are mainly concerned with α-nitroacrylates. Only a few synthetic procedures and scattered spectral characteristics are available for their acyl and cyano analogs. Nevertheless, structural features of nitroethenes of the indole series containing an ester, acyl, or cyano group in the geminal position with respect to the nitro group are of undoubted interest.

It is known that in most cases the condensation of aldehydes with nitro-substituted CH acids in the presence of bases gives no desired geminally activated (het)aryl-substituted nitroethenes but leads to the formation of 2,4-dinitroglutaric acid derivatives, substituted (dihydro)isoxazole *N*-oxides [18–22], or 5-hydroxy-6-oxo-1,2-oxazine-3-carboxylates (isolated as salts) [23]. Furthermore, base-catalyzed reactions of aldehydes with nitroacetone involved only the methyl group of the latter [24], whereas nitroacetophenone readily decomposed in the presence of strong bases [25].

Some geminally activated nitroethenes could be obtained from Schiff bases or acetals. For example, ethyl β-(1-acetylindol-3-yl)-α-nitroacrylate [19, 20] and methyl β-(indol-3-yl)-α-nitroacrylate [26, 27] were synthesized from nitroacetic acid esters. Direct alkenylation of nitroacetic acid ester with (hetero) aromatic aldehydes in anhydrous CCl_4–THF in the presence of $TiCl_4$ and *N*-methylmorpholine (pyridine) was also successful [28–30]. The condensation of indole-3-carbaldehyde and its analogs with ethyl nitroacetate, nitroacetone, and nitroacetophenone in ethanol

[1] Supplementary materials are available for this article at doi 10.1134/S1070363219050037 and are accessible for authorized users.

Scheme 1.

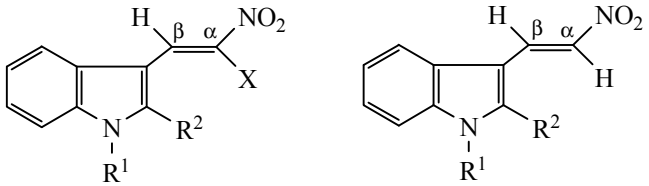


1–5 **6–22**

$R^1 = R^2 = H$ (**1**); R^1 = Me, $R^2 = H$ (**2**); R^1 = Bn, $R^2 = H$ (**3**); $R^1 = R^2$ = Me (**4**); R^1 = C(O)Me, $R^2 = H$ (**5**); X = C(O)OEt: R^1 = Bn, $R^2 = H$ (**6**); $R^1 = R^2$ = Me (**7**); R^1 = C(O)Me, $R^2 = H$ (**8**); X = C(O)Me: $R^1 = R^2 = H$ (**9**); R^1 = Me, $R^2 = H$ (**10**); R^1 = Bn, $R^2 = H$ (**11**); $R^1 = R^2$ = Me (**12**); X = C(O)Ph : $R^1 = R^2 = H$ (**13**); R^1 = Me, $R^2 = H$ (**14**); R^1 = Bn, $R^2 = H$ (**15**); $R^1 = R^2$ = Me (**16**); R^1 = C(O)Me, $R^2 = H$ (**17**); X = CN: $R^1 = R^2 = H$ (**18**); R^1 = Me, $R^2 = H$ (**19**); R^1 = Bn, $R^2 = H$ (**20**); $R^1 = R^2$ = Me (**21**); R^1 = C(O)Me, $R^2 = H$ (**22**).

in the presence of aprotic and protic acids also seems promising [19, 31, 32]; it made it possible to obtain a wide series of (hetero)aryl-substituted nitroethenes [33–35]. Various geminal alkoxycarbonyl- and benzoyl-nitroethenes (including indole-containing analogs) were synthesized by heating aldehydes and the corresponding CH acids in boiling benzene in the presence of acetic acid and β-alanine or ε-amino-

Table 1. ^{1}H NMR spectra of (*E*)-benzoyl(cyano)nitroethenes **13**–**18** and **20**–**24**[a]

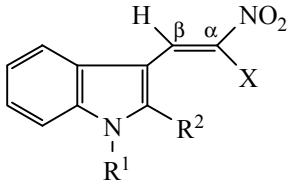


13–18, 20–22 **23**, **24**

Compound no.	X	R^1	R^2	δ, ppm, *J*, Hz		
				H^α (H^β)	R^1	H_{arom}
13	C(O)Ph	H	H	8.80 s	12.33 s	7.10–8.0 m
14	C(O)Ph	Me	H	8.77 s	3.76 s	7.30–7.94 m
15	C(O)Ph	CH_2Ph	H	8.69 s	5.24 s	6.90–7.90 m
16[b]	C(O)Ph	Me	Me	8.70 s	3.69 s	6.95–8.00 m
17	C(O)Ph	C(O)Me	H	8.59 s	2.52 s	7.40–8.44 m
18	CN	H	H	8.93 s	13.06 s	7.27 m, 7.53, 8.00 m, 8.54 m
20	CN	CH_2Ph	H	9.08 s	5.68 s	7.31–7.33 m, 7.66 m, 8.13 m, 8.80 m
21[c]	CN	Me	Me	8.78 s	3.81 s	7.32–7.40 m, 7.67 m, 8.14 m
22	CN	C(O)Me	H	9.09 s	2.70 s	7.42–7.47 m, 8.14 m, 8.33 m, 8.80 m
23	–	CH_2Ph	H	8.13 d (7.61 d) $J_{\alpha\beta}$ = 14.0	5.18 s	7.19–7.43 m
24	–	C(O)Me	H	8.17 d (7.81 d) $J_{\alpha\beta}$ = 13.7	2.71 s	7.40–7.87 m, 8.48–8.52 m

[a] The ^{1}H NMR spectra of **13**, **18**, and **20**–**22** were recorded in DMSO-d_6, and of **14**–**17**, **23**, and **24**, in $CDCl_3$.
[b] 2-Me: δ 2.57 ppm.
[c] 2-Me: δ 2.60 ppm.

Table 2. $^{13}C–\{^1H\}$ NMR spectra of (*E*)-benzoyl(cyano)nitroethenes **13**–**18** and **20**–**22**[a]



13–18, 20–22

Comp. no.	X	R^1	R^2	δ_C, ppm (*J*, Hz)			
				C^α	C^β	R^1	X
13	C(O)Ph	H	H	138.40	132.77	–	190.41 (C=O)
14	C(O)Ph	CH_3	H	139.14	131.04	34.01	190.29 (C=O)
15	C(O)Ph	CH_2Ph	H	140.01	130.13	51.28 (CH_2)	189.43 (C=O)
16	C(O)Ph	CH_3	CH_3	138.98	134.02	30.66	189.70 (C=O)
17	C(O)Ph	$C(O)CH_3$	H	144.02	129.04	23.82 (CH_3), 168.53 (C=O)	188.80 (C=O)
18	CN	H	H	115.31	142.58	–	114.70 (CN, $^3J_{CNH\beta}$ = 10.4)
20	CN	CH_2Ph	H	115.92	141.90	51.12 (CH_2)	114.44 (CN, $^3J_{CNH\beta}$ = 10.6)
21	CN	CH_3	CH_3	113.95	142.43	31.93	114.96 (CN, $^3J_{CNH\beta}$ = 10.1)
22	CN	$C(O)CH_3$	H	111.00	141.70	24.38 (CH_3), 170.40 (C=O)	113.38 (CN)

[a] The $^{13}C–\{^1H\}$ NMR spectra of **13**, **18**, and **20**–**22** were recorded in DMSO-d_6, and of **14**–**17**, in $CDCl_3$. Carbon atoms of the benzene and indole ring resonated in the region δ_C 107.28–157.43 ppm; the 2-Me signal was located at δ_C 11.94 (**16**) or 12.22 ppm (**21**).

caproic acid [34–38]. The condensation of aldehydes with nitroacetonitrile successfully afforded geminal cyanonitroethenes in the presence of $AlkNH_2 \cdot HCl$ + Na_2CO_3, β-alanine, or propylamine as condensing agent, on silica gel, under microwave irradiation [4, 39, 40] or without a catalyst [41]. Some geminal cyanonitroethenes were obtained in this way using crude nitroacetonitrile [19, 31, 39]. It should be noted that the reaction of (hetero)aromatic aldehydes with nitroacetonitrile at a ratio of 1:2 in the presence of an equimolar amount of a base (diethylamine or sodium acetate) led to the formation of 2,4-dinitroglutaronitrile salts which were converted to the corresponding cyanonitroethenes by the action of acids [42, 43].

In this work, we performed condensation of indole-3-carbaldehydes **1**–**5** with ethyl nitroacetate, nitroacetone, nitroacetophenone, and nitroacetonitrile and obtained 3-(2-nitrovinyl)indoles **6**–**22** containing an ester, acetyl, benzoyl, or cyano group in the geminal position with respect to the nitro group (Scheme 1). The reactions were carried out in anhydrous ethanol in the presence of thionyl chloride or phosphoryl chloride (**7**, **9**–**15**; method *a*) or in the absence of a condensing agent[2] (**18**–**22**; method *b*). Compounds **6**, **8**, and **15**–**17** were synthesized by heating the reactants in boiling benzene in the presence of β-alanine and acetic acid with simultaneous removal of liberated water (method *c*). The yields reached 93%. Compounds **7**, **12**, **16**, **17**, **21**, and **22** were not reported previously. The properties of compounds **6**, **8**, and **15** (method *c*) were consistent with those of samples prepared previously by other methods [20, 29, 31].

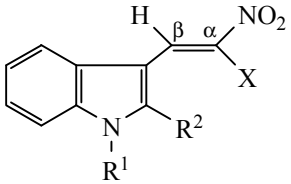
The structure of nitroethenes **6**–**22**[3] was studied by IR, UV, and ^1H and $^{13}C–\{^1H\}$ NMR spectroscopy, including $^1H–^{13}C$ HMQC, $^1H–^{13}C$ HMBC, and $^1H–^1H$ NOESY experiments. The ^1H NMR spectra of benzoyl and cyano derivatives **13**–**18** and **20**–**22**[4] indicated their stereochemical homogeneity (Table 1). The olefinic proton resonated at δ 8.59–9.09 ppm, i.e., shifted downfield than the corresponding proton in

[2] Crude nitroacetonitrile [44] was used.

[3] Structurally related compounds used as models were considered as indole-containing geminally substituted 1-nitroethenes.

[4] The ^1H and $^{13}C–\{^1H\}$ NMR, IR, and electronic absorption spectra of cyano analog **19** were given in [45].

Table 3. Electronic absorption[a] and IR[b] spectra of (*E*)-benzoyl(cyano)nitroethenes **13**–**18** and **20**–**24**



13–18, 20–22

Comp. no.	X	R^1	R^2	λ_{max}, nm	ε, L mol^{-1} cm^{-1}	NOO^- (NO_2)	C=O (CN) [NH]	C=C, C=N^+
13	C(O)Ph	H	H	422	17300	1277, 1228, 1220	1670 [3337 sh]	1606, 1580
14	C(O)Ph	CH_3	H	430	17000	1288, 1244, 1229	1672	1620, 1608
15	C(O)Ph	CH_2Ph	H	426	16400	1321, 1292, 1176	1672	1620, 1608
16	C(O)Ph	CH_3	CH_3	440	18500	1286, 1260, 1229	1668	1601, 1579
17	C(O)Ph	$C(O)CH_3$	H	386	12800	1321, 1231, 1202	1724, 1676	1632, 1546
18	CN	H	H	440	30000	1278, 1262, 1238	(2219) [3352 sh]	1593, 1575
20	CN	CH_2Ph	H	440	36200	1297, 1274, 1167	(2219)	1591, 1576
21	CN	CH_3	CH_3	439	39330	1300, 1285, 1237	(2211)	1593, 1580
22	CN	$C(O)CH_3$	H	407	18840	(1524, 1324)	(2227) 1728	1611, 1601
23	–	CH_2Ph	H	397	17900	1310, 1265	–	1625, 1500
24	–	$C(O)CH_3$	H	354	19000	1513, 1337	1723	1623

[a] The UV spectra of **13–17, 21–23** were recorded in acetonitrile, and of **18**, **20**, and **24**, in ethanol; given are long-wavelength bands in the region λ > 300 nm.

[b] The IR spectra of **14**–**17**, **23**, and **24** were recorded in chloroform, and of **13**, **18**, and **20**–**22**, in KBr.

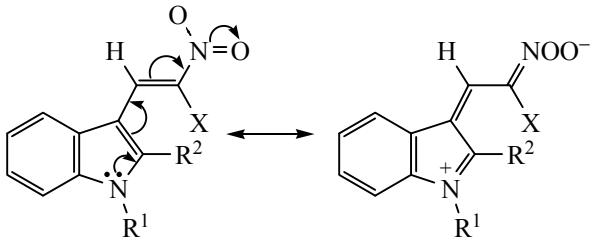
model *E*-nitroethenes[5]; this suggests *E* configuration of the exocyclic double bond in **13**–**18** and **20**–**22** (Table 1).

The $^{13}C–\{^1H\}$ NMR spectra of **13**–**18** and **20**–**22** displayed signals of all carbon atoms present in their molecules (Table 2). In the spectra of **13**–**17**, the carbon atom linked to the nitro and benzoyl groups shifted downfield (δ_C 138.40–144.02 ppm) than that of cyano analogs **18** and **20**–**22** (δ_C 111.00–115.92 ppm), presumably due to anisotropic effect of the cyano group [49]. The $^1H–^{13}C$ coupling constant between the olefinic proton and carbon nucleus of CN group ($^3J_{CH}$ = 10.1–10.6 Hz) confirmed their *trans* orientation, in keeping with published data [39, 50].

The *E* configuration of the exocyclic double bond in **13**–**18** and **20**–**22** assigned on the basis of the ^1H NMR data is also consistent with the electronic absorption spectra of these compounds (Table 3). In fact, introduction of a benzoyl or cyano group into indolylnitroethene molecules induces a red shift of the long-wavelength absorption band.

[5] The spectral parameters of model nitroethene **26** were given in [46]. Model compounds **23**–**25** were synthesized as described in [47, 48]; their spectral characteristics were measured in this work.

Scheme 2.



X = C(O)Ph, CN.

The IR spectra of (*E*)-benzoyl(cyano)nitroethenes **13**–**18**, **20**, and **21** (Table 3) are similar to the spectra of model (*E*)-nitroethenes. They lacked absorption bands typical of a covalently bonded nitro group but contained bands at 1546–1632 (C=C, C=N$^+$) and 1167–1321 cm^{-1} (NOO$^-$). This spectral pattern suggests high degree of polarization of molecules **13**–**18**, **20**, and **21** due to efficient *p*,π-conjugation involving electron pair on the indole nitrogen atom, C=C bond, and nitro group (Scheme 2). A similar spectral pattern was observed previously for geminal cyanonitroethenes containing a pyrrole, *N*-methylpyrrole, thiophene, or furan ring [39, 41]. Unlike compounds **13**–**18**, **20**, and **21**, the IR spectrum of *N*-acetylindole **22** showed absorption bands typical of a covalently bonded nitro group (1524, 1324 cm^{-1}).

According to the ^{1}H NMR data, among geminal ethoxycarbonyl- and acetylnitroethenes, only compound **9** was obtained as a single stereoisomer (Table 4). In the ^{1}H NMR spectrum of **9**, the olefinic proton resonated at δ 7.75 ppm, i.e., shifted upfield than the corresponding proton of model (*E*)-nitrovinylindole **25** (δ 8.38 ppm in DMSO-d_6). Therefore, compound **9** was assigned *Z* configuration of the exocyclic double bond. The ^{1}H NMR spectra of the other compounds (**6**–**8** and **10**–**12**) displayed two sets of signals. In particular, the olefinic proton signals were located at δ 7.74–8.01 (*Z* isomer) and 8.22–8.62 ppm (*E* isomer); in most cases, the *Z* isomer predominated (Table 4). The presence of two isomers of **6**–**8** and **10**–**12** is also supported by their electronic spectra which showed two absorption bands in the long-wavelength region (Table 4).

It should be noted that α-nitro-β-(indol-3-yl) acrylates and their *N*-methyl analogs synthesized previously were also isolated as equilibrium mixtures of *Z* and *E* isomers [51]. Only the *Z* isomer of methyl α-nitro-β-(1-acetyl-indol-3-yl)acrylate was isolated in the pure state [52].

The ^{13}C–{^{1}H} NMR spectra of **6**–**8** and **10**–**12** are given in Table 5. The carbonyl carbon nuclei resonated in the region δ_C 159.32–195.31 ppm. As in the spectra of benzoyl analogs **13**–**17** (Table 2), signals of C$^\alpha$ were located downfield (δ_C 134.49–144.43 ppm) from the signals of C$^\beta$ (δ_C 126.59–134.10 ppm).

The IR spectra of *Z*/*E* isomer mixtures **6**–**8** and **10**–**17** were fairly complex, but we were able to distinguish therein absorption bands due to covalently bonded nitro group of the *Z* isomers. Effective conjugation between the lone electron pair on the indole nitrogen atom, C=C bond, and carbonyl group of the acetyl (ester) fragment of the *Z* isomer is likely to induce reduction of the intensity of the carbonyl stretching band in comparison to the C=C stretching band (Scheme 3), whereas characteristics of the NO_2 stretching bands remain almost unchanged.

The conformation with respect to the C^3–C$^\beta$ bond of some indolylnitroethenes was determined by analysis of the NOESY data. The ^{1}H–^{1}H NOESY spectrum of **21** (DMSO-d_6) showed cross-peaks between β-H and 2-Me protons, indicating *s-trans* conformation of the molecule. On the other hand, in the ^{1}H–^{1}H NOESY spectra of **20** and **22** (DMSO-d_6) we observed a correlation between β-H and 4-H, which is possible for the *s-cis* conformation. A similar pattern was typical of benzoylnitroethene **14** in $CDCl_3$, whereas its analog **16** was assigned *s-trans* configuration in the same solvent (Scheme 4).

Scheme 3.

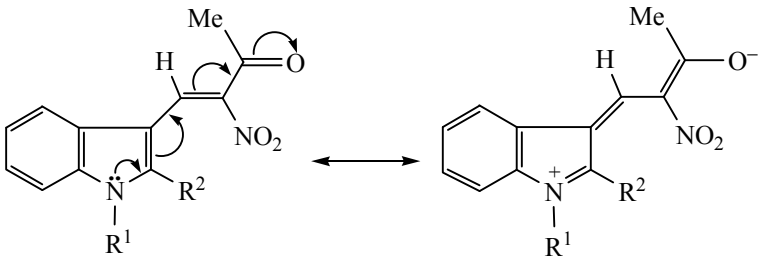
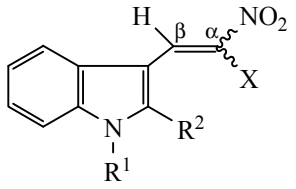
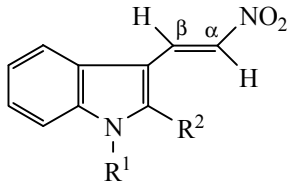


Table 4. [1]H NMR and electronic absorption spectra of ethoxycarbonyl(acetyl)nitroethenes **6**–**12**, **25**, and **26**[a]



6–12

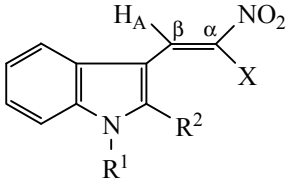


25, **26**

Comp. no.	X	R^1	R^2	*Z*/*E* ratio	δ, ppm (*J*, Hz)	δ, ppm (*J*, Hz)				λ_{max}, nm (MeCN)	ε, L mol^{-1} cm^{-1}
						α-H (β-H)	R^1 (NH)	OCH_2Me (Me)	H_{arom}		
6	$COOCH_2Me$	$PhCH_2$	H	~1.1:1	*Z*	7.96 s	5.27 s	4.37 q, 1.37 t (^3J = 7.2)	7.13–7.82 m	358[b]	5600
					E	8.49 s	5.31 s	4.34 q, 1.30 t (^3J = 7.2)	7.06–7.94 m	411[b]	6400
7[c]	$COOCH_2Me$	Me	Me	~1:1.2	*Z*	7.90 s	3.70 s	4.369 q, 1.37 t (^3J = 7.2)	7.15–7.45 m	344	7340
					E	8.43 s	3.73 s	4.368 q, 1.23 t (^3J = 7.2)		429	16280
8	$COOCH_2Me$	C(O)Me	H	~3.3:1	*Z*	7.74 s	2.60 s	4.36 q, 1.34 t (^3J = 7.2)	7.30–8.40 m	332	11470
					E	8.22 d ($^4J_{\beta,2}$ = 0.7)	2.64 s	4.39 q, 1.33 t (^3J = 7.2)	8.18–8.40 m	385 sh	5900
9	C(O)Me	H	H	100:0		7.75 s	(12.37 s)	(2.52 s)	7.30–8.05 m	390	6300
10	C(O)Me	Me	H	~5:1	*Z*	8.01 s	3.85 s	(2.50 s)	7.22–7.90 m 8.29 s	367	15500
					E	8.44 s	3.88 s	(2.49 s)	7.22–7.80 m	430	8200
11	C(O)Me	$PhCH_2$	H	~1.6:1	*Z*	7.94 s	5.34 s	(2.48 s)	7.10–7.85 m	366	20000
					E	8.62 s	5.40 s	(2.55 s)	7.93 s, 8.66 s	429	8300
12[d]	C(O)Me	Me	Me	~2.9:1	*Z*	7.94 s	3.73 s	(2.46 s)	7.08–7.37 m	360	11500
					E	8.42 s	3.73 s	(2.63 s)		440	8300
25	–	H	H	0:100		8.38 d (7.98 d) $^3J_{\alpha\beta}$ = 13.4	(12.23)	–	7.22–8.22 m	400[b]	22300
26[e]	–	Me	Me	0:100		8.32 d (7.75 d) $^3J_{\alpha\beta}$ = 13.1	3.77 s	–	7.27–8.02 m	415	20200

[a] The [1]H NMR spectra of **6**–**8**, **11**, **12**, and **26** were recorded in $CDCl_3$, and of **9**, **10**, and **25**, in DMSO-d_6.
[b] The UV spectrum was recorded in ethanol.
[c] 2-Me: δ 2.53 (*Z*), 2.55 ppm (*E*).
[d] 2-Me: δ 2.56 (*Z*), 2.54 ppm (*E*).
[e] 2-Me: δ 2.57 ppm.

Table 5. ^{13}C NMR spectra of ethoxycarbonyl(acetyl)nitroethenes **6**–**8** and **10**–**12**[a]



6–8, 10–12

Comp. no.	X	R^1	R^2	Isomer	C^α	C^β	R^1	X
6	$COOCH_2CH_3$	CH_2Ph	H	*Z*	134.49	126.59	51.22 (CH_2)	14.31 (CH_3), 62.44 (CH_2), 60.46 (C=O)
				E	135.42	130.77	51.22 (CH_2)	13.99 (CH_3), 62.58 (CH_2), 162.81 (C=O)
7[b]	$COOCH_2CH_3$	CH_3	CH_3	*Z*	134.42	130.54	30.49 (CH_3)	14.36 (CH_3), 62.30 (CH_2), 161.36 (C=O)
				E	136.20	133.27	30.60 (CH_3)	13.87 (CH_3), 62.50 (CH_2), 163.16 (C=O)
8	$COOCH_2CH_3$	$COCH_3$	H	*Z*	139.26	127.71	23.86 (CH_3) 168.8 (C=O)	14.13 (CH_3), 63.19 (CH_2), 159.32 (C=O)
				E	140.65	128.73	23.90 (CH_3) 168.8 (C=O)	13.92 (CH_3), 63.22 (CH_2), 161.57 (C=O)
10	$C(O)CH_3$	CH_3	H	*Z*	144.43	127.27	34.00	25.62 (CH_3), 188.25 (C=O)
				E	141.49	131.99	34.27	30.35 (CH_3), 194.99 (C=O)
11	$C(O)CH_3$	CH_2Ph	H	*Z*	143.42	127.07	51.50 (CH_2)	26.11 (CH_3), 188.55 (C=O)
				E	142.30	133.02	56.65 (CH_2)	30.41 (CH_3), 194.41 (C=O)
12[c]	$C(O)CH_3$	CH_3	CH_3	*Z*	142.66	130.99	29.94	26.45 (CH_3), 189.19 (C=O)
				E	141.70	134.10	29.94	30.68 (CH_3), 195.31 (C=O)

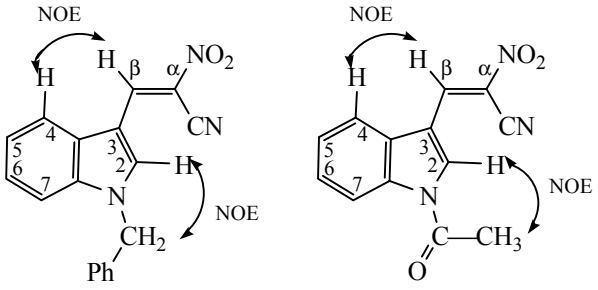
[a] The $^{13}C-\{^1H\}$ NMR spectra of **6**–**8**, **11**, and **12** were recorded in $CDCl_3$, and of **10**, in DMSO-d_6. Carbon atoms of the benzene and indole rings resonated in the region δ_C 105.38–148.51 ppm.
[b] 2-Me: δ_C 11.60 (*Z*), 11.67 ppm (*E*).
[c] 2-Me: δ_C 11.77 (*Z*), 12.13 ppm (*E*).

Both isomers of α-nitroacrylate **7** displayed in the $^1H-^1H$ NOESY spectrum ($CDCl_3$) cross-peaks between β-H and 2-Me [δ 7.90/2.53 (*Z*) and 8.43/2.55 ppm (*E*)], which suggests *s-trans* configuration of the vinylindole fragment in both *Z*-**7** and *E*-**7** (Scheme 5).

The $^1H-^1H$ NOESY spectrum of **10** (DMSO-d_6) showed cross-peaks between β-H and 4-H of both isomers, indicating *s-cis* conformation of the vinylindole fragment therein. In addition, a cross-peak between β-H and methyl protons of the acetyl fragment was observed for the *Z* isomer of **10**, which corresponds to *s-trans* conformation of the enone fragment (Scheme 6). Likewise, the *Z* isomer of **12** in $CDCl_3$ was assigned *s-trans* configuration of both vinylindole and enone fragments.

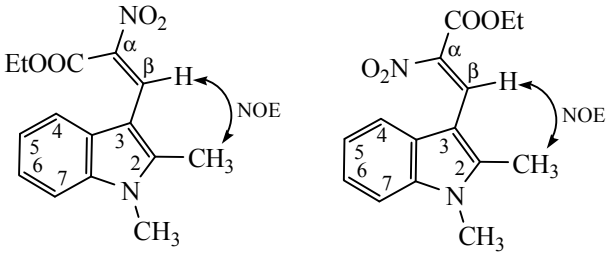
In summary, we have synthesized a series of indolyl-substituted nitroethenes containing an acetyl, benzoyl, ethoxycarbonyl, or cyano group geminal to the nitro group by condensation of indole-3-carbaldehydes with the corresponding CH acids. The proposed procedure

Scheme 4.



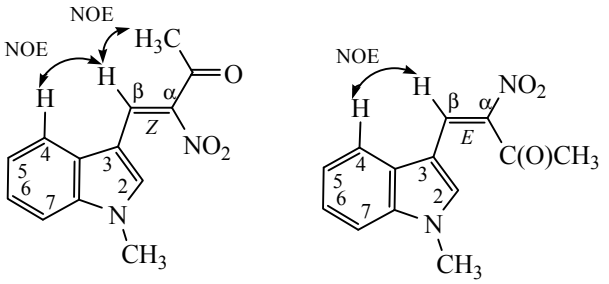
20 **22**

Scheme 5.



s-trans-E-**7** *s-trans-Z*-**7**

Scheme 6.



s-cis-Z-**10** *s-cis-E*-**10**

is characterized by high efficiency and preparative convenience. Analysis of spectral parameters of the synthesized compounds showed that geminal benzoyl- and cyanonitroethenes have *E* configuration of the exocyclic double bond and that most acetyl and ethoxycarbonyl analogs are mixtures of *E* and *Z* isomers, the latter prevailing. The configuration of some nitroethenes with respect to the C^3–C^β bond has been determined on the basis of the ^{1}H–^{1}H NOESY data.

EXPERIMENTAL

Physicochemical studies were performed using the equipment of the Center for Collective Use of the Faculty of Chemistry of the Herzen State Pedagogical University of Russia. The ^{1}H, ^{13}C–{^{1}H}, ^{1}H–^{13}C HMQC, and ^{1}H–^{13}C HMBC NMR spectra were recorded on a Jeol JNM-ECX400A spectrometer at 399.78 (^{1}H) and 100.53 MHz (^{13}C) using $CDCl_3$ or DMSO-d_6 as solvent; the chemical shifts were measured relative to the residual proton and carbon signals of the solvent. The IR spectra were recorded on a Shimadzu IR Prestige-21 spectrometer with Fourier transform from solutions in chloroform (c = 40 mg/mL) or KBr pellets. The electronic absorption spectra were measured in ethanol or acetonitrile on a Shimadzu UV 2401PC spectrophotometer using quartz cells with a cell path length l of 1.01 mm. The elemental analyses were obtained on a EuroVector EA 3000 CHN Dual analyzer.

Ethyl 3-(1-benzyl-1*H*-indol-3-yl)-2-nitroprop-2-enoate (6). A mixture of 0.67 g (5 mmol) of ethyl nitroacetate, 1.17 g (5 mmol) of 1-benzyl-1*H*-indole-3-carbaldehyde (**3**), 0.19 g of β-alanine, and 0.8 mL of glacial acetic acid in 20 mL of anhydrous benzene was refluxed for 5 h in a flask equipped with a Dean–Stark trap. After cooling, the mixture was washed with brine, the organic phase was dried over calcined $MgSO_4$, the solvent was removed, and the residue was subjected to chromatography on silica gel. Elution with benzene gave 1.42 g (81%) of **6** as red–orange oil, R_f 0.53 (hexane–acetone, 3:1). Found, %: N 7.89. $C_{20}H_{18}N_2O_4$. Calculated, %: N 8.00.

Ethyl 3-(1,2-dimethyl-1*H*-indol-3-yl)-2-nitroprop-2-enoate (7). Thionyl chloride (2 drops) was added to a suspension of 0.35 g (2 mmol) of 1,2-dimethyl-1*H*-indole-3-carbaldehyde (**4**) and 0.25 mL (2 mmol) ethyl nitroacetate in 2 mL of anhydrous ethanol. The mixture was heated until it became homogeneous and was left to stand for 24 h at room temperature. The precipitate was filtered off and dried. Yield 0.42 g (73%), yellow crystals, mp 107–108°C (from EtOH). Found, %: N 9.85. $C_{15}H_{16}N_2O_4$. Calculated, %: N 9.72.

Ethyl 3-(1-acetyl-1*H*-indol-3-yl)-2-nitroprop-2-enoate (8) was synthesized as described above for compound **6** from 1-acetyl-1*H*-indole-3-carbaldehyde (**5**) and ethyl nitroacetate; reaction time 2 h. The solvent was evaporated to 1/3 of the initial volume, and the yellow solid was filtered off and dried. Yield 55%, mp 137–138°C (from EtOH); published data [20]: mp 140–141°C (from EtOH).

4-(1*H*-Indol-3-yl)-3-nitrobut-3-en-2-one (9). A mixture of 0.206 g (2 mmol) of nitroacetone, 0.29 g (2 mmol) of 1*H*-indole-3-carbaldehyde (**1**), and

2 drops of phosphoryl chloride in 3 mL of anhydrous ethanol was heated until it became homogeneous and was left to stand for 24 h at room temperature. The solution was poured onto crushed ice, and the precipitate was filtered off and washed with ethanol on a filter. Yield 0.3 g (65%), yellow crystals, mp 157–158°C (from EtOH); published data [31]: mp 159–160°C (from EtOH).

4-(1-Methyl-1*H*-indol-3-yl)-3-nitrobut-3-en-2-one (10) was synthesized as described above for compound **7** from 1-methyl-1*H*-indole-3-carbaldehyde (**2**) and nitroacetone. After 24 h, the mixture was poured onto crushed ice. Yield 93%, yellow crystals, mp 154–155°C (from MeCN). Found, %: C 63.75; H 4.84; N 11.53. $C_{13}H_{12}N_2O_3$. Calculated, %: C 63.93; H 4.92; N 11.48.

4-(1-Benzyl-1*H*-indol-3-yl)-3-nitrobut-3-en-2-one (11) was synthesized as described above for compound **10** from 1-benzyl-1*H*-indole-3-carbaldehyde (**3**) and nitroacetone. Yield 80%, orange crystals, mp 137–138°C (from *i*-PrOH). Found, %: C 71.36; H 5.23; N 8.63. $C_{19}H_{16}N_2O_3$. Calculated, %: C 71.25; H 5.00; N 8.75.

4-(1,2-Dimethyl-1*H*-indol-3-yl)-3-nitrobut-3-en-2-one (12) was synthesized as described above for compound **10** from aldehyde **4** and nitroacetone. Yield 64%, yellow crystals, mp 170–171°C (from EtOH). Found, %: C 64.96; H 5.57; N 10.70. $C_{14}H_{14}N_2O_3$. Calculated, %: C 65.10; H 5.42; N 10.85.

3-(1*H*-Indol-3-yl)-2-nitro-1-phenylprop-2-en-1-one (13). Phosphoryl chloride (2 drops) was added to a mixture of 0.72 g (5 mmol) of aldehyde **1** and 0.82 g (5 mmol) nitroacetophenone in 3 mL of anhydrous ethanol. The mixture was heated until it became homogeneous. After 24 h, the mixture was poured into an ice–water mixture and extracted with diethyl ether. The extract was dried over calcined Na_2SO_4, and the solvent was removed. Yield 1.35 g (93%), mp 131–132°C (from EtOH); published data [31]: mp 131–132°C (from EtOH).

3-(1-Methyl-1*H*-indol-3-yl)-2-nitro-1-phenylprop-2-en-1-one (14). A mixture of 0.41 g (2.5 mmol) of nitroacetophenone, 0.4 g (2.5 mmol) of aldehyde **2**, and 2 drops of thionyl chloride in 2 mL of anhydrous ethanol was heated until it became homogeneous and was left to stand for 24 h at room temperature. The precipitate was filtered off and dried. Yield 0.62 g (81%), orange crystals, mp 191–192°C (from MeCN). Found, %: C 70.50; H 4.72; N 9.28. $C_{18}H_{14}N_2O_3$. Calculated, %: C 70.59; H 4.58; N 9.15.

3-(1-Benzyl-1*H*-indol-3-yl)-2-nitro-1-phenylprop-2-en-1-one (15). *a*. The procedure was analogous to the synthesis of **14**. Yield 76%, orange crystals, mp 116–118°C (from *i*-PrOH). Found, %: C 75.35; H 4.85; N 7.25. $C_{24}H_{18}N_2O_3$. Calculated, %: C 75.39; H 4.71; N 7.32.

b. A mixture of 0.82 g (5 mmol) of nitroacetophenone, 1.17 g (5 mmol) of aldehyde **3**, 0.19 g of β-alanine, and 4 mL of glacial acetic acid in 40 mL of anhydrous benzene was refluxed for 4 h in a flask equipped with a Dean–Stark trap. After cooling, the mixture was washed with water and dried over calcined $MgSO_4$, the solvent was removed, and the precipitate was filtered off and dried. Yield 1.62 g (85%), orange crystals, mp 124–126°C (from *i*-PrOH). The product showed no depression of the melting point on mixing with a sample prepared as described in *a*.

3-(1,2-Dimethyl-1*H*-indol-3-yl)-2-nitro-1-phenylprop-2-en-1-one (16) was synthesized as described above for compound **15** (*b*) from aldehyde **4** and nitroacetophenone; reaction time 4.5 h. Yield 58%, orange crystals, mp 183–184°C (from PhH). Found, %: C 71.35; H 5.20; N 8.60. $C_{19}H_{16}N_2O_3$. Calculated, %: C 71.25; H 5.0; N 8.75.

3-(1-Acetyl-1*H*-indol-3-yl)-2-nitro-1-phenylprop-2-en-1-one (17) was synthesized as described above for compound **15** (*b*) from aldehyde **5** and nitroacetophenone; reaction time 2 h. Yield 73%, yellow crystals, mp 142–143°C (from *i*-PrOH). Found, %: N 8.51. $C_{19}H_{14}N_2O_3$. Calculated, %: N 8.38.

3-(1*H*-Indol-3-yl)-2-nitroprop-2-enenitrile (18). A suspension of 1.45 g (10 mmol) of aldehyde **1** in 15 mL of anhydrous ethanol was added to 0.86 g (10 mmol) of crude nitroacetonitrile. The mixture turned dark, and an orange crystalline solid separated on slight heating. The mixture was left to stand for 24 h at room temperature, and the precipitate was filtered off and dried. Yield 1.86 g (87%), mp 219–220°C (from $MeNO_2$); published data [31]: mp 215°C (from $MeNO_2$).

3-(1-Methyl-1*H*-indol-3-yl)-2-nitroprop-2-enenitrile (19) was synthesized in a similar way from aldehyde **3** and nitroacetonitrile. Yield 66%, mp 190–191°C (from $MeNO_2$). Found, %: C 63.58; H 4.05; N 18.48. $C_{12}H_9N_3O_2$. Calculated, %: C 63.44; H 3.96; N 18.50.

3-(1-Benzyl-1*H*-indol-3-yl)-2-nitroprop-2-enenitrile (20) was synthesized in a similar way from aldehyde **3** and nitroacetonitrile; reaction time 3 h. Yield 51%, mp

213–214°C ($MeNO_2$); published data [31]: mp 211°C (from $MeNO_2$).

3-(1,2-Dimethyl-1*H*-indol-3-yl)-2-nitroprop-2-enenitrile (21) was synthesized in a similar way from aldehyde **4** and nitroacetonitrile; reaction time 3 h. Yield 78%, mp 191–192°C (from $MeNO_2$). Found, %: N 17.51. $C_{13}H_{11}N_3O_2$. Calculated, %: N 17.43.

3-(1-Acetyl-1*H*-indol-3-yl)-2-nitroprop-2-enenitrile (22) was synthesized in a similar way from aldehyde **5** and nitroacetonitrile. Yield 78%, mp 201–202°C (from $MeNO_2$). Found, %: N 16.38. $C_{13}H_9N_3O_3$. Calculated, %: N 16.47.

CONFLICT OF INTEREST

No conflict of interest was declared by the authors.

REFERENCES

1. Perekalin, V.V., Sopova, A.S., and Lipina, E.S., *Nepredel'nye nitrosoedineniya* (Unsaturated Nitro Compounds), Leningrad: Khimiya, 1982.
2. Perekalin, V.V., Lipina, E.S., Berestovitskaya, V.M., and Efremov, D.A., *Nitroalkenes. Conjugated Nitro-compounds*, Chichester: Wiley, 1994.
3. Karakhanov, R.A., Kelarev, V.I., and Polivin, Yu.N., *Russ. Chem. Rev*., 1993, vol. 62, no. 2, p. 169. doi 10.1070/RC1993v062n02ABEH000011
4. Berestovitskaya, V.M., Baichurin, R.I., and Aboskalova, N.I., *Sopryazhennye nitroeteny, geminal'no aktivirovannye slozhnoefirnoi, tsiano- i atsil'noi gruppami* (Conjugated Nitroethenes Geminally Activated by Ester, Cyano, and Acyl Groups), St. Petersburg: Asterion, 2014.
5. *Izbrannye metody sinteza i modifikatsii geterotsiklov. Khimiya sinteticheskikh indol'nykh sistem* (Selected Methods of Synthesis and Modification of Heterocycles. Chemistry of Sunthetic Indole Systems), Kartsev, V.G., Ed., Moscow: IBS, 2004, vol. 3.
6. Shul'ts, E.E., Kartsev, V.G., and Tolstikov, G.A., *Khimiya i biologicheskaya aktivnost' indol'nykh alkaloidov* (Chemistry and Biological Activity of Indole Alkaloids), Moscow: ICSPF, 2018.
7. Sharma, V., Kumar, P., and Pathak, D., *J. Heterocycl. Chem*., 2010, vol. 47, no. 3, p. 491. doi 10.1002/jhet.349
8. Kaushik, N.K., Kaushik, N., Attri, P., Kumar, N., Kim, C.H., Verma, A.K., and Choi, E.H., *Molecules*, 2013, vol. 18, no. 6, p. 6620. doi 10.3390/molecules18066620
9. Singh, T.P. and Singh, O.M., *Mini Rev. Med. Chem*., 2018, vol. 18, no. 1, p. 9. doi 10.2174/1389557517666170807123201
10. Mal'tsev, O.V., Beletskaya, I.P., and Zlotin, S.G., *Russ. Chem. Rev*., 2011, vol. 80, no. 11, p. 1067. doi RC2011v080n11ABEH004249
11. Mashkovskii, M.D., *Lekarstvennye sredstva* (Medicines), Moscow: Novaya Volna, 2012, 16th ed.
12. Zhungietu, G.I., Budylin, V.A., and Kost, A.N., *Preparativnaya khimiya indola* (Preparative Indole Chemistry), Kishinev: Shtiintsa, 1975
13. Baron, M., Metay, E., Lemaire, M., and Popowycz, F., *J. Org. Chem*., 2012, vol. 77, no. 7, p. 3598. doi 10.1021/jo2026096
14. Aksenov, A.V., Aksenov, N.A., Skomorokhov, A.A., Aksenova, I.V., Gryaznov, G.D., Voskressensky, L.G., and Rubin, M.A., *Chem. Heterocycl. Compd*., 2016, vol. 52, no. 11, p 923. doi 10.1007/s10593-017-1988-x
15. Abdelwaly, A., Salama, I., Gomaa, M.S., and Helal, M.A., *Med. Chem. Res*., 2017, vol. 26, no. 12, p. 3173. doi 10.1007/s00044-017-2011-x
16. Wang, Y.-C., Wang, J.-L., Burgess, K.S., Zhang, J.-W., Zheng, Q.-M., Pu, Y.-D., Yan, L.-J., and Chen, X.-B., *RSC Adv*., 2018, vol. 8, no. 11, p. 5702. doi 10.1039/c7ra13207g
17. Zhmurov, P.A., Ushakov, P.Yu., Novikov, R.A., Sukhorukov, A.Yu., and Ioffe, S.L., *Synlett*, 2018, vol. 29, no. 14, p. 1871. doi 10.1055/s-0037-1610213
18. Dornow, A. and Menzel, H., *Justus Liebigs Ann. Chem*., 1954, vol. 588, no. 1, p. 40. doi 10.1002/jlac.19545880105
19. Aboskalova, N.I., *Cand. Sci. (Chem.) Dissertation*, Leningrad, 1971.
20. Aboskalova, N.I., Polyanskaya, A.S., and Perekalin, V.V., *Dokl. Chem*., 1967, vol. 176, no. 4, p. 861.
21. Vinograd, L.Kh. and Suvorov, N.N., *Chem. Heterocycl. Compd*., 1970, vol. 6, no. 11, p. 1403. doi 10.1007/BF00476782
22. Umezawa, S. and Zen, S., *Bull. Chem. Soc. Jpn*., 1963, vol. 36, no. 9, p. 1150. doi 10.1246/bcsj.36.1150
23. Baranov, M.S. and Yampolsky, I.V., *Tetrahedron Lett*., 2013, vol. 54, no. 7, p. 628. doi 10.1016/j.tetlet.2012.11.132
24. Dornow, A. and Sassenberg, W., *Justus Liebigs Ann. Chem*., 1957, vol. 602, no. 1, p. 14. doi 10.1002/jlac.19576020102
25. Zalukaev, L.P., *Sintez i reaktsii al'fa-nitroketonov* (Synthesis and Reactions of α-Nitro Ketones), Riga: Akad. Nauk Latv. SSR, 1958.
26. Babievskii, K.K., *Doctoral (Chem.) Dissertation*, Moscow, 1980.
27. Kochetkov, K.A., Babievskii, K.K., Belikov, V.M., Garbalinskaya, N.S., and Bakhmutov, V.I., *Bull. Acad. Sci. USSR, Div. Chem. Sci*., 1980, vol. 29, no. 3, p. 458. doi 10.1007/BF00949634
28. Lehnert, W., *Tetrahedron*, 1972, vol. 28, no. 3, p. 663. doi 10.1016/0040-4020(72)84029-8
29. Rodríguez, R., Viñets, I., Diez, A., Rubiralta, M., and Giralt, E., *Synth. Commun*., 1996, vol. 26, no. 16, p. 3029. doi 10.1080/00397919608004608

30. Rodríguez, R., Diez, A., Rubiralta, M., and Giralt, E., *Heterocycles*, 1996, vol. 43, no. 3, p. 513. doi 10.3987/COM-95-7327
31. Aboskalova, N.I., Polyanskaya, A.S., Perekalin, V.V., Demireva, Z.I., and Sokolova, L.N., *J. Org. Chem. USSR*, 1972, vol. 8, no. 6, p. 1349.
32. Polyanskaya, A.S., Perekalin, V.V., Aboskalova, N.I., and Sokolova, L.N., USSR Inventor's Certificate no. 335246; *Byull. Izobret*., 1972, no. 13.
33. Fel'gendler, A.V., Aboskalova, N.I., and Berestovitskaya, V.M., *Russ. J. Gen. Chem*., 2000, vol. 70, no. 7, p. 1087.
34. Bakhareva, S.V., *Cand. Sci. (Chem.) Dissertation*, St. Petersburg, 2001.
35. Berestovitskaya, V.M., Aboskalova, N.I., Ishmaeva, E.A., Bakhareva, S.V., Berkova, G.A., Vereshchagina, Ya.A., Fel'gendler, A.V., and Fattakhova, G.R., *Russ. J. Gen. Chem*., 2001, vol. 71, no. 12, p. 1942. doi 10.1023/A:1014200612456
36. Baichurina, L.V., Baichurin, R.I., Aboskalova, N.I., and Berestovitskaya, V.M., *Russ. J. Gen. Chem*., 2010, vol. 80, no. 10, p. 2022. doi 10.1134/S1070363210100221
37. Velezheva, V.S., Erofeev, Yu.V., and Suvorov, N.N., *J. Org. Chem. USSR*, 1980, vol. 16, no. 10, p. 1839.
38. Baichurin, R.I., Baichurina, L.V., Aboskalova, N.I., and Berestovitskaya, V.M., *Russ. J. Gen. Chem*., 2013, vol. 83, no. 9, p. 1764. doi 10.1134/S1070363213090223
39. Baichurin, R.I., Aboskalova, N.I., Trukhin, E.V., and Berestovitskaya, V.M., *Russ. J. Gen. Chem*., 2015, vol. 85, no. 8, p. 1845. doi 10.1134/S1070363215080101
40. Woliński, P., Jasiński, R., *Czamopismo Techniczne/Tech. Trans.,* 2018, vol. 2, p. 109. doi 10.4467/2353737XCT.18.024.7997
41. Polyanskaya, A.S., Perekalin, V.V., Aboskalova, N.I., Demireva, Z.I., Sokolova, L.N., and Abdulkina, Z.A., *J. Org. Chem. USSR*, 1979, vol. 15, no. 10, p. 859.
42. Shadrin, V.Yu., *Cand. Sci. (Chem.) Dissertation*, Leningrad, 1987.
43. Garming, A., Redwan, D., Gelbke, P., Kern, D., and Dierkes, U., *Justus Liebigs Ann. Chem*., 1975, no. 10, p. 1744. doi 10.1002/jlac.197519751003
44. Ried, W. and Köhler, E., *Justus Liebigs Ann. Chem*., 1956, vol. 598, no. 2, p. 145. doi 10.1002/jlac.19565980207
45. Berestovitskaya, V.M., Baichurin, R.I., Aboskalova, N.I., Baichurina, L.V., Trukhin, E.V., Fel'gendler, A.V., and Gensirovskaya, M.A., *Russ. J. Gen. Chem*., 2016, vol. 86, no. 6, p. 1266. doi 10.1134/S1070363216060086
46. Berestovitskaya, V.M., Ishmaeva, E.A., Litvinov, I.A., Vasil'eva, O.S., Vereshchagina, Ya.A., Ostroglyadov, E.S., Fattakhova, G.R., Beskrovnyi, D.V., and Aleksandrova, S.M., *Russ. J. Gen. Chem*., 2004, vol. 74, no. 7, p. 1108. doi 10.1023/B:RUGC.0000045874.46434.ea
47. Bulatova, N.N. and Suvorov, N.N., *Chem. Heterocycl. Compd*., 1969, vol. 5, no. 5, p. 602. doi 10.1007/BF00957368
48. Young, E.H.P., *J. Chem. Soc*., 1958, no. 10, p. 3493. doi 10.1039/JR9580003493
49. Ionin, B.I., Ershov, B.A., and Kol'tsov, A.I., *YaMR-spektroskopiya v organicheskoi khimii* (NMR Spectroscopy in Organic Chemistry), Leningrad: Khimiya, 1983.
50. Troschütz, R. and Grün, L., *Archiv Pharm*., 1993, vol. 326, no. 11, p. 857. doi 10.1002/ardp.19933261104
51. Babievskii, K.K., Bakhmutov, V.I., Kochetkov, K.A., Burmistrov, V.A., and Belikov, V.M., *Bull. Acad. Sci. USSR, Div. Chem. Sci*., 1977, vol. 26, no. 2, p. 384. doi 10.1007/BF00921860
52. Aboskalova, N.I., Babievskii, K.K., Belikov, V.M., Perekalin, V.V., and Polyanskaya, A.S., *J. Org. Chem. USSR*, 1973, vol. 9, no. 5, p. 1082.