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α-Indolyl-β-nitroacrylates. Synthesis and Structure

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Abstract—A one-pot procedure has been developed for the synthesis of α-indolyl-β-nitroacrylates by reaction of β-bromo-β-nitroacrilates with indole and substituted indoles. All indolylnitroacrilates thus obtained have *Z* configuration of the double bond. According to the X-ray diffraction data, ethyl 2-(1-methyl-1*H*-indol-3-yl)-3-nitroacrylate is characterized by *s-trans* conformation of the double C=C bond and indole ring; its crystal packing involves intermolecular hydrogen bonds C–H···O and C–H···π with formation of centrosymmetric dimers which give rise to bilayer supramolecular structures.

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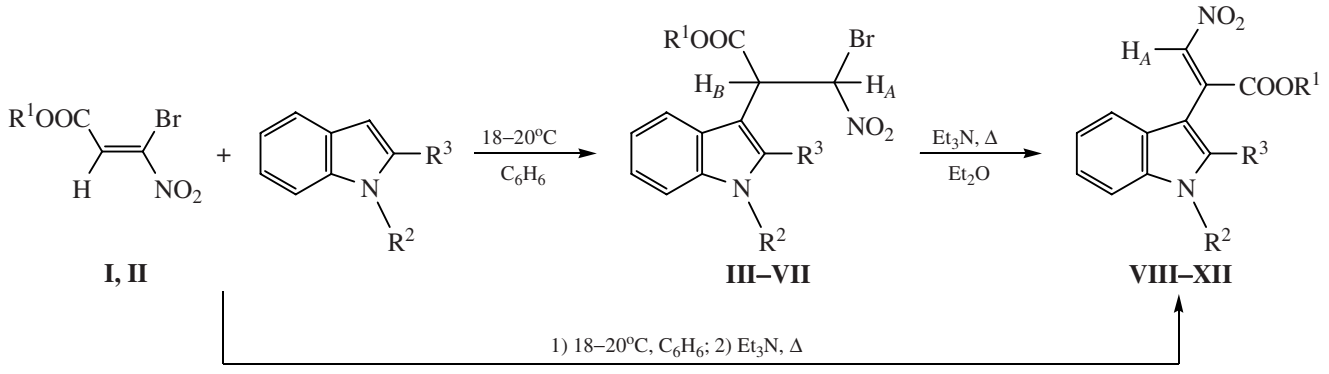
Hetaryl derivatives of 3-nitroactylic acid have been studied relatively poorly despite increased interest of synthetic chemists in 3-nitroacrylic acid and its esters, which are used in the synthesis of practically important compounds such as antibiotic Oryzoxymycin [1], alkaloid Reserpine [2], and many others [3, 4]. Indole ring is a structural unit of widespread natural compounds, e.g., tryptamine (sympatholytic, anticholineesterase agent [5]), serotonin (CNS mediator), and melatonin (epiphyseal hormone of pineal gland) [6], as well as of numerous synthetic drugs, e.g., Indometacin (antiphlogistic agent), Mexamine (used for the treatment of radiation sickness syndrome), Thymogen (immunomodulator), Indopan (stimulator and antidepressant), etc. [6–8]. Introduction of a pharmacophoric indole heteroring [9] into 3-nitroacrylate molecule could give rise to novel functionalized nitroethenes.

Methyl and ethyl 3-bromo-3-nitroacrylates **I** and **II** reacted with indole and substituted indoles along the substitutive addition pathway to give compounds **III**–**VII**, and subsequent dehydrohalogenation of the latter on heating with an equimolar amount of triethylamine



R^1 = Me (**I**), Et (**II**); R^2 = R^3 = H, R^1 = Me (**III, VIII**), Et (**IV, IX**); R^1 = R^2 = Me, R^3 = H (**V, X**); R^1 = Et, R^2 = Me, R^3 = H (**VI, XI**), R^2 = H, R^3 = Me (**VII, XII**).

Table 1. IR and ^{1}H NMR spectra of alkyl indolylbromonitropropanoates **III–VII**

Comp. no.	Yield, %	mp °C, (R_f)	Diastereo-isomer[a]	^{1}H NMR spectrum ($CDCl_3$), δ, ppm (J, Hz)					IR spectrum ($CHCl_3$), ν, cm^{-1}		
				Indole[b]	H_A (J_{AB})	H_B (J_{AB})	(OCH_3) OCH_2CH_3	NH, ($N–CH_3$)	C=O	NO_2	NH
III	89	(0.66)	**a**	7.20–7.74	6.59 (11.0)	4.88 (11.0)	(3.77)	8.59	1735	1570	3475
			b		6.53 (10.3)	4.93 (10.3)	(3.70)	8.54		1355	
IV	84	(0.60, 0.75)	**a**	7.00–7.70	6.79 (8.5)	4.75 (8.5)	1.15–1.40,	8.10	1730	1570	3480
			b		6.63 (10.0)	4.81 (10.0)	4.05–4.30	8.04		1355	
V	93	160–161	**a**	7.13–7.70	6.53 (11.0)	4.83 (11.0)	(3.80)	(3.69)	1735	1570	–
			b		6.48 (10.3)	4.88 (10.3)	(3.76)	(3.73)		1355	
VI	86	78–84	**a**	6.87–7.73	6.51 (8.8)	4.78 (8.8)	1.10–1.40,	(3.75)	1710	1570	–
			b		6.48 (10.0)	4.85 (10.0)	4.05–4.35	(3.83)	1730	1360	
VII	69	(0.84, 0.96)	**a**	7.10–7.75	6.70 (10.6)	4.75 (10.6)	1.15–1.35	8.10	1710	1570	3440
			b		6.60 (10.6)	4.75 (10.6)	4.05–4.40	8.03	1730	1355	

[a] Diastereoisomer with a larger difference in the chemical shifts of H_A and H_B signals is denoted as "**a**," and the other, as "**b**"; the **a/b** diastereoisomer ratio for compounds **III–VII** is 1 : 1, 3 : 2, 1 : 3, 2 : 1, and 3 : 2, respectively. [b] Protons in the methyl group on the indole ring in diastereoisomers **VIIa** and **VIIb** appear as singlets at δ 2.34 and 2.48 ppm, respectively.

in anhydrous benzene led to the formation of previously unknown methyl and ethyl α-indolyl-β-nitroacrylates **VIII–XII**. Our experimental results allowed us to develop a one-pot procedure for the synthesis of new compounds **VIII–XII**. For this purpose, a mixture of 3-bromo-3-nitroacrylate **I** or **II** with indole or its substituted derivative in benzene was kept for 1.5 h at 18–20°C, an equimolar amount of triethylamine was added, and the mixture was heated for 3.5–4 h under reflux. In this case, the yields were generally lower (22–62%), but the one-pot procedure is considerably simpler.

The structure of indolylbromonitropropanoates **III–VII** and indolylnitropropenoates **VIII–XII** was determined on the basis of their IR, UV, and ^{1}H and ^{13}C NMR spectra (Tables 1, 2), as well as by comparing their spectral parameters with those of structurally related indolylbromonitroethyl- and indolylnitroethenylphosphonates [10, 11]. Compounds **III–VII** displayed in the ^{1}H NMR spectra double sets of signals from all structural fragments, indicating that these compounds are mixtures of *erythro* and *threo* diastereoisomers (Table 1). The IR spectra of **III–VII** contained strong absorption bands due to stretching vibrations of the nonconjugated nitro (1570, 1355–1360 cm^{-1}) and carbonyl groups (1710–1735 cm^{-1}), and bands belonging to symmetric and asymmetric stretching vibrations of the nitro groups appeared separately ($\Delta\nu \approx 210–215$ cm^{-1}), which is typical of compounds having a halogen atom and a nitro group at the same carbon atom [12].

The ^{1}H NMR spectral patterns of **VIII–XII** were fairly similar, and they indicated configurational homogeneity of these compounds (Table 2). For example, the ^{1}H NMR spectrum of indolylnitroacrylate **VIII** contained a signal at δ 7.69 ppm from the olefinic protons, protons of the methoxy group resonated at δ 4.02 ppm, protons in the indole ring gave signals at δ 7.31–7.33, 7.47–7.53, and 7.73 ppm, and the NH proton appeared as a downfield signal at δ 9.96 ppm. The ^{13}C–{^{1}H} NMR spectrum of **VIII** was fully consistent with the assumed structure, δ_C, ppm: 166.1 (C=O); 139.3, 137.0 (C=C); 131.1, 129.2, 124.2, 123.5, 122.7, 120.1, 112.3, 107.8 (indole ring); 53.2 (CH_3O).

The IR spectra of α-indolyl-β-nitroacrylates **VIII–XII** displayed a complicated pattern; they resembled the IR spectrum of model 2-(1*H*-indol-3-yl)-1-nitroethene with *trans* orientation of the heteroring and nitro group [12]. Apart from the band at 1730–1735 cm^{-1} due to ester carbonyl group, the spectra contained strong broadened absorption bands at 1305–1315 and 1250–1230 cm^{-1}, which may be assigned to vibrations of ionized nitro group, and strong bands in the region 1600–1570 cm^{-1}, belonging to vibrations of the indole ring and conjugated bond system (C=C and $C=N^+$). The observed IR spectral pattern, as with the simplest β-indolylnitroethene [12–16], suggests

Table 2. IR, UV, and ^{1}H NMR spectra of alkyl α-indolyl-β-nitroacrylates **VIII–XII**

Comp. no.	Yield,[a] %		mp,[b] °C	^{1}H NMR spectrum ($CDCl_3$), δ, ppm				IR spectrum ($CHCl_3$), ν, cm^{-1}				Electronic absorption spectrum (EtOH)	
	a	*b*		indole	H_A	(OCH_3) OCH_2CH_3	NH $(N–CH_3)$	C=O	C=C C=N	NOO^-	NH	λ_{max}, nm	ε
VII	56	22	156–157	7.31–7.33,	7.69	(4.02)	9.96	1735	1590	1305,	3350	216	21800
I				7.47–7.53,						1250		260	6900
				7.73								278	8200
												406	19200
IX	55	–	168–169	7.25–7.45,	7.70	1.40,	9.00	1730	1600	1315,	3245–	220	23500
				7.55		4.42				1250	3480	280	9400
												410	16200
X	73	62	129–131	7.34–7.40,	7.65	(4.03)	(3.84)	1735	1600	1310,	–	219	25000
				7.73						1230		284	9000
												411	19000
XI	64	44	122–124	7.34–7.42,	7.67	1.42,	(3.84)	1730	1600	1315,	–	219	23300
				7.73–7.77		4.50				1230		284	7200
												411	16800
XII	79	–	164–165	7.20–7.50,	7.42	1.42,	8.70	1730	1570	1310,	3245–	220	27200
				7.65[в]		4.50				1250	3480	280	13000
												430	24400

[a] Method *a*: synthesis from adducts **III–VII**; method *b*: one-pot synthesis. [b] Melting points of compounds **VIII–XII** after recrystallization from methanol. [c] Protons in the methyl group on the indole ring in compound **XII** resonate in the ^{1}H NMR spectrum at δ 2.45 ppm.

effective *p*,π- and π,π-conjugation in molecules **VIII–XII** with participation of unshared electron pair on the indole nitrogen atom, π-electrons in the indole ring, double C=C bond, and nitro group. This means that molecules **VIII–XII** have strongly polarized structure. In fact, compounds **VIII–XII** showed in the electronic spectra long-wave absorption bands with their maxima at λ 406–430 nm (ε = 16200–24400). These bands are displaced to the red region relative to the corresponding bands in the spectrum of α-indolyl-β-nitroethene (λ_{max} = 390, ε = 21200), presumably due to some contribution of the alkoxycarbonyl group to the electron system [11]. In addition, intermolecular charge-transfer interaction involving the indole ring (as donor) of one molecule and nitroacrylate fragment (as acceptor) of another molecule in ethanol cannot be ruled out.

Considerably increased intensity of the long-wave absorption band in the electronic spectra of α-indolyl-β-nitroacrylates **VIII–XII** (λ_{max} = 406–430 nm, ε = 16800–24400) as compared to α-indolyl-β-nitroethenylphosphonates (λ_{max} = 430–440 nm, ε = 2000–5600) [11] allowed us to presume *trans* orientation of the indolyl substituent and the nitro group with respect to the double C=C bond (*Z* configuration) in molecules **VIII–XII**; however, these data are insufficient to draw unambiguous conclusion.

The geometric structure of compounds **VIII–XII** was rigorously proved by X-ray analysis of a single crystal of ethyl 2-(1-methyl-1*H*-indol-3-yl)-3-nitroacrilate (**XI**). It was found that molecule **XI** has *Z* configuration with *s-trans* orientation of the exocyclic double C=C bond and indole ring, which favors effective conjugation. The structure of molecule **XI** is shown in Fig. 1, and the coordinates of atoms and bond lengths and bond and dihedral angles are given in Tables 3–6. The indole ring is planar within the experimental error [0.030(4) Å], the nitropropene fragment $C^{12}C^1C^2N^3O^1O^2$ is also planar and is slightly turned with respect to the indole ring plane (the torsion angle $C^{11}C^3C^1C^2$ is 15.9°), and the ester fragment $C^{12}(O^{12})O^{13}$ is orthogonal to the $C^{12}C^1C^2N^3O^1O^2$ plane (Table 4).

Table 3. Coordinates ($\times 10^4$) and equivalent thermal parameters ($Å^2 \times 10^3$) of non-hydrogen atoms in the molecule of ethyl 2-(1-methyl-1*H*-indol-3-yl)-3-nitroacrylate (**XI**)

Atom	*x*	*y*	*z*	*U*(eq)
O^{13}	9418(2)	5846(3)	3255(2)	48(1)
O^{12}	7822(2)	4638(3)	2019(2)	55(1)
C^3	8025(2)	4445(3)	4425(2)	36(1)
C^{11}	7621(2)	3730(3)	5146(2)	34(1)
C^1	8661(2)	3810(3)	3877(2)	35(1)
N^5	7135(2)	6288(3)	4955(2)	43(1)
C^4	7685(3)	6003(3)	4335(3)	40(1)
O^2	9848(3)	2541(4)	2815(3)	83(1)
C^6	7065(2)	4905(3)	5454(3)	39(1)
N^3	9864(3)	1856(3)	3605(3)	53(1)
C^{10}	7621(3)	2205(4)	5525(3)	42(1)
C^2	9234(3)	2438(4)	4151(3)	44(1)
C^{12}	8591(2)	4770(3)	2927(2)	37(1)
C^7	6544(3)	4638(4)	6133(3)	48(1)
O^1	10426(3)	647(4)	3963(3)	89(1)
C^9	7108(3)	1929(4)	6197(3)	50(1)
C^{16}	6708(3)	7797(4)	5093(3)	58(1)
C^8	6571(3)	3121(4)	6507(3)	51(1)
C^{14}	9413(4)	6931(5)	2430(3)	60(1)
C^{15}	10069(3)	6285(6)	1866(3)	70(1)

Considerable polarization of molecule **XI** follows from some redistribution of bond lengths therein: the C^1–C^2 bond [1.348(4) Å] is longer, while the C^2–N^3 bond [1.416(4) Å] is shorter than the corresponding standard double and single bonds. Analogous bond length variation was found in the molecule of 2-(1*H*-indol-3-yl)-1-nitroethene by X-ray diffraction [13].

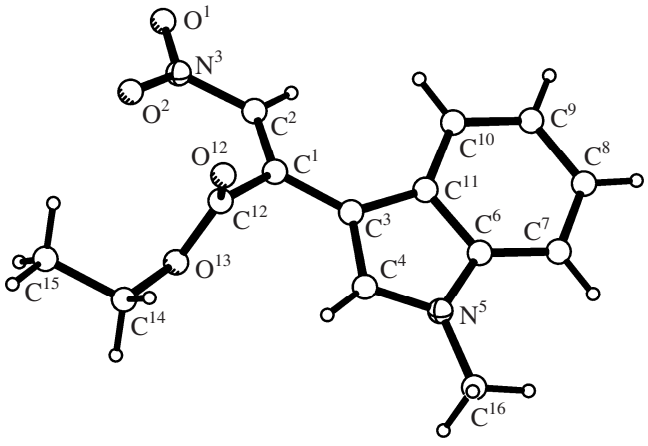


Fig. 1. Structure of the molecule of ethyl 2-(1-methyl-1*H*-indol-3-yl)-3-nitroacrylate (**XI**) in crystal (with atom numbering) according to the X-ray diffraction data.

Table 4. Selected torsion angles (τ, deg) in the molecule of ethyl 2-(1-methyl-1*H*-indol-3-yl)-3-nitroacrylate (**XI**)

Angle	τ, deg	Angle	τ, deg
$C^1C^3C^{11}C^{10}$	–4.6(6)	$C^1C^3C^4N^5$	–178.2(3)
$C^2C^1C^{12}O^{13}$	–94.5(3)	$C^2C^1C^{12}O^{12}$	91.2(4)
$C^3C^1C^2N^3$	–179.2(3)	$C^3C^1C^{12}O^{12}$	–86.0(4)
$C^4C^3C^1C^2$	163.4(3)	$C^3C^1C^{12}O^{13}$	88.3(3)
$C^{11}C^3C^1C^{12}$	161.3(3)	$O^2N^3C^2C^1$	–4.7(6)
$C^{12}O^{13}C^{14}C^{15}$	–87.4(4)	$C^4C^3C^1C^{12}$	–19.4(4)
$C^{14}O^{13}C^{12}C^1$	–176.3(3)	$C^{11}C^3C^1C^2$	–15.9(5)
$C^{14}O^{13}C^{12}O^{12}$	–2.2(5)	$C^{12}C^1C^2N^3$	3.8(5)
$O^1N^3C^2C^1$	175.0(3)		

The crystal packing of compound **XI** lacks classical hydrogen bonds, but is determined by intermolecular C–H···O and C–H···π interactions. A couple of identical hydrogen bonds between the H^{10} hydrogen atom in the benzene fragment of one molecule **XI** and $O^{1'}$ oxygen atom in the nitro group of the other molecule ($H^{10}\cdots O^{1'}$ 2.55 Å, $C^{10}H^{10}O^{1'}$ 144°, symmetry operation $-x$, $2 - y$, $1 - z$) gives rise to centrosymmetric dimers. Each molecule of the H-dimer acts as both donor and acceptor in two additional C–H···O interactions with the neighboring H-dimers related to the former molecule through a screw axis (interaction between the H^8 hydrogen atom in the benzene ring and $O^{2''}$ atom of the nitro group, C^8–$H^8\cdots O^{2''}$, with the following parameters: $H^8\cdots O^{2''}$ 2.55 Å, C^8–$H^8\cdots O^{2''}$ 166°, symmetry operation $1/2 + x$, $3/2 - y$, $-1/2 + z$; Fig. 2). As a result of combination of the above interactions, bilayer supramolecular structure is formed (Fig. 3).

Such mutual arrangement of molecules **XI** in crystal gives rise to additional interactions between electronic systems of the aromatic fragments and C–H···π interactions. Methyl hydrogen atoms (H^{151}) in the ethyl groups of two centrosymmetric molecules belonging to the same bilayer are involved in C–H···π interactions, leading to specific dimers (the $H^{151}\cdots C_g$ distance, where C_g is the centroid of the benzene ring, is 2.71 Å, and the angle $C^{15}H^{151}C_g$ is 159°; Fig. 4). As a result, a fairly high packing factor (0.68) is reached.

Thus we have proposed a convenient preparative procedure for the synthesis of indolyl-substituted β-nitroacrylates which can be used as key structures for

the design of potential biologically active compounds having a pharmacophoric indole ring and readily modifiable nitro and ester groups; the structure of the products has been reliably determined by spectral methods and X-ray analysis.

EXPERIMENTAL

The IR spectra were recorded from solutions in chloroform (c = 0.1–0.001 M) or pastes in mineral oil on an InfraLYuM FT-02 spectrometer with Fourier transform. The ^{1}H and ^{13}C NMR spectra were measured on Bruker AC-200 and WM-400 spectrometers at 200.13 (^{1}H), 50.323 (^{13}C), and 400.13 MHz (^{1}H), respectively, using chloroform-*d* as solvent and tetramethylsilane as internal reference; the chemical shifts were determined with an accuracy of ±0.5 Hz. The electronic absorption spectra were recorded from solutions in ethanol on SF 2000 and Shimadzu UV2401 spectrophotometers using quartz cells (cell path lingth 0.1 and 1 cm). The products were isolated and purified by recrystallization and column chromatography on Chemapol silica gel LD 100–250 and 100–400 μm (Czechia), the substrate–to sorbent ratio being 1:(10–20) (by weight); eluents were selected according to eluotropic series given in [17]. The progress of reactions and the purity of products were monitored by thin-layer chromato-graphy on Silufol UV-254 plates; development with iodine vapor or under UV light.

The X-ray diffraction study of a single crystal of compound **XI** was performed at 20°C on a NONIUS B.V. CAD-4 diffractometer (graphite monochromator, λCuK_α irradiation, ω-scanning, $\theta \le 74.24°$) at the X-Ray Department, Spectral and Analytical Center, Arbuzov Institute of Organic and Physical Chemistry, Kazan Research Center, Russian Academy of Sciences. Monoclinic crystals, $C_{14}H_{14}N_2O_4$, with the following unit cell parameters (20°C): a = 12.899(2), b = 8.548(2), c = 13.662(3) Å; β = 116.46(3)°; V = 1348.6(5) Å^3; d_{calc} = 1.35 g cm^{-3}; M 274.27; Z = 4; space group $P2_1/n$. Total of 2853 reflections were measured, 1794 of which were with $I \ge 2\sigma(I)$. No drop in the intensities of three control reflections was observed during data acquisition, and correction for extinction was not introduced (μ_{Cu} = 0.84 mm^{-1}). The structure was solved by the direct method using SIR program [18] and was refined first in isotropic and then in anisotropic approximation using SHELXL software package [19]. The coordinates of hydrogen atoms were

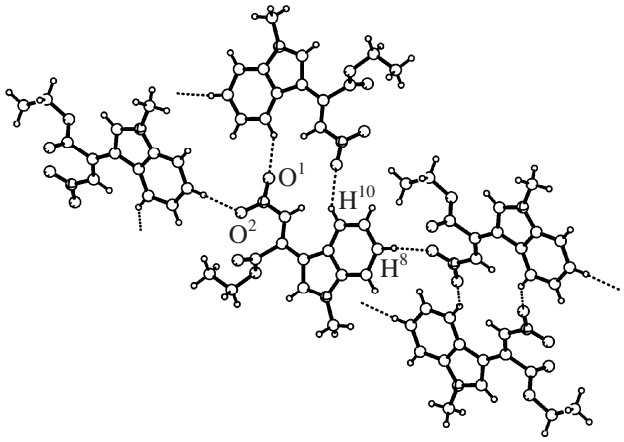


Fig. 2. C–H···O interactions (dotted lines) between molecules **XI** in crystal.

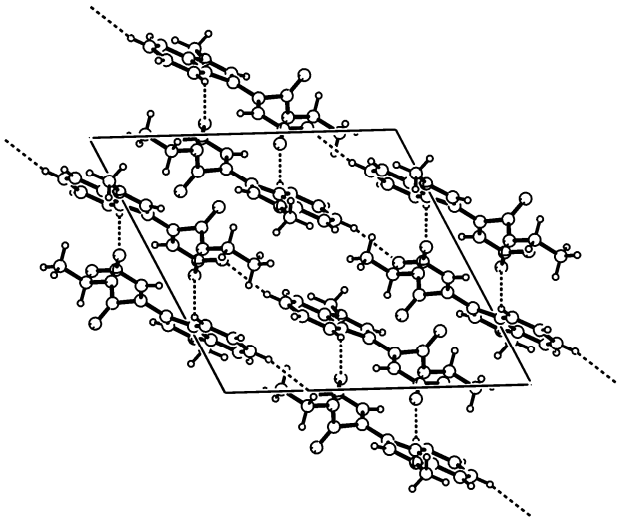


Fig. 3. Bilayer supramolecular structure formed by molecules **XI** in crystal via C–H···O interactions (dotted lines). View along the 0y crystallographic axis.

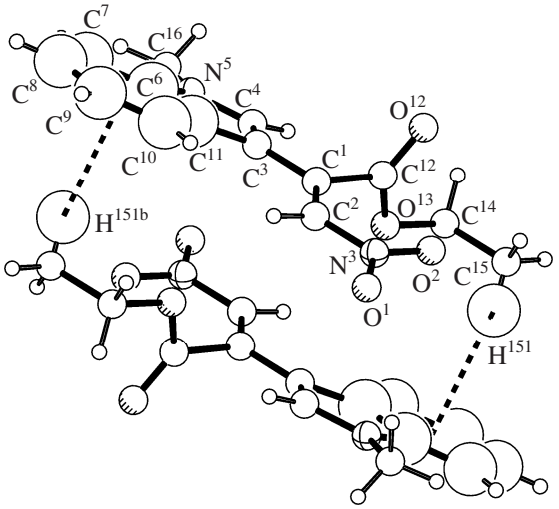


Fig. 4. C–H···π interactions (dotted lines) between molecules **XI** in crystal. The H^{151} hydrogen atom and carbon atoms of the benzene ring are shown as large circles for the sake of clarity.

Table 5. Bond angles (ω, deg) in the molecule of ethyl 2-(1-methyl-1*H*-indol-3-yl)-3-nitroacrylate (**XI**)[a]

Angle	ω, deg	Angle	ω, deg
$C^{12}O^{13}C^{14}$	117.0(3)	$C^4C^3C^{11}$	105.8(2)
$O^2N^3O^1$	121.9(3)	$C^4C^3C^1$	123.0(3)
$O^2N^3C^2$	120.7(3)	$C^{11}C^3C^1$	131.2(3)
$O^1N^3C^2$	117.4(3)	$N^5C^4C^3$	110.6(3)
$C^4N^5C^6$	108.9(2)	$C^7C^6N^5$	128.9(3)
$C^4N^5C^{16}$	125.5(3)	$N^5C^6C^{11}$	107.9(3)
$C^6N^5C^{16}$	125.6(3)	$C^{10}C^{11}C^3$	135.0(3)
$C^2C^1C^3$	123.5(3)	$C^6C^{11}C^3$	106.9(3)
$C^2C^1C^{12}$	122.0(3)	$O^{12}C^{12}O^{13}$	125.8(3)
$C^3C^1C^{12}$	114.4(2)	$O^{12}C^{12}C^1$	123.0(3)
$C^1C^2N^3$	122.1(3)	$O^{13}C^{12}C^1$	110.9(2)
		$O^{13}C^{14}C^{15}$	111.0(3)

calculated on the basis of stereochemical criteria and were refined according to the rider model. The final divergence factors were $R = 0.0746$ and $R_w = 0.2142$ (for 1794 reflections with $F^2 \geq 2\sigma$). All calculations were performed using MolEN [20] and WinGX [21], and the molecular structures were plotted using PLATON program [22]. The complete set of crystallographic data for compound **XI** was deposited to the Cambridge Crystallographic Data Center (entry no. CCDC 664370).

Initial alkyl 3-bromo-3-nitroacrylates **I** and **II** were synthesized according to the procedure developed by us previously [23].

Methyl 3-bromo-2-(1*H*-indol-3-yl)-3-nitropropanoate (III). A solution of 0.62 g of indole in 5 ml of anhydrous benzene was added dropwise to a solution of 1.13 g of methyl 3-bromo-3-nitroacrylate (**I**) in 5 ml of anhydrous benzene. The mixture was kept for 2 h at room temperature, and the solvent was distilled off to obtain 1.70 g of a dark orange oil, which was subjected to chromatography on silica gel. From the fraction eluted with benzene we isolated 1.55 g (89%) of oily compound **III**, R_f 0.66. Found, %: N 8.57. $C_{12}H_{11}BrN_2O_4$. Calculated, %: N 8.56.

Ethyl 3-bromo-2-(1*H*-indol-3-yl)-3-nitropropanoate (IV) was synthesized in a similar way from 0.89 g of ethyl 3-bromo-3-nitroacrylate (**II**) and 0.47 g of indole in 10 ml of anhydrous benzene (the mixture was kept for 6–7 h at room temperature). The oily residue was subjected to chromatography on silica gel. From the fraction eluted with chloroform we isolated 1.15 g (84%) of oily compound **IV**, R_f 0.60, 0.75. Found, %: C 46.10, 46.12; H 4.05, 4.07; N 8.40, 8.42. $C_{13}H_{13}BrN_2O_4$. Calculated, %: C 45.75; H 3.81; N 8.21.

Methyl 3-bromo-2-(1-methyl-1*H*-indol-3-yl)-3-nitropropanoate (V) was synthesized as described above for compound **III** from 0.94 g of methyl 3-bromo-3-nitroacrylate (**I**) and 0.59 g of 1-methyl-1*H*-indole in 10 ml of anhydrous benzene (the mixture was kept for 7 h at room temperature). We isolated 1.4 g (93%) of compound **V** as an oily residue which crystallized on storage, mp 160–161°C (from ethanol). Found, %: N 8.33. $C_{13}H_{13}BrN_2O_4$. Calculated, %: N 8.21.

Ethyl 3-bromo-2-(1-methyl-1*H*-indol-3-yl)-3-nitropropanoate (VI) was synthesized as described above for compound **III** from 1.12 g of ethyl 3-bromo-3-nitroacrylate (**II**) and 0.65 g of 1-methyl-1*H*-indole in 10 ml of anhydrous benzene (the mixture was kept for 6–7 h at room temperature). The oily residue, 1.65 g, was subjected to chromatography on silica gel. From the fraction eluted with carbon tetrachloride–benzene (1:1) we isolated 1.53 g (86%) of compound **VI**, which crystallized on storage. Yellow crystals, mp 78–84°C (from ethanol). Found, %: C 47.42, 47.47; H 4.55, 4.54; N 7.67, 7.65. $C_{14}H_{15}BrN_2O_4$. Calculated, %: C 47.32; H 4.23; N 7.89.

Ethyl 3-bromo-2-(2-methyl-1*H*-indol-3-yl)-3-nitropropanoate (VII) was synthesized as described above

Table 6. Bond lengths (*d*, Å) in the molecule of ethyl 2-(1-methyl-1*H*-indol-3-yl)-3-nitroacrylate (**XI**)

Bond	*d*, Å	Bond	*d*, Å	Bond	*d*, Å	Bond	*d*, Å
O^{12}–C^{12}	1.200(4)	N^5–C^4	1.347(4)	C^3–C^4	1.390(4)	C^{10}–C^9	1.371(5)
O^{13}–C^{12}	1.326(4)	N^5–C^6	1.388(4)	C^3–C^{11}	1.439(4)	C^{11}–C^{10}	1.403(4)
O^{13}–C^{14}	1.457(4)	N^5–C^{16}	1.448(4)	C^6–C^7	1.384(5)	C^{14}–C^{15}	1.481(6)
O^1–N^3	1.232(4)	C^1–C^2	1.348(4)	C^6–C^{11}	1.404(4)		
O^2–N^3	1.221(4)	C^1–C^3	1.441(4)	C^7–C^8	1.388(5)		
C^2–N^3	1.416(4)	C^1–C^{12}	1.503(4)	C^8–C^9	1.399(5)		

for compound **III** from 0.89 g ethyl 3-bromo-3-nitroacrylate (**II**) and 0.52 g of 2-methyl-1*H*-indole in 10 ml of anhydrous benzene (the mixture was kept for 6–7 h at room temperature). The oily residue, 1.40 g, was subjected to chromatography on silica gel. From the fraction eluted with benzene–chloroform (1:1) we isolated 0.98 g (69%) of compound **VII** as a dark brown oily substance, R_f 0.84, 0.96. Found, %: C 47.40, 47.34; H 4.41, 4.43; N 7.93, 7.92. $C_{14}H_{15}BrN_2O_4$. Calculated, %: C 47.32; H 4.23; N 7.89.

Methyl-2-(1*H*-indol-3-yl)-3-nitroacrylate (VIII). *a*. A solution of 0.39 ml of triethylamine in 8 ml of anhydrous diethyl ether was added dropwise to a solution of 0.92 g of methyl 3-bromo-2-(1*H*-indol-3-yl)-3-nitropropanoate (**III**) in 20 ml of anhydrous diethyl ether, and the mixture was heated for 7 h under reflux. The precipitate of triethylamine hydrobromide was filtered off, the solvent was distilled off from the filtrate, and the oily residue crystallized upon addition of anhydrous diethyl ether. Yield 0.38 g (56%), yellow crystals, mp 156–158°C (from methanol–water, 1:1). Found, %: C 58.42; H 4.50; N 11.85. $C_{12}H_{10}N_2O_4$. Calculated, %: C 58.54; H 4.09; N 11.38.

b. A solution of 0.41 g of indole in 5 ml of anhydrous benzene was added dropwise to a solution of 0.74 g of methyl 3-bromo-3-nitroacrylate (**I**) in 7 ml of anhydrous benzene. The mixture was kept for 100 min at room temperature, a solution of 0.49 ml (0.36 g) of triethylamine in 5 ml of anhydrous benzene was added dropwise, and the mixture (it turned dark) was heated for 4 h under reflux. The precipitate of triethylamine hydrobromide, 0.41 g, was filtered off, the filtrate poured into a Petri dish and evaporated, and the residue was kept for 2 days in a vacuum desiccator over potassium hydroxide. The product was subjected to chromatography on silica gel to isolate (by elution with chloroform) 0.19 g (22%) of crystalline compound **VIII**, mp 156–157°C (from methanol). The product showed no depression of the melting point on mixing with a sample prepared as described above in *a*.

Ethyl 2-(1*H*-indol-3-yl)-3-nitroacrylate (IX) was synthesized in a similar way (method *a*) from 1.36 g of ethyl 3-bromo-2-(1*H*-indol-3-yl)-3-nitropropanoate (**IV**) and 0.55 ml of triethylamine in 15 ml of anhydrous diethyl ether (the mixture was heated for 2.5 h under reflux). Yield 0.57 g (55%), orange crystals, mp 168–169°C (from methanol). Found, %: C 60.25, 60.27; H 5.03, 5.05; N 11.04, 11.06. $C_{13}H_{12}N_2O_4$. Calculated, %: C 60.00; H 4.62; N 10.77.

Methyl 2-(1-methyl-1*H*-indol-3-yl)-3-nitroacrylate (X). *a*. The procedure was the same as described for compound **VIII** (method *a*); the reaction was carried out with 0.28 g of methyl 3-bromo-2-(1-methyl-1*H*-indol-3-yl)-3-nitropropanoate (**V**) and 0.12 ml of triethylamine in 14 ml of anhydrous diethyl ether (the mixture was heated for 8 h). The oily residue crystallized upon addition of anhydrous diethyl ether. Yield 0.16 g (73%), yellow crystals, mp 130–132°C (from aqueous methanol, 1:1).

b. A solution of 0.46 ml of 1-methyl-1*H*-indole in 5 ml of anhydrous benzene was added dropwise to a solution of 0.77 g of methyl 3-bromo-3-nitroacrylate (**I**) in 10 ml of anhydrous benzene. The mixture was kept for 1.5 h at room temperature, a solution of 0.51 ml of triethylamine in 5 ml of anhydrous benzene was added, and the mixture (it turned dark) was heated for 3.5 h under reflux. The precipitate of triethylamine hydrobromide, 0.52 g, was filtered off, the mother liquor was poured into a Petri dish, and the residue was kept for 2 days in a vacuum desiccator over potassium hydroxide. The oily residue crystallized upon addition of anhydrous diethyl ether. Yield 0.59 g (62%), mp 129–131°C (from methanol). The product showed no depression of the melting point on mixing with a sample prepared as described above in *a*. Found, %: C 60.15, 60.17; H 4.83, 4.83; N 10.74, 10.70. $C_{13}H_{12}N_2O_4$. Calculated, %: C 60.00; H 4.65; N 10.76.

Ethyl 2-(1-methyl-1*H*-indol-3-yl)-3-nitroacrylate (XI) was synthesized in a similar way (method *a*) from 1.78 g of ethyl 3-bromo-2-(1-methyl-1*H*-indol-3-yl)-3-nitropropanoate (**VI**) and 0.70 ml of triethylamine in 15 ml of anhydrous diethyl ether (the mixture was heated for 2 h under reflux). We isolated 0.20 g of yellow crystals, and the residue, 0.76 g, was subjected to chromatography on silica gel. From the benzene fraction we isolated 0.67 g of an oily substance which crystallized on treatment with anhydrous methanol. Overall yield of **XI** 0.87 g (64%), mp 122–124°C (from methanol). Found, %: C 61.74, 61.70; H 5.62, 5.61; N 10.15, 10.17. $C_{14}H_{14}N_2O_4$. Calculated, %: C 61.30; H 5.14; N 10.21.

b. 1-Methyl-1*H*-indole, 0.41 ml, was added to a solution of 0.72 g of ethyl 3-bromo-3-nitroacrylate (**II**) in 15 ml of anhydrous benzene. The mixture was kept for 1.5 h at room temperature, a solution of 0.45 ml of triethylamine in 8 ml of anhydrous benzene was added dropwise, and the mixture was heated for 4 h under reflux. The precipitate of triethylamine hydrobromide was filtered off, the filtrate was poured into a Petri dish

and evaporated, and the dark red oily residue was kept for 2 days in a vacuum desiccator over alkali. The product crystallized on treatment with anhydrous diethyl ether. Yield 0.38 g (44%), mp 122–124°C (from methanol). $^{13}C–\{^1H\}$ NMR spectrum, δ, ppm: 165.68 (C=O); 139.53, 138.13 (C=C); 135.36, 128.22, 124.36, 123.84, 122.61, 120.32, 110.50, 106.35 (indole); 62.39 (CH_2O); 33.40 (NCH_3); 13.64 (CH_3). Found, %: C 61.42, 61.37; H 5.41, 5.42; N 10.26, 10.29. $C_{14}H_{14}N_2O_4$. Calculated, %: C 61.30; H 5.14; N 10.21.

Ethyl 2-(2-methyl-1*H*-indol-3-yl)-3-nitroacrylate (XII) was synthesized in a similar way (method *a*) from 0.36 g of ethyl 3-bromo-2-(2-methyl-1*H*-indol-3-yl)-3-nitropropanoate (**VII**) and 0.10 g of triethylamine in 20 ml of anhydrous diethyl ether (the mixture was heated under reflux for 2 h). Yield 0.22 g (79%), mp 164–165°C (from methanol). Found, %: C 61.53, 61.52; H 5.18, 5.20; N 10.37, 10.35. $C_{14}H_{14}N_2O_4$. Calculated, %: C 61.30; H 5.14; N 10.21.

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