X-RAY AND NMR SPECTROSCOPIC STUDY OF SUBSTITUTED 2-ALKYLIDENE-7-DIETHYLAMINOBENZOPYRANS

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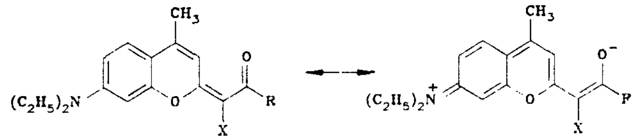
The structures of 4-methyl-7-diethylamino-2-(acetylcarbethoxymethylene)- and 4-methyl-7-diethylamino-2-(cyanocarbethoxymethylene)benzopyran were investigated by X-ray structural analysis. It was shown that the crystalline compounds have strong intramolecular charge separation and a single conformation in which the largely acceptor substituent, exomethylene, is near atom 3-H of the benzopyran fragment. Based on low temperature NMR spectra, it was concluded that an analogous conformation predominates in solution.

Earlier [1] we reported the synthesis of a series of 2-alkylidene-7-dialkylaminobenzopyrans from 7-aminocoumarins. In particular, compounds II and III were obtained from 4-methyl-7-diethylaminocoumarin (I).

In this work, we study the question of the degree of charge separation in alkylideneaminobenzopyrans in molecules such as II and III, which can be strongly polarized to the point of having the quinoid structures IIa and IIIa



II, III IIa, IIIa

II, IIa R=CH_3, X=$CO_2C_2H_5$; III, IIIa R=OC_2H_5, X=CN

Besides this, it was necessary to establish the configuration of the substituents in the alkylidene portion of these molecules. Therefore, we carried out the X-ray investigation of II and III (Fig. 1, Table 1).

Structural studies of compounds in the 7-aminobenzopyran system are exceedingly rare; thus, only the structure of 4-methyl-7-diethylaminocoumarin (I) [2] has been described. In contrast to I, the geometrical parameters of which are similar to those found in coumarin itself (IV) [3], in the structure of II and III a series of interesting features is observed. The substitution of the carbonyl oxygen atom by a methylene fragment leads to a significant change in the geometry of the benzopyran system in II and III when compared to I and IV. A lengthening of the $C_{(3)}-C_{(4)}$, $C_{(4a)}-C_{(5)}$, $C_{(6)}-C_{(7)}$, and $C_{(7)}-C_{(8)}$ bonds and a shortening of the $C_{(2)}-C_{(3)}$, $C_{(5)}-C_{(6)}$, and $C_{(8)}-C_{(8a)}$ bonds occur. Thus, in the investigated molecules a distinct tendency toward equalization of the C–C bonds in the pyran ring and a localization of the double bond in the benzene ring are present. Considering that in II and III the C=O moiety of the acetyl and carbethoxyl groups are more or less located in the plane of the benzopyran system, it is possible to propose a substantial contribution to the observed geometry of II and III from forms IIa and IIIa with charge separation (see above). The contribution of forms IIa and IIIa, however, are not reflected in the $C_{(7)}-N$ distance, which is identical within experimental error for compounds I-III.

It is interesting that the range of bond distances and the conformation of the $C_{(4a)}-C_{(4)}-C_{(3)}-C_{(2)}-O_{(1)}-C_{(9)}X-C_{(10)}R-O_{(2)}$ fragments in II and III are practically equal to those found, for example, in 1,1-dicarbomethoxy-4-dimethylaminobutadiene-1,3 [4]. Based on structural an-

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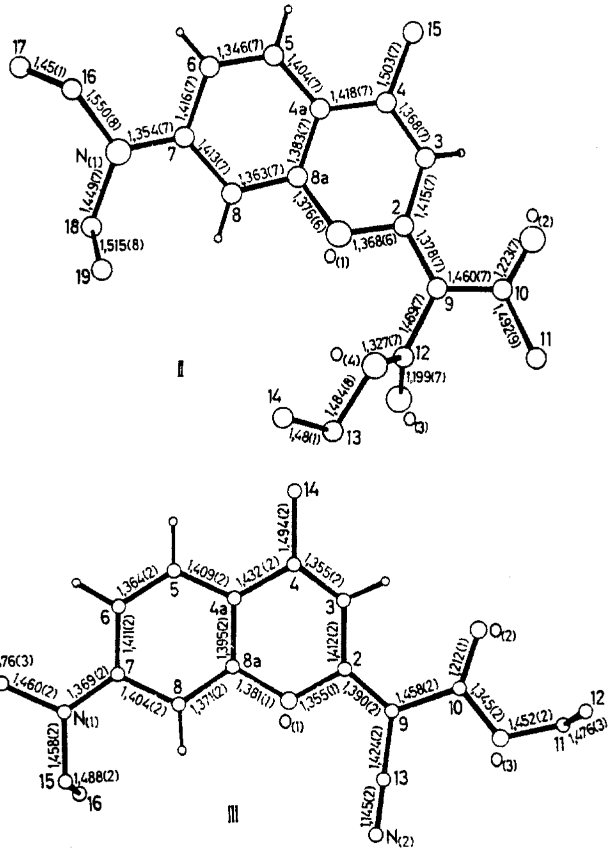

Fig. 1. Views of compound II and III and bond distances in them.

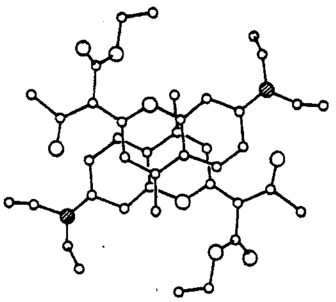

Fig. 2. Projection of the dimer of II on the benzopyran plane.

alysis of a series of similar compounds having polyene chains of various lengths with electron accepting and donating substituents in the α- and ω-positions, a conclusion about the lesser degree of delocalization of the double bonds in the middle of a long polyene chain when the planarity of the ends of the chain are preserved was made in [5]. Evidently, this conclusion can be applied to compounds of type II and III, since by comparison with coumarins I and IV, in them the $C_{(4)}$–$C_{(4a)}$ and $C_{(4a)}$–$C_{(5)}$ bonds change least and are in the middle of the conjugated chain. As in the polyenes mentioned above, the conjugation energy in II and III can be very large, since the coplanarity of the benzopyran and carbonyl group of the acetyl or carbethoxy substituent is preserved in spite of the short intramolecular contacts $O_{(2)}$–3-H, 2.27(3) and 2.22(1) Å, in compounds II and III, respectively. The interaction O–3-H, evidently is the reason for a shift of the 3-H proton signal of II into the weak field region fo the NMR spectrum (see below). Exchange of the cyano group, located in the plane of the $C_{(2)}$–$C_{(9)}$ double bond in III, by a carbethoxy group in II, for which the plane of the carboxyl group $C_{(9)}$–$C_{(12)}$–$O_{(3)}$–$O_{(4)}$ is at an angle of 55° with the double bond, does not lead to a change in the geometry of the delocalized system.

TABLE 1. Bond Angles ω in Compound II and III

Compound II		Compound III	
angle	ω°	angle	ω°
$C_{(2)}O_{(1)}C_{(8a)}$	122,3(4)	$C_{(2)}O_{(1)}C_{(8a)}$	121,38(9)
$C_{(12)}O_{(4)}C_{(13)}$	119,8(5)	$C_{(10)}O_{(3)}C_{(11)}$	116,6(1)
$C_{(7)}NC_{(16)}$	119,2(4)	$C_{(7)}N_{(1)}C_{(15)}$	121,1(1)
$C_{(7)}NC_{(18)}$	122,0(4)	$C_{(7)}N_{(1)}C_{(17)}$	122,5(1)
$C_{(16)}NC_{(18)}$	116,0(4)	$C_{(15)}N_{(1)}C_{(17)}$	116,3(1)
$O_{(1)}C_{(2)}C_{(3)}$	116,5(4)	$O_{(1)}C_{(2)}C_{(3)}$	118,8(1)
$O_{(1)}C_{(2)}C_{(9)}$	114,1(4)	$O_{(1)}C_{(2)}C_{(9)}$	114,0(1)
$C_{(3)}C_{(2)}C_{(9)}$	129,4(5)	$C_{(3)}C_{(2)}C_{(9)}$	127,2(1)
$C_{(2)}C_{(3)}C_{(4)}$	122,6(5)	$C_{(2)}C_{(3)}C_{(4)}$	121,9(1)
$C_{(3)}C_{(4)}C_{(4a)}$	119,2(4)	$C_{(3)}C_{(4)}C_{(4a)}$	118,7(1)
$C_{(3)}C_{(4)}C_{(15)}$	119,6(4)	$C_{(3)}C_{(4)}C_{(14)}$	120,7(1)
$C_{(4a)}C_{(4)}C_{(15)}$	121,2(4)	$C_{(4a)}C_{(4)}C_{(14)}$	120,6(1)
$C_{(4)}C_{(4a)}C_{(5)}$	126,4(4)	$C_{(4)}C_{(4a)}C_{(5)}$	126,3(1)
$C_{(4)}C_{(4a)}C_{(8a)}$	118,2(4)	$C_{(4)}C_{(4a)}C_{(8a)}$	118,7(1)
$C_{(5)}C_{(4a)}C_{(8a)}$	115,3(4)	$C_{(5)}C_{(4a)}C_{(8a)}$	115,0(1)
$C_{(4a)}C_{(5)}C_{(6)}$	122,4(5)	$C_{(4a)}C_{(5)}C_{(6)}$	122,6(1)
$C_{(5)}C_{(6)}C_{(7)}$	122,0(5)	$C_{(5)}C_{(6)}C_{(7)}$	121,4(1)
$NC_{(7)}C_{(6)}$	122,7(5)	$N_{(1)}C_{(7)}C_{(6)}$	122,1(1)
$NC_{(7)}C_{(8)}$	121,4(4)	$N_{(1)}C_{(7)}C_{(8)}$	121,0(1)
$C_{(6)}C_{(7)}C_{(8)}$	116,0(4)	$C_{(6)}C_{(7)}C_{(8)}$	116,9(1)
$C_{(7)}C_{(8)}C_{(8a)}$	120,2(5)	$C_{(7)}C_{(8)}C_{(8a)}$	120,3(1)
$O_{(1)}C_{(8a)}C_{(4a)}$	121,0(4)	$O_{(1)}C_{(8a)}C_{(4a)}$	120,4(1)
$O_{(1)}C_{(8a)}C_{(8)}$	114,9(4)	$O_{(1)}C_{(8a)}C_{(8)}$	115,8(1)
$C_{(4a)}C_{(8a)}C_{(8)}$	124,0(4)	$C_{(4a)}C_{(8a)}C_{(8)}$	123,9(1)
$C_{(2)}C_{(9)}C_{(10)}$	122,0(4)	$C_{(2)}C_{(9)}C_{(10)}$	123,1(1)
$C_{(2)}C_{(9)}C_{(12)}$	119,8(4)	$C_{(2)}C_{(9)}C_{(13)}$	118,8(1)
$C_{(10)}C_{(9)}C_{(12)}$	117,9(4)	$C_{(10)}C_{(9)}C_{(13)}$	118,1(1)
$O_{(2)}C_{(10)}C_{(9)}$	124,2(5)	$O_{(2)}C_{(10)}O_{(3)}$	122,7(1)
$O_{(2)}C_{(10)}C_{(11)}$	117,2(5)	$O_{(2)}C_{(10)}C_{(9)}$	126,6(1)
$C_{(9)}C_{(10)}C_{(11)}$	118,5(5)	$O_{(3)}C_{(10)}C_{(9)}$	110,8(1)
$O_{(3)}C_{(12)}O_{(4)}$	121,8(5)	$O_{(3)}C_{(11)}C_{(12)}$	111,8(1)
$O_{(3)}C_{(12)}C_{(9)}$	124,5(5)	$N_{(2)}C_{(13)}C_{(9)}$	179,4(1)
$O_{(4)}C_{(12)}C_{(9)}$	113,7(5)	$N_{(1)}C_{(15)}C_{(16)}$	114,1(2)
$O_{(4)}C_{(13)}C_{(14)}$	111,2(6)	$N_{(1)}C_{(17)}C_{(18)}$	114,4(2)
$NC_{(16)}C_{(17)}$	107,3(5)		
$NC_{(18)}C_{(19)}$	113,0(5)		

TABLE 2. Coordinates of Nonhydrogen ($\cdot 10^4$) and Hydrogen ($\cdot 10^3$) Atoms in III

Non-hydrogen atom	x	y	z	Hydrogen atom	x	y	z
$O_{(1)}$	3563(1)	1134(3)	4720(2)	3-H	274(2)	304(4)	354(2)
$O_{(2)}$	3569(2)	4173(4)	3159(2)	5-H	144(2)	16(4)	458(2)
$O_{(3)}$	5172(2)	1936(5)	4325(3)	6-H	172(2)	−129(4)	555(2)
$O_{(4)}$	4730(2)	2344(4)	5264(2)	8-H	364(2)	−57(4)	566(2)
$N_{(1)}$	2869(2)	−1945(5)	6311(2)	11,1-H	496(2)	474(4)	405(2)
$C_{(2)}$	3472(2)	2148(5)	4220(2)	11,2-H	467(2)	515(4)	330(2)
$C_{(3)}$	2802(2)	2417(5)	3868(3)	11,3-H	500(2)	387(4)	337(2)
$C_{(4)}$	2265(2)	1741(5)	4028(2)	13,1-H	561(2)	236(4)	583(2)
$C_{(4a)}$	2378(2)	753(5)	4579(2)	13,2-H	543(2)	114(4)	555(2)
$C_{(5)}$	1885(2)	30(5)	4838(3)	15,1-H	123(2)	208(4)	392(2)
$C_{(6)}$	2037(2)	−846(5)	5388(3)	15,2-H	135(2)	125(4)	338(2)
$C_{(7)}$	2708(2)	−1103(5)	5741(3)	15,3-H	155(2)	279(4)	336(2)
$C_{(8)}$	3209(2)	−421(5)	5466(3)	16,1-H	190(2)	−172(4)	681(2)
$C_{(8a)}$	3034(2)	481(5)	4919(2)	16,2-H	258(2)	−205(4)	735(2)
$C_{(9)}$	4058(2)	2757(5)	4133(2)	17,1-H	208(2)	−339(4)	609(2)
$C_{(10)}$	4068(3)	3773(5)	3579(3)	17,2-H	246(2)	−419(4)	683(2)
$C_{(11)}$	4722(4)	4420(7)	3540(4)	17,3-H	186(2)	−312(4)	709(2)
$C_{(12)}$	4704(2)	2306(6)	4565(3)	18,1-H	354(2)	−321(4)	681(2)
$C_{(13)}$	5320(3)	1772(8)	5765(4)	18,2-H	380(2)	−248(4)	618(2)
$C_{(14)}$	5156(3)	1443(9)	6466(4)	19,1-H	434(2)	−172(4)	736(2)
$C_{(15)}$	1570(3)	2048(6)	3615(3)	19,2-H	386(2)	−44(4)	691(2)
$C_{(16)}$	2353(3)	−2174(6)	6792(3)	19,3-H	369(2)	−122(4)	751(2)
$C_{(17)}$	2128(4)	−3566(8)	6694(4)				
$C_{(18)}$	3558(2)	−2299(5)	6624(3)				
$C_{(19)}$	3901(3)	−1267(7)	7167(3)				

The significant contribution of forms IIa and IIIa to the geometry of II and III is reflected in the crystal packing which is characteristic for compounds with strong dipole-dipole interactions. Because of these interactions, molecules of II form discrete centrosymmetric dimers,

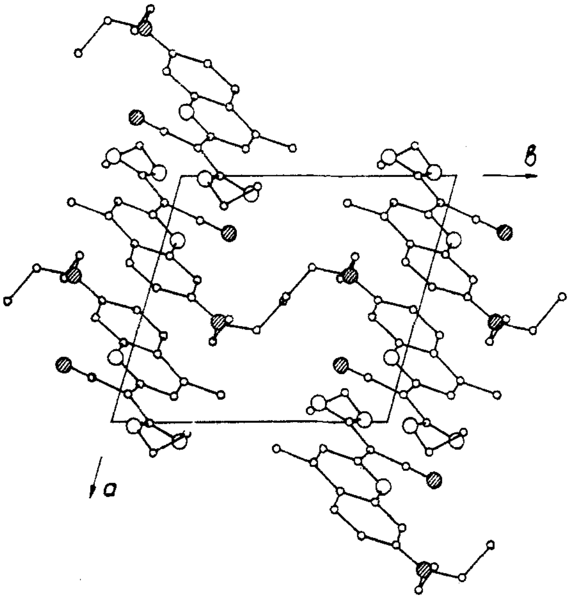

Fig. 3. Projection of III on the aOb Plane.

the structure of which is shown as a projection on the least squares plane of the benzopyran system in Fig. 2. The distance between the planes of the bicyclic fragments in the dimer is short (3.426 Å), which is consistent with relatively strong interactions between molecules. In III, the molecules also are stacked antiparallel, but do not form dimers (Fig. 3). The interplanar distances in the stacks are 3.478 and 3.372 Å.

Thus , we established that in the crystals, II and III have the methylenebenzopyran structure with strong charge separation. Now we will settle the question of the form of II and III in solution. Earlier [1], we developed a hypothesis about the rapid spinning in solution of the methylene fragment around the $C_{(2)}-C_{(9)}$ bond, which should be weakened in polarized structures such as IIa and IIIa (see above). For confirmation of this supposition, low temperature NMR spectra of II in CD_2Cl_2 were investigated. The changes in the NMR spectra upon lowering the temperature from 20 to −70°C are shown in Fig. 4. At 20°C the signal of proton 3-H is missing, but the signals of the remaining protons are still rather sharp. Successive lowering of the temperature (−20°C) leads initially to a broadening and then a splitting ($\leq$-50°C)of most of the signals, which supports the existence at low temperature of two conformers with different orientations of the $COCH_3$ and $CO_2C_2H_5$ groups. In this case, signals from the 3-H protons are observed in the region 7.69 and 6.75 ppm. By comparing the low temperature NMR spectra of II with spectra of previously synthesized [1] methylenebenzopyrans, it can be concluded that the weaker field signals belong to the Z-conformer (with the acetyl group close to the 3-H proton), and the strong field signals to the E-conformer. Based on the integrated intensities, the ratio of conformers Z:E can be calculated. At −70°C in CD_2Cl_2 solution, it is approximately 2:1. Thus, in solution, II also exists primarily in the Z-conformer.

It is interesting to note that in deuterochloroform the NMR spectra at 20°C are analogous to spectra taken at −20°C in CD_2Cl_2. This fact is consistent with greater resistance to internal rotation in II in $CDCl_3$, which possibly is explained by the lower mobility of $CDCl_3$ compared to CD_2Cl_2 as a result of the larger molecular weight and volume.

EXPERIMENTAL

The synthesis of II and III is given in [1]. Crystals for the X-ray analysis were grown by slow evaporation of solutions of II and III in hexane-acetone, 3:1.

NMR spectra were recorded on a Bruker WM-250 in CD_2Cl_2 and $CDCl_3$, with HMDS as an internal standard.

X-Ray Investigation of II. Red crystals of II, $C_{20}H_{25}NO_4$, are monoclinic, at 20°C a = 20.372(2), b = 9.849(1), c = 19.133(2) Å, β = 102.057(9)°, Z = 8, space group C2/c. The cell constants and intensities of 1471 reflections with $I \leq 2\sigma$ were measured on an automatic 4-circle Hilger-Watts Y-290 diffractometer (λMoK_α, graphite monochromator, $\theta/2\theta$-scanning, $\theta \leq 30$°C). The structure was solved by direct methods and was refined by anisotropic full matrix least squares for all nonhydrogen atoms. Difference maps showed all hydrogen atoms except for that bonded to $C_{(14)}$, which had a large temperature factor. The H atom coordinates were refined

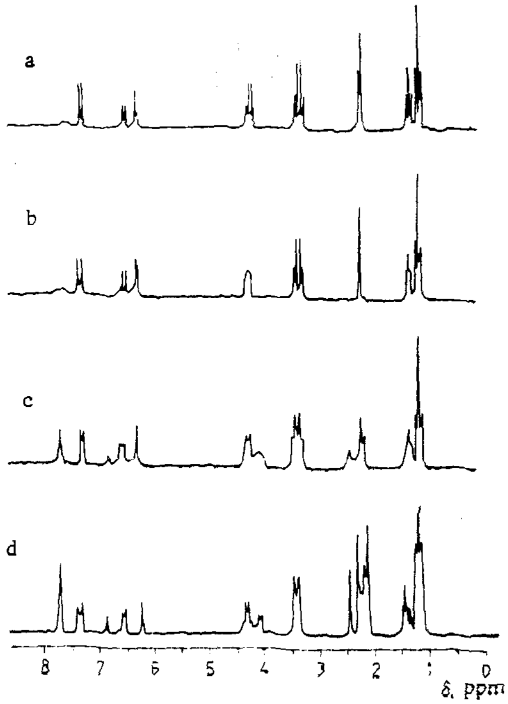

Fig. 4. NMR spectra of II (in CDCl$_2$.
a) 20°C; b) −20°C; c) −50°C; d) −70°C.

TABLE 3. Coordinates of Nonhydrogen ($\cdot 10^4$) and Hydrogen ($\cdot 10^3$) Atoms in III

Nonhydrogen atom	x	y	z	Hydrogen atom	x	y	z
$O_{(1)}$	2605(1)	520(1)	5328(1)	3-H	35(2)	−280(2)	528(1)
$O_{(2)}$	−772(2)	2686(1)	6886(1)	5-H	326(2)	−196(2)	209(2)
$O_{(3)}$	−136(1)	−864(1)	8411(1)	6-H	497(2)	15(2)	151(2)
$N_{(1)}$	5954(2)	2887(2)	2685(1)	8-H	446(2)	254(2)	454(1)
$N_{(2)}$	2337(2)	2298(2)	7896(2)	11,1-H	−137(2)	−114(2)	959(2)
$C_{(2)}$	1562(2)	−654(2)	5693(2)	11,2-H	−208(2)	−230(2)	852(2)
$C_{(3)}$	1065(2)	−2041(2)	4977(2)	12,1-H	−17(3)	−362(2)	914(2)
$C_{(4)}$	1645(2)	−2242(2)	3963(2)	12,2-H	−115(2)	−339(2)	1024(2)
$C_{(4a)}$	2775(2)	−1001(2)	3601(2)	12,3-H	48(3)	−232(2)	1027(2)
$C_{(5)}$	3508(2)	−1015(2)	2586(2)	14.1-H	50(2)	−446(2)	365(2)
$C_{(6)}$	4540(2)	232(2)	2284(2)	14,2-H	42(2)	−362(2)	245(2)
$C_{(7)}$	4938(2)	1620(2)	2984(2)	14,3-H	191(2)	−401(2)	307(2)
$C_{(8)}$	4250(2)	1648(2)	4017(2)	15,1-H	669(2)	452(2)	433(2)
$C_{(8a)}$	3213(2)	376(2)	4293(2)	15,2-H	722(2)	505(2)	323(2)
$C_{(9)}$	1100(2)	−329(2)	6769(2)	16,1-H	470(3)	524(2)	211(2)
$C_{(10)}$	−21(2)	−1428(2)	7319(2)	16,2-H	391(2)	432(2)	337(2)
$C_{(11)}$	−1217(2)	−1845(2)	9063(2)	16,3-H	518(2)	605(2)	354(2)
$C_{(12)}$	−453(3)	−2887(3)	9732(2)	17,1-H	698(2)	199(2)	158(2)
$C_{(13)}$	1791(2)	1128(2)	7390(2)	17,2-H	780(2)	364(2)	189(2)
$C_{(14)}$	1095(2)	−3723(2)	3223(2)	18,1-H	647(3)	334(2)	−7(2)
$C_{(15)}$	6266(3)	4330(2)	3375(2)	18,2-H	492(3)	253(2)	27(2)
$C_{(16)}$	4923(3)	5029(2)	3125(2)	18,3-H	574(3)	420(2)	63(2)
$C_{(17)}$	6744(2)	2887(2)	1647(2)				
$C_{(18)}$	5836(3)	3214(3)	499(2)				

with fixed B_{iso} = 5 Å^2. Refinement in the final stage used 1426 reflections with $I \geq 4.3\ \sigma$. The final R factors were R = 0.069, Rw = 0.066. All calculations were done on an IBM Eclipse S/200 using INEXTL programs [6]. The coordinates of nonhydrogen atoms and hydrogen atoms are given in Table 2.

X-Ray Investigation of III. Bright orange crystals of III, $C_{19}H_{22}N_2O_3$, are triclinic, at 20°C, a = 8.822(3), b = 9.308(2), c = 11.214(1) Å, α = 92.07(1), β = 100.46(2), γ = 105.67(2)°, Z = 2, space group P$\bar{1}$. The cell constants and intensities of 2049 independent reflections with $I \geq 3\sigma$ were measured on a Nonius CAD-4 automatic 4-circle diffractometer (λMoK$_\alpha$, graphite monochromator, relative scanning speed ω:θ = 1.2:1, θ ≤ 28°C). The structure was solved by direct methods and was refined by anisotropic full matrix least squares for all nonhydrogen atoms. All hydrogen atoms, found in difference maps, were refined isotropically. Refinement in the final stages used 1909 reflections with $I \geq 5\sigma$. The final R factors were $R = 0.035$ and $R_w = 0.049$. All calculations were done on an IBM PDP-11/23PLUS using SDP-PLUS programs [7]. The coordinates of nonhydrogen and hydrogen atoms are given in Table 3.

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NITRILE OXIDES OF THE THIOPHENE SERIES: INFLUENCE OF STERIC FACTORS ON STABILITY AND REACTIVITY IN REACTIONS OF 1,3-DIPOLAR CYCLOADDITION

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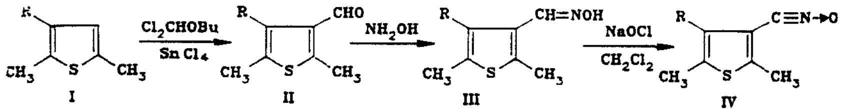
The synthesis of a series of di- and trialkyl-substituted thiophenecarbonitrile oxides is described. Their addition to styrene is studied together with the quantitative evaluation of the influence of different alkyl groups on the rate of the 1,3-dipolar cycloaddition reaction by the method of competing reactions.

The first examples of nitrile oxides of the the thiophene series, the stability of which was determined by the presence of an electron-accepting substituent together with the C≡N→O group, were previously studied in our laboratory [1]. Moreover, there are well known examples of the aromatic series where the stability is determined by the steric effects of the two alkyl groups in the ortho positions relative to the nitrile oxide function. Thiophene analogs of such compounds are described below; the extent of the shielding influence of different alkyl groups on the stability of the substances and the rates of their reaction with styrene were evaluated quantitatively. The synthesis of the products was performed by the following scheme:



I—IV a R=H; b $R=CH_3$; c $R=CH_2CH_3$; d $R=CH(CH_3)_2$

We also undertook attempts to synthesize analogs of the compounds (IV) in which both the alkyl groups adjoining the nitrile oxide group differ from methyl. It was to be expected that the most sterically hindered compound would have two tertbutyl groups. Taking into account the known ease of cleavage of the tert-butyl groups during electrophilic substitution in the presence of Lewis acids, it is impossible to synthesize such a compound by the formylation of 2-methyl-3,5-di-tertbutylthiophene (V) under the conditions utilized for the isolation of the aldehydes (II). Therefore, it was planned to carry out the bromination of compound (V)

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