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Stereoisomerism in the Series of Isoindole-Based Quaternary Salts

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Abstract—Steric structure of quaternary ammonium salts of the 3-[alkyl(aryl)amino]-1-[alkyl(aryl)iminio]-1*H*-isoindole series was studied by ^{1}H NMR spectroscopy and X-ray analysis. The examined salts are characterized by *E*,*E* configuration of substituents with respect to the exocyclic C–N bonds, and the presence of *ortho*- and *meta*-substituents in the benzene rings on the nitrogen atoms gives rise to atropisomers. Sterically hindered *N*-(2,4,6-trimethylphenyl) derivative was found to exist as *Z*,*Z* isomer which undergoes irreversible thermal isomerization into the more stable *E*,*E* isomer through intermediate *Z*,*E* structure. The reactions of 1,1,3-trichloro-1*H*-isoindole with secondary aromatic amines having an electron-withdrawing substituent in the *ortho* position in the presence of organic bases (triethylamine, *N*,*N*-dimethylbenzylamine) are accompanied by decomposition of the latter and formation of unsymmetrically substituted salts of the 3-[alkyl(aryl)amino]-1-(dialkyliminio)-1*H*-isoindole series, which contain both arylamine residue and dialkylamino group and are also characterized by atropisomerism.

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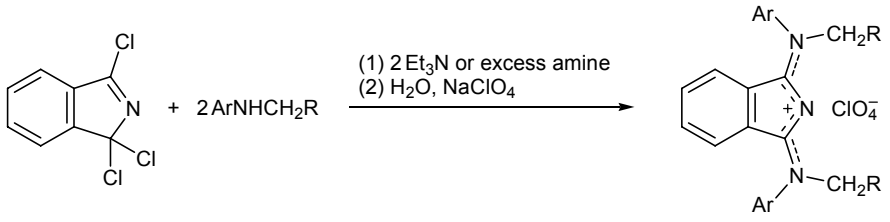
Compounds of the aminoimino-1*H*-isoindole series can exist as different tautomers and geometric isomers [1]. The latter appear due to the presence of double exocyclic C=N bonds. For instance, 1,3-bis(arylimino)-2,3-dihydro-1*H*-isoindoles generally exist as mixtures of tautomers, as well as of *Z*,*E* isomers [2]. Their NMR spectra contain two sets of signals corresponding to *Z*,*E* and *Z*,*Z* isomers. By contrast, quaternary isoindolium salts of the 3-amino-1-iminio-1*H*-isoindole series are stable as *E*,*E* isomers of 1,3-bis-[alkyl(aryl)amino] derivatives and *Z*,*Z* isomers of the salts derived from cyclic fatty–aromatic amines [3].

3-Amino-1-iminio-1*H*-isoindole salts cannot be synthesized by direct alkylation of the corresponding bases, 1,3-bis(arylimino)-2,3-dihydro-1*H*-isoindoles; however, such salts are readily available via nucleophilic replacement of chlorine in 1,1,3-trichloro-1*H*-isoindole (**I**) by secondary amine residues in the presence of excess amine [3]. With a view to examine the effect of steric factors on the state of equilibrium between stereoisomers we synthesized 1,3-bis(arylamino)isoindolium salts having *ortho* substituents in the aromatic ring. The reaction readily occurred in anhydrous aprotic solvent, such as chloroform, aceto-

Scheme 1.



I **IIa–IId**, **IIIa–IIIg** (*E*,*E* isomer)

II, R = H, Ar = 2-MeC_6H_4 (**a**), 2-MeOC_6H_4 (**b**), 2-ClC_6H_4 (**c**), 2,4,6-$Me_3C_6H_2$ (**d**); **III**, R = Ph, Ar = Ph (**a**), 3-MeC_6H_4 (**b**), 2-MeC_6H_4 (**c**), 2-MeOC_6H_4 (**d**), 2-ClC_6H_4 (**e**), 2-BrC_6H_4 (**f**), 2,4,6-$Me_3C_6H_2$ (**g**).

Table 1. ^{1}H NMR spectra of aryl{3-[(aryl)methylamino]-1*H*-isoindol-1-ylidene}methylammonium perchlorates **IIa**–**IIc** at 298 K

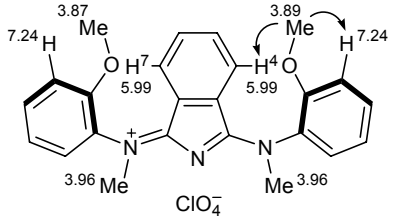
Comp. no.	Solvent	Stereoisomer ratio, %	Chemical shifts δ±0.02 ppm, J = 8 Hz				
			CH_3, s	NCH_3, s	4-H, 7-H, d.d	5-H, 6-H, d.d	other aromatic protons, m
IIa	$CDCl_3$	57:43	2.30,2.32	4.00	5.79	7.13, 7.12	7.49
	TFA-*d*		2.41	4.32	6.25		7.44–7.82
	DMSO-d_6	54:46	2.26, 2.28	3.97	5.73	7.32	7.61
IIb	$CDCl_3$	71:29	3.87, 3.89	3.96	5.97, 5.99	7.13	7.08–7.73
	TFA-*d*		4.00	4.31	6.50		7.28–7.95
	DMSO-d_6		3.83	3.95	5.95	7.35	7.20–7.75
IIc	$CDCl_3$	52:48		4.06, 4.04	5.92, 5.89	7.17, 7.25	7.50–7.90
	TFA-*d*			4.21	6.20	7.42	7.64–7.94
	DMSO-d_6			4.00, 3.98	5.85, 5.84	7.42	7.60–8.10

nitrile, or hexane, and in most cases another organic base (e.g., triethylamine) can be used to bind liberated hydrogen chloride. Salts **IIa**–**IId** and **IIIa**–**IIIg** were isolated as readily crystallizable perchlorates which are poorly soluble in water (see also [4] and references therein).

It turned out that introduction of only one *ortho* substituent did not lead to the appearance of *Z*,*Z* isomer, and salts **IIa**–**IIc** and **IIIa**–**IIIg** have *E*,*E* configuration. This follows from the characteristic diamagnetic shift of signals from the 4-H and 7-H protons in the isoindole residue to the region δ 5.7–6.5 ppm [3] (Table 1) due to effect of ring current in the *N*-aryl groups.

Variation of the size of substituents does not change the stereoisomer ratio. It might be expected that increase in the size of the *N*-aryl group would affect the torsion angle formed by the benzene ring and heterocyclic fragment, which should affect the position of the 4-H and 7-H signals. However, the presence of a methyl group in the *ortho* position (compound **IIa**) induces only a small diamagnetic shift (Δδ = 0.1 ppm, DMSO-d_6) as compared to unsubstituted salt [3], while the 4-H and 7-H signals of salt **IIb** having *ortho*-methoxy groups are displaced downfield (δ 5.95–5.99 ppm). Signals in the spectrum of salt **IIb** in CD_2Cl_2 solution were assigned using NOE technique. Irradiation at a frequency corresponding to δ 3.89 ppm increased the intensity of a doublet in the aromatic region at δ 7.24 ppm, as well as the intensity of multiplet signal from 4-H and 7-H in the isoindole fragment. Irradiation at a frequency corresponding to the other methyl protons (δ 3.96 ppm) did not produce appreciable change of the spectral pattern. Therefore, we concluded that the signal at δ 3.96 ppm belongs to the *N*-methyl protons and that the singlets at δ 3.87 and 3.89 ppm arise from protons in the methoxy groups.

The chemical shifts of 4-H and 7-H are sensitive to the solvent nature. They are fairly similar in the spectra recorded from solutions in $CDCl_3$ and DMSO-d_6, while in going to trifluoroacetic acid (CF_3COOD) they decrease by about 0.2–0.5 ppm, presumably as a result of protonation of the endocyclic nitrogen atom and formation of bis-quaternary salt.



Although substituents in the *ortho* positions of the benzene rings do not favor formation of *Z*,*Z* isomers, they give rise to atropisomerism related to restricted internal rotation of the benzene rings about the C–N bonds. This follows from the presence of two sets of signals in the ^{1}H NMR spectra of solutions of *N*-methyl-substituted salts **IIa**–**IIc** (Table 1). The ^{1}H NMR spectrum of salt **IIa** in $CDCl_3$ at 298 K contains two signals from protons in the *ortho*-methyl groups with an intensity ratio of 57:43, a singlet from the *N*-methyl groups, a doublet of doublets from 4-H and 7-H, and two overlapped doublets of doublets from 5-H and 6-H. Differences in the chemical shifts become more appreciable in going to *ortho*-chloro derivative **IIc**. The positions of all signals in the spectrum recorded from a solution in TFA-*d* are averaged;

Table 2. ^{1}H NMR spectra of aryl{3-[(aryl)benzylamino]-1*H*-isoindol-1-ylidene}benzylammonium perchlorates **IIIa**–**IIIg** at 298 K

Comp. no.	Solvent	Stereoisomer ratio, %	Chemical shifts δ±0.2 ppm, J = 8 Hz							
			CH_3, s	NCH_2, d, J = 14 Hz	Δδ	NCH_2, d, J = 14 Hz	Δδ	4-H, 7-H. d.d	5-H, 6-H, d.d	other aromatic protons, m
IIIa	$CDCl_3$			5.73		5.73		5.84	7.11	7.23–7.64
	TFA-*d*			5.75		5.75		6.08		7.20–7.68
	DMSO-d_6			5.72		5.72				
IIIb	$CDCl_3$	59:41	1.91, 2.13	5.63, 5.72	0.09	5.53, 6.00	0.69	5.77, 5.79	7.12	7.38 (C_6H_5), 7.04–7.60
	TFA-*d*	61:39	2.01, 2.15	5.71, 5.85	0.14	5.53, 6.01	0.48	6.11	7.32	7.11–7.82
	DMSO-d_6	57:43	1.93, 2.20	5.66, 5.74	0.08	5.24, 6.10	0.86	5.72		7.05–7.65
IIIc	$CDCl_3$	42:58	3.68, 3.80	5.34, 5.78	0.44	5.09, 6.03	0.94	5.97		7.33 (C_6H_5), 6.95–7.69
	TFA-*d*	58:42	3.73, 3.83	5.68, 5.77	0.09	5.51, 5.94	0.43	6.32		7.40 (C_6H_5), 7.16–7.80
	DMSO-d_6	45:55	3.56, 3.69	5.50, 5.64	0.14	5.23, 5.91	0.68	5.95	7.16	7.00–7.70
IIId	$CDCl_3$	52:48	2.38	5.59, 5.72	0.13	5.52, 5.79	0.27	5.86	7.10	7.35 (C_6H_5), 7.42 (*o*-H), 6.93–7.18
	TFA-*d*		2.40	5.73		5.73		6.17		7.14–8.00
	DMSO-d_6	50:50	2.36	5.62, 5.78	0.16	5.55, 5.86	0.31	5.89		7.40 (C_6H_5), 7.25–7.83
IIIe	$CDCl_3$	53:47		5.37, 6.02	0.65	5.30, 6.10	0.80	5.86, 5.90	7.16, 7.27	7.20–7.70
	TFA-*d*	50:50		5.32, 6.17	0.85	5.17, 6.28	1.11	6.04	7.24	7.04–7.68
	DMSO-d_6	57:43		5.68, 5.83	0.15	5.29, 6.16	0.87	5.86	7.71	7.42–8.00
IIIf	$CDCl_3$	44:56		5.28, 6.08	0.80	5.18, 6.18	1.00	5.83		7.38 (C_6H_5), 7.15–7.85
	TFA-*d*	46:54		5.31, 6.31	1.00	5.19, 6.39	1.20	6.07	7.30	7.06–8.00
	DMSO-d_6	46:54		5.56, 5.93	0.37	5.18, 6.24	1.06	5.85		7.43–8.10

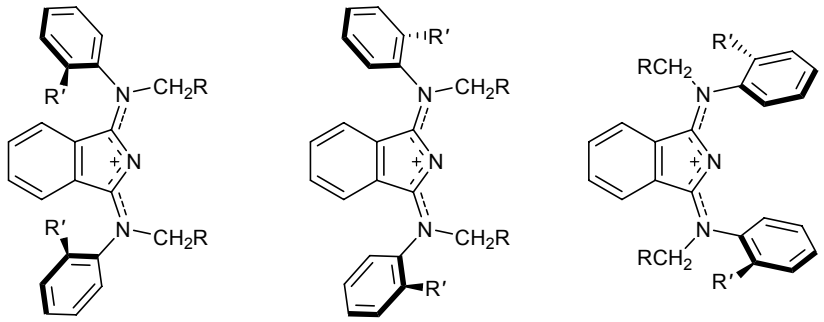
in DMSO-d_6 signals from particular *N*-methyl groups can be observed; and the ^{1}H NMR spectrum in $CDCl_3$ contains two sets of signals from both *N*-methyl protons and 4-H/7-H and 5-H/6-H.

N-Benzyl derivatives **IIIb**–**IIIf** also displayed two sets of signals with different intensities, corresponding to the NCH_2 protons (Table 2). These protons are diastereotopic, and their signals appear as two *AB* systems with larger or smaller difference in the chemical shifts. Methylene protons in *meta*-substituted salt **IIId** are also magnetically nonequivalent.

The presence of two sets of signals in the ^{1}H NMR spectra may be rationalized assuming that the examined compounds exist as mixtures of atropisomers, symmetrical *meso* form and two enantiomers.

The stereoisomer ratio of salts **IIa**–**IIc** ranges from 2:3 to 1:1, while one atropisomer of *ortho*-methoxy derivative **IIb** in $CDCl_3$ considerably predominates (70%). No signal splitting was observed in the ^{1}H NMR spectra of salts **IIa**–**IIc** dissolved in TFA-*d*. Salts **IId** and **IIIg** obtained, respectively, from *N*-methylmesidine and *N*-benzylmesidine possess two *ortho* substituents in each benzene ring on the nitrogen atoms; therefore, they have no chiral elements and do not give rise to atropisomers.

The ratio of atropisomers does not depend on the temperature: The ^{1}H NMR spectrum of salt **IIb** in DMSO-d_6 does not change on heating to 413 K. This means that the stereoisomers are formed with approximately equal probabilities and are incapable of under-



meso Enantiomers

going interconversion; i.e., they are approximately equivalent in energy.

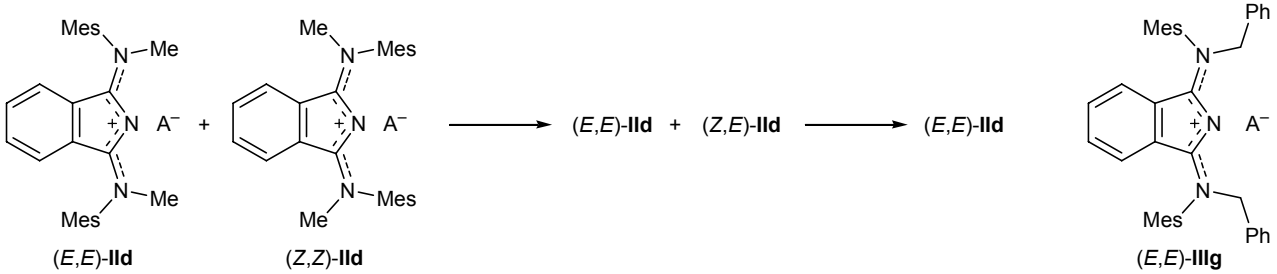
As follows from the spectral data for *N*-benzyl-substituted salts **IIIb**–**IIIf** (Table 2), differences in the chemical shifts of anisochronous protons in two stereoisomers are fairly large. The differences Δδ for *meta* substituted derivative **IIId** are 0.27 and 0.13 ppm in $CDCl_3$ and 0.31 and 0.16 ppm in DMSO-d_6. The Δδ value for one stereoisomer of *ortho*-methyl-substituted salt **IIIb** considerably increases (0.69 against 0.09 ppm in $CDCl_3$ and 0.86 against 0.08 ppm in DMSO-d_6). As the size of the substituent increases (in going from methyl group in **IIIb** to bromine atom in **IIIf**), Δδ successively rises in all solvents, e.g., to 1.00 ppm in $CDCl_3$. Simultaneously, the difference in the chemical shifts of the corresponding protons in the second stereoisomer also increases (from 0.09 to 0.80 ppm).

Nonequivalence of the methylene protons is different in different solvents. No anisochronicity is observed for salt **IIId** in TFA-*d*, but it appears in going to $CDCl_3$ and DMSO-d_6. The Δδ values for salts **IIIb** and **IIIc** in TFA-*d* differ insignificantly; however, the difference Δδ between *ortho*-chloro and *ortho*-bromo derivatives **IIIe** and **IIIf** exceeds 1 ppm in the same solvent, and compound **IIIf** is characterized by the largest Δδ values in this series (1.20 and 1.00 ppm). On the whole, Δδ successively increases in going from $CDCl_3$ to DMSO-d_6 and then to TFA-*d* for the chloro- and bromo-substituted salts. On the other hand, the maximal Δδ value for salt **IIIb** is observed in DMSO-d_6, and for **IIIc**, in $CDCl_3$ (Table 2).

Rise in temperature differently affects the position of signals from diastereotopic protons of two diastereoisomers. The chemical shifts of the CH_2 protons in the stereoisomer of **IIIc** characterized by lower Δδ value (0.14 ppm) remain unchanged as the temperature rises to 433 K (DMSO-d_6). The position of signals of the second stereoisomer changes to a considerable extent, from Δδ = 0.68 ppm at 298 K to 0.41 ppm at 433 K, approaching the corresponding signals of the first stereoisomer. Presumably, the existence of temperature dependence for only one isomer is the result of internal nonequivalence of $\Delta\delta_i$, and the value Δδ = 0.68 ppm includes the contributions of both conformational anisochronicity of $\Delta\delta_c$ (which depends on the populations of all possible rotamers) and internal difference in the δ values for each conformer [5, 6].

Increase of steric hindrances due to introduction of bulky 2,4,6-trimethylphenyl (mesityl) group leads to the formation of a mixture of *Z*,*Z*- and *E*,*E*-isomeric iminium salts **IId** in the reaction of 1,1,3-trichloro-1*H*-isoindole (**I**) with *N*-methylmesidine (Scheme 2). On the other hand, the reaction of **I** with *N*-benzylmesidine gives only one *E*,*E* isomer **IIIg** (like salts **IIIa**–**IIIc**). The *E*,*E* and *Z*,*Z* isomers of **IId** in DMSO-d_6 at 298 K display in the ^{1}H NMR spectrum signals from

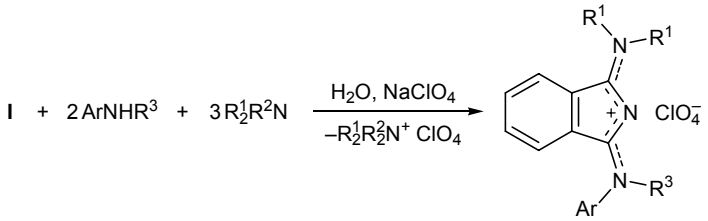
Scheme 2.



(*E*,*E*)-**IId** (*Z*,*Z*)-**IId** (*E*,*E*)-**IId** (*Z*,*E*)-**IId** (*E*,*E*)-**IIIg**

Mes = 2,4,6-$Me_3C_6H_2$; A = ClO_4^-.

Scheme 3.



(*E*)-**IVa**, (*E*)-**IVb**

Ar = 2-ClC_6H_4, $R^1 = R^3$ = Me, R^2 = $PhCH_2$ (**a**); Ar = 2-BrC_6H_4, $R^1 = R^2$ = Et, R^3 = $PhCH_2$ (**b**).

both stereoisomers with approximately equal intensities. The signals were assigned taking into account that the 4-H and 7-H signals of the *E*,*E* isomer appear in a stronger field (δ 5.85 ppm, d.d, *J* = 8 Hz,) due to shielding by ring current in the trimethylphenyl ring. The 4-H and 7-H protons in the *Z*,*Z* isomer are not shielded by the trimethylphenyl substitutents, and they resonate in a weaker field (δ 8.33 ppm). The *E*,*E* isomer is characterized by a doublet of doublets at δ 7.28 ppm (*J* = 8 Hz) from 5-H/6-H and a singlet at δ 3.86 ppm from the NCH_3 protons. The *Z*,*Z* isomer displays signals at δ 7.88 (*J* = 8 Hz, 5-H/6-H), 6.75 (*m*-H), and 3.92 ppm (NCH_3).

Raising the temperature to 363 K is accompanied by reduction in the intensity of signals belonging to the *Z*,*Z* isomer and appearance of new signals: two singlets from the methyl groups in the mesityl substitutents, two signals with equal intensities (δ 3.45 and 4.03 ppm) from the *N*-methyl groups, and one signal corresponding to *meta* protons in the mesityl group (δ 7.01 ppm). The signal belonging to 4-H/7-H is transformed into a doublet at δ 8.33 ppm with a coupling constant *J* of 8 Hz, and the second doublet with the same coupling constant appears in a stronger field (δ 5.93 ppm). The 5-H/6-H signals constitute a part of an *ABCD* spin system (δ 7.5 ppm). The intensity of signals from the *E*,*E* isomer does not change.

The observed temperature-induced variations of the spectral pattern are related to stereoisomer transformations involving disappearance of the *Z*,*Z* isomer and appearance of the *Z*,*E* isomer. Magnetically anisotropic effect of the trimethylphenyl ring in the latter spans only one 4-H proton, and its signal is displaced upfield (δ 5.93 ppm, d), whereas the 7-H signal remains in a weak field (δ 8.33, d).

Further raising the temperature to 413 K leads to subsequent variations in the spectrum of compound **IId**. The intensity of signals assigned to the *Z*,*E* isomer decreases, and the intensity of signals from the *E*,*E* isomer simultaneously increases. When the solution of

Table 3. ^{1}H NMR spectra of isoindolium perchlorates **IVa** and **IVb**

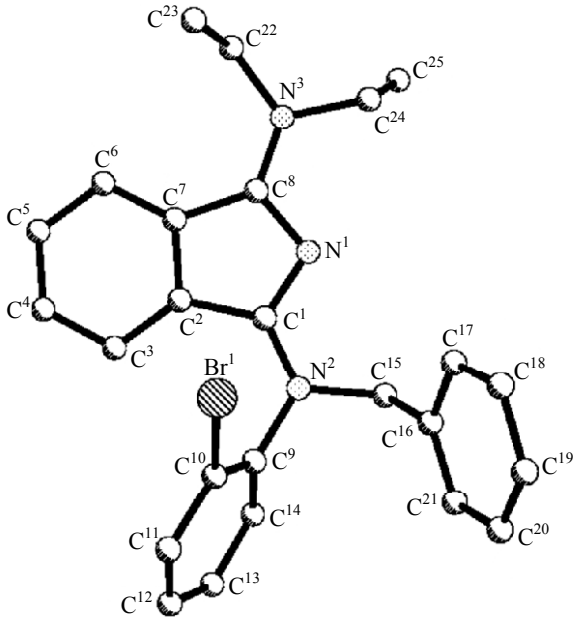
Comp. no.	Ar	R^1	R^3	Solvent	Temperature, K	Chemical shifts δ±0.02 ppm						
						NCH_3,[a] CH_2	NCH_3,[b] CCH_3	NCH_3, CH_2	4-H[a]	5-H	6-H	7-H[a]
IVa	2-ClC_6H_4	Me	Me	$CDCl_3$	303	3.97	3.86	3.86	5.90	7.28	7.62	8.09
				CD_2Cl_2	303	3.91	3.87	3.84	5.97	7.34	7.63	8.04
				DMSO-d_6	308	3.88	3.82	3.78	5.88	7.50	7.66	8.28
					453	3.89	3.87	3.80[b]				8.20
IVb	2-BrC_6H_4	Et	$PhCH_2$	$CDCl_3$	303	4.29, 4.33[c]	1.59, 1.64[c]	4.84, 6.02[d]	5.84	7.28	7.71	8.08
				DMSO-d_6	308	4.24[e]	1.49[e]	5.08, 5.88[d]	5.93	7.43	7.69	8.13
					373	4.22 4.24	1.49 1.51	5.13 5.85	5.93	7.46	7.73	8.16

[a] Doublet, *J* = 7.7 Hz.
[b] Broadened signal.
[c] *J* = 7 Hz.
[d] *AB* System, *J* = 14 Hz.
[e] Broadened signal at 308 K in DMSO-d_6.

IId was kept for 15 min at that temperature, the ^{1}H NMR spectrum contained signals from only the *E*,*E* isomer and was almost identical to the spectrum of salt **IIIg** with analogous structure but having benzyl groups on the nitrogen atoms, which originally had *E*,*E* structure. The spectrum of **IId** did not change after cooling to 303 K and subsequent keeping for 3 days at room temperature. When a solution of *N*-benzyl derivative **IIIg** in $CDCl_3$–$(CD_3)_2CO$ (1:1) was cooled to 198 K, its ^{1}H NMR spectrum contained signals belonging to only the *E*,*E* isomer.

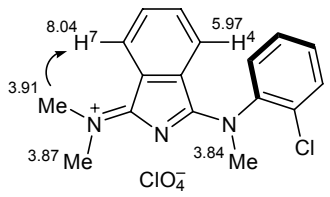
The above findings led us to conclude that the *E*,*E* isomer is thermodynamically more stable and that the transformation *Z*,*Z*→*Z*,*E*→*E*,*E* is irreversible. This transformation may follow rotational mechanism involving rotation of all nitrogen-containing groups about the single C–N bonds.

The reactions of 1,1,3-trichloro-1*H*-isoindole (**I**) with secondary amines whose basicity is reduced due to the presence of electron-withdrawing substituents (such as chlorine or bromine atoms) should be carried out using excess amine as base in acetonitrile. When triethylamine or *N*,*N*-dimethylbenzylamine was added to bind liberated hydrogen chloride, these amines underwent decomposition with formation of unsymmetrically substituted salts like **IVa** and **IVb**, as was observed previously for weakly basic primary aromatic amines [7] (Scheme 3).



Structure of the molecule of 3-[benzyl(2-bromophenyl)-amino]-1*H*-isoindol-1-ylidene(dimethyl)ammonium perchlorate (**IVb**) according to the X-ray diffraction data.

The orientation of aromatic and alkyl substituents at one of the exocyclic nitrogen atoms in perchlorates **IVa** and **IVb** was the same as in symmetric salts **IIa**–**IId** and **IIIa**–**IIIg** (*E* configuration). This followed from the upfield shift of the 4-H signal (Table 3). Magnetic nonequivalence of protons in the two methyl groups on the nitrogen atom suggests a considerable contribution of a structure in which the positive charge is localized on the dimethylamino group.



IVa

The ^{1}H NMR signals of salt **IVa** were unambiguously assigned on the basis of the results of NOE experiments, as well as of the temperature variation of the spectral pattern. Irradiation of protons in one of the three methyl groups (δ 3.91 ppm, CD_2Cl_2) gave a response on the 7-H doublet at δ 8.04 ppm. The intensity of the latter insignificantly increased upon irradiation of protons resonating at δ 3.87 ppm. Therefore, the third signal (δ 3.84 ppm) was assigned to the methyl protons in the methyl(2-chlorophenyl)amino group.

Raising the temperature of a solution of salt **IVa** in DMSO-d_6 to 433 K resulted in broadening of the singlet at δ 3.78 ppm, whereas the two other signals (δ 3.82 and 3.88 ppm) were displaced toward each other, their width remaining unchanged. The difference in their chemical shifts was 0.02 ppm at 453 K. Simultaneously, the doublet at δ 5.88 ppm (4-H) gradually broadened and then disappeared at 453 K, obviously due to faster rotation of the methyl(2-chlorophenyl)amino group and averaging of anisotropic effect of the *N*-phenyl ring.

Like symmetric salts **IIa**–**IIc** and **IIIb**–**IIIf**, perchlorates **IVa** and **IVb** exist as mixtures of atropisomers. The ^{1}H NMR spectrum of *o*-bromophenyl derivative **IVb** contained signals from diastereotopic protons in the *N*-benzyl group (*AB* system, δ 5.08, 5.88 ppm) due to the presence of two enantiomers. The difference in the chemical shifts of the methylene protons increases to 1.18 ppm in $CDCl_3$ (Table 3). The signals from the two nonequivalent *N*-ethyl groups are broadened at 308 K, and they become narrower on heating to 373 K, the difference between the chemical shifts (Δδ = 0.02 ppm) remaining unchanged. The

same applies to the *AB* pattern formed by diastereotopic methylene protons in the benzyl group ($\Delta\delta$ = 0.72 ppm).

Our conclusions were confirmed by the X-ray diffraction data for salt **IVb** with perchlorate as counterion (see figure). Delocalization of the positive charge over the NCNCN fragment leads to shortening of the N^2–C^1 [1.329(7) Å] and N^3–C^8 bonds [1.315(7) Å] (average length 1.36 Å [8]) and extension of the C^1–N^1 [1.339(7) Å] and C^8–N^1 bonds [1.368(8) Å] (average length 1.28 Å). The N^2 and N^3 atoms have planar–trigonal bond configuration. A small turn about the C^1–N^2 bond is observed [the torsion angles $C^2C^1N^2C^9$ and $N^1C^1N^2C^{15}$ are 17.9(9) and –10.6(8)°, respectively], and the methylene carbon atoms in the ethyl groups lie in the isoindole ring plane [the torsion angles $C^{22}N^3C^8C^7$ and $C^{24}N^3C^8N^1$ are 3(1)° and –1.1(9)°, respectively]. The ethyl groups are oriented in opposite directions almost orthogonally to the isoindole ring plane [the torsion angles $C^8N^3C^{22}C^{23}$ and $C^8N^3C^{24}C^{25}$ are 78.9(9)° and 104.6(8)°, respectively]. Substituents on N^2 are arranged in such a way that the bromophenyl ring is oriented *cis* with respect to the benzene fragment of isoindole, despite obviously stronger steric strain inducing rotation of the C^9–C^{14} ring plane relative to the plane of the bicyclic fragment [the torsion angle $C^1N^2C^9C^{10}$ is –60.9(8)°]. The C^{16}–C^{21} benzene ring is almost orthogonal to the isoindole ring plane [the torsion angle $N^2C^{15}C^{16}C^{17}$ is –82.8(6)°]. Probably, such orientation of substituents is stabilized by weak intramolecular C–H$\cdots\pi$ hydrogen bond: C^3–$H^3\cdots$X ($H^3\cdots$X 2.81 Å, C^3–$H^3\cdots$X 143°, where X is the centroid of the C^9–C^{14} ring.

Molecules **IVb** in crystal are linked to dimers via intermolecular stacking interactions between the isoindole fragments of a reference molecule and that related to it through the symmetry operation (–*x*, 1 – *y*, 2 – *z*) (the distance between the ring centroids is 3.64 Å, and their planes are strictly parallel). Also, a shortened intermolecular contact was found in crystal: $Br^1\cdots Br^1$ 3.55 Å (–*x*, 2 – *y*, 2 – *z*) (the sum of the van der Waals radii is 3.94 Å [9]).

The revealed stereochemical specificity of quaternary salts of the isoindole series are likely determined by the presence in their molecules of a fragment which can be regarded as aza vinylog of biphenyl (or quaternized Schiff base). This fragment firmly holds *Z,Z* configuration of the phenyl rings about the $C{=}N^+$ bond, which leads to atropisomerism. Salts **IVa** and **IVb** possess only one such fragment, so that they could exist as two enantiomers, while the presence of two fragments in symmetric salts **IIa**–**IIc** and **IIIb**–**IIIf** is responsible for the appearance of achiral *meso* structure in addition to two enantiomers [5].

EXPERIMENTAL

The ^{1}H NMR spectra were recorded on a Bruker WP-100SY spectrometer (100.13 MHz) and a Varian Mercury 400 instrument (400 MHz) using tetramethylsilane as internal reference. Thin-layer chromatography was performed using Silufol UV-254 plates. The melting points were determined on a Boetius melting point apparatus. Chloroform and acetonitrile were distilled over P_2O_5 just before use. 1,1,3-Trichloro-1*H*-isoindole (**I**) was synthesized by reaction of phthalimide with phosphorus(V) chloride according to the procedure described in [10].

X-Ray diffraction data for compound IVb. Triclinic crystals, $C_{25}H_{25}BrN_3\cdot ClO_4$, with the following unit cell parameters (at 20°C): a = 10.531(3), b = 10.858(4), c = 12.384(4) Å; α = 94.99(3), β = 110.49(3), γ = 107.68(3)°; V = 1244(1) Å^3; M_r = 546.84; Z = 2; space group $\bar{I}$; d_{calc} = 1.460 g/cm^3; $\mu(MoK_\alpha)$ = 1.796 mm^{-1}; $F(000)$ = 560. The unit cell parameters and intensities of 4547 reflections (4021 independent reflections with R_{int} = 0.100) were measured on a Siemens P3/PC automatic four-circle diffractometer (MoK_α irradiation, graphite monochromator, 2θ/θ scanning, $2\theta_{max}$ = 50°). A correction for absorption was introduced semiempirically on the basis of the ψ-scanning data. The structure was solved by the direct method using SHELX97 software package [11]. The positions of hydrogen atoms were determined by difference syntheses of electron density and were refined according to the riding model with $U_{iso} = nU_{eq}$ (where n = 1.5 for methyl hydrogen atoms, and n = 1.2 for the other hydrogen atoms). The structure was refined with the Cl–O bond length in the disordered perchlorate ion constrained to 1.414(3) Å. Full-matrix least-squares refinement (by F^2) in anisotropic approximation for non-hydrogen atoms was terminated at wR_2 = 0.143 for 4021 reflections [R_1 = 0.056 for 1937 reflections with $F > 4\sigma(F)$, S = 0.880]. The complete set of crystallographic data for compound **IVb** was deposited to the Cambridge Crystallographic Data Centre (entry no. CCDC 751355).

Alkyl{3-[alkyl(aryl)amino]-1*H*-isoindol-1-ylidene}(aryl)ammonium perchlorates IIa, IIb, IId and IIIa–IIId (*general procedure*). A mixture of

20 mmol of the corresponding *N*-alkylaniline and 20 mmol of triethylamine in 20 ml of hexane was added dropwise under stirring to a boiling solution of 2.20 g (10 mmol) of 1,1,3-trichloro-1*H*-isoindole (**I**) in 50 ml of hexane. The mixture was heated for 1 h under reflux, and the yellow precipitate was filtered off, dried, and dissolved in 100 ml of water. The aqueous solution was filtered, and the product was precipitated from the filtrate by adding $NaClO_4$ and recrystallized from ethanol.

Methyl{3-[methyl(2-methylphenyl)amino]-1*H*-isoindol-1-ylidene}(2-methylphenyl)ammonium perchlorate (IIa). Yield 90%, yellow crystals, mp 259–260°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 2.30 s and 2.32 s (6H, CH_3), 4.00 s (6H, CH_3), 5.79 d.d (2H, 4-H, 7-H, J = 8 Hz), 7.12 d.d and 7.13 d.d (2H, 5-H, 6-H, J = 8 Hz), 7.49 m (8H, H_{arom}). Found, %: Cl 7.79; N 9.53. $C_{24}H_{24}ClN_3O_4$. Calculated, %: Cl 7.83; N 9.26.

2-Methoxyphenyl{3-[(2-methoxyphenyl)methylamino]-1*H*-isoindol-1-ylidene}methylammonium perchlorate (IIb). Yield 70%, yellow crystals, mp 309–310°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.87 s and 3.89 s (6H, OCH_3), 3.96 s (6H, NCH_3), 5.97 d.d and 5.99 d.d (2H, 4-H, 7-H, J = 8 Hz), 7.13 d.d (2H, 5-H, 6-H, J = 8 Hz), 7.73–7.08 m (8H, H_{arom}). Found, %: Cl 7.71; N 9.06. $C_{24}H_{24}ClN_3O_6$. Calculated, %: Cl 7.31; N 8.65.

(*Z*,*Z*/*E*,*E*)-Methyl{3-[methyl(2,4,6-trimethylphenyl)amino]-1*H*-isoindol-1-ylidene}(2,4,6-trimethylphenyl)ammonium perchlorate (IId) was synthesized in a similar way using chloroform as solvent. When the reaction was complete, the mixture was evaporated, the oily residue was treated with 100 ml of water, the aqueous solution was filtered, and the product was precipitated from the filtrate as perchlorate by adding $NaClO_4$. Yield 82%, yellow crystals, mp 281–282°C. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 1.97 s (6H, *Z*,*Z*, *o*-CH_3), 2.15 s (9H, *Z*,*Z*, *p*-CH_3 and *E*,*E*, *o*-CH_3), 2.37 s (3H, *E*,*E*, *p*-CH_3), 3.86 s (3H, *E*,*E*, NCH_3), 3.92 s (3H, *Z*,*Z*, NCH_3), 5.85 d.d (1H, *E*,*E*, 4-H, 7-H, J = 8 Hz), 6.75 s (2H, *Z*,*Z*, *m*-H), 7.15 s (2H, *E*,*E*, *m*-H), 7.28 d.d (1H, *E*,*E*, 5-H, 6-H, J = 8 Hz), 7.88 d.d (1H, *Z*,*Z*, 5-H, 6-H, J = 8 Hz), 8.33 d.d (1H, *Z*,*Z*, 4-H, 7-H, J = 8 Hz). Found, %: Cl 6.94; N 8.11. $C_{28}H_{32}ClN_3O_4$. Calculated, %: Cl 6.96; N 8.24.

Benzyl{3-[benzyl(phenyl)amino]-1*H*-isoindol-1-ylidene}phenylammonium perchlorate (IIIa). Yield 90%, yellow crystals, mp 233–234°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 5.73 s (4H, NCH_2), 5.84 d.d (2H, 4-H, 7-H, J = 8 Hz), 7.11 d.d (2H, 5-H, 6-H, J = 8 Hz), 7.23–7.64 m (20H, H_{arom}). Found, %: Cl 6.25; N 7.13. $C_{34}H_{28}ClN_3O_4$. Calculated, %: Cl 6.13; N 7.27.

Benzyl{3-[benzyl(2-methylphenyl)amino]-1*H*-isoindol-1-ylidene}(2-methylphenyl)ammonium perchlorate (IIIb). Yield 82%, yellow crystals, mp 272–273°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.91s and 2.13 s (6H, NCH_3), 5.63 m and 5.72 m (2H, NCH_2), 5.53 m and 6.00 m (2H, NCH_2), 5.77 d.d and 5.79 d.d (2H, 4-H, 7-H, J = 8 Hz), 7.12 d.d (2H, 5-H, 6-H, J = 8 Hz), 7.38 m (10H, C_6H_5), 7.04–7.60 m (8H, H_{arom}). Found, %: Cl 5.80; N 6.76. $C_{36}H_{32}ClN_3O_4$. Calculated, %: Cl 5.85; N 6.93.

Benzyl{3-[benzyl(2-methoxyphenyl)amino]-1*H*-isoindol-1-ylidene}(2-methoxyphenyl)ammonium perchlorate (IIIc). Yield 80%, yellow crystals, mp 190–191°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.68 s and 3.80 s (6H, OCH_3), 5.34 m and 5.78 m (2H, NCH_2), 5.09 m and 6.03 m (2H, NCH_2), 5.97 d.d (2H, 4-H, 7-H, J = 8 Hz), 6.95–7.69 m (20H, 5-H, 6-H, H_{arom}). Found, %: Cl 5.68; N 6.60. $C_{36}H_{32}ClN_3O_6$. Calculated, %: Cl 5.56; N 6.58.

Benzyl{3-[benzyl(3-methylphenyl)amino]-1*H*-isoindol-1-ylidene}(3-methylphenyl)ammonium perchlorate (IIId). Yield 78%, yellow crystals, mp 226–227°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 2.38 s (6H, CH_3), 5.59 m and 5.72 m (2H, NCH_2), 5.52 m and 5.79 m (2H, NCH_2), 5.86 d.d (2H, 4-H, 7-H, J = 8 Hz), 7.10 d.d (2H, 5-H, 6-H, J = 8 Hz), 7.35 m (10H, C_6H_5), 7.42 d (2H, *o*-H), 6.93–7.18 m (8H, H_{arom}). Found, %: Cl 5.33; N 7.18. $C_{36}H_{32}ClN_3O_4$. Calculated, %: Cl 5.85; N 6.93.

Condensation of 1,1,3-trichloro-1*H*-isoindole (I) with weakly basic *N*-alkylanilines (*general procedure*). A solution of 40 mmol of the corresponding *N*-alkylaniline in 10 ml of acetonitrile was added dropwise under stirring to a solution of 2.20 g (10 mmol) of 1,1,3-trichloro-1*H*-isoindole (**I**) in 30 ml of acetonitrile. The mixture was heated for 1 h under reflux and cooled, a saturated solution of $NaClO_4$ was added, and the yellow precipitate or oily substance was separated, dried, and recrystallized from ethanol.

2-Chlorophenyl{3-[2-chlorophenyl(methyl)amino]-1*H*-isoindol-1-ylidene}methylammonium perchlorate (IIc). Yield 85%, yellow crystals, mp 207–208°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 4.04 s and 4.06 s (52:48, 6H, NCH_3), 5.89 d.d and 5.92 d.d (2H, 4-H, 7-H, J = 8 Hz), 7.17 d.d and 7.25 d.d (2H, 5-H, 6-H, J = 8 Hz), 7.50–7.90 m (8H, H_{arom}). Found, %: Cl 21.65; N 8.18. $C_{22}H_{18}Cl_3N_3O_4$. Calculated, %: Cl 21.54; N 8.49.

Benzyl{3-[benzyl(2-chlorophenyl)amino]-1*H*-isoindol-1-ylidene}(2-chlorophenyl)ammonium perchlorate (IIIe). Yield 75%, yellow crystals, mp 251–252°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 5.37 m and 6.02 m (2H, NCH_2), 5.30 m and 6.10 m (2H, NCH_2), 5.86 d.d and 5.90 d.d (2H, 4-H, 7-H, J = 8 Hz), 7.16 d.d and 7.27 d.d (2H, 5-H, 6-H, J = 8 Hz), 7.20–7.70 m (20H, C_6H_5, H_{arom}). Found, %: Cl 16.25; N 6.38. $C_{34}H_{26}Cl_3N_3O_4$. Calculated, %: Cl 16.44; N 6.49.

Benzyl{3-[benzyl(2-bromophenyl)amino]-1*H*-isoindol-1-ylidene}(2-bromophenyl)ammonium perchlorate (IIIf). Yield 90%, yellow crystals, mp 247–248°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 5.28 m and 6.08 m (2H, NCH_2), 5.18 m and 6.18 m (2H, NCH_2), 5.83 d.d (2H, 4-H, 7-H, J = 8 Hz), 7.38 (10H, C_6H_5), 7.15–7.85 m (10H, 5-H, 6-H, H_{arom}). Found, %: N 5.65. $C_{34}H_{26}Br_2ClN_3O_4$. Calculated, %: N 5.71.

Benzyl{3-[benzyl(2,4,6-trimethylphenyl)amino]-1*H*-isoindol-1-ylidene}(2,4,6-trimethylphenyl)ammonium perchlorate (IIIg). Yield 75%, yellow crystals, mp 292–293°C. ^{1}H NMR spectrum ($CDCl_3$–DMSO-d_6, 1:1), δ, ppm: 1.84 s (12H, *o*-CH_3), 2.40 s (6H, *p*-CH_3), 5.59 s (4H, CH_2), 5.87 d.d (2H, 4-H, 7-H, J = 8 Hz), 7.03 s (4H, *m*-H), 7.22 d.d (2H, 5-H, 6-H, J = 8 Hz), 7.39 s (10H, C_6H_5). Found, %: Cl 5.30; N 6.21. $C_{40}H_{40}ClN_3O_4$. Calculated, %: Cl 5.37; N 6.35.

2-Chlorophenyl{3-[2-chlorophenyl(methyl)-amino]-1*H*-isoindol-1-ylidene}methylammonium perchlorate (IVa). A mixture of 1.42 g (10 mmol) of *N*-methyl-2-chloroaniline and 7.89 g (40 mmol) of *N*,*N*-dimethylbenzylamine was added dropwise under stirring to a solution of 2.20 g (10 mmol) of 1,1,3-trichloro-1*H*-isoindole (**I**) in 50 ml of acetonitrile, and the mixture was heated for 1 h under reflux. The mixture gradually turned red and was left overnight. The solvent was distilled off under reduced pressure, and the dry residue was dissolved in 100 ml of water. The solution was treated with activated charcoal on heating to the boiling point and filtered, and compound **IVa** was precipitated from the filtrate by adding $NaClO_4$ and recrystallized from water. Yield 60%, yellow crystals, mp 138–139°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.86 s (6H, NCH_3), 3.97 s (3H, NCH_3), 5.90 d (1H, 4-H, J = 7.7 Hz), 7.28 d.d (1H, 5-H), 7.62 d.d (1H, 6-H), 8.09 d (1H, 7-H, J = 7.7 Hz), 7.55–7.78 m (4H, H_{arom}). Found, %: Cl 17.70; N 10.70. $C_{17}H_{17}Cl_2N_3O_4$. Calculated, %: Cl 17.80; N 10.55.

3-[Benzyl(2-bromophenyl)amino]-1*H*-isoindol-1-ylidene(dimethyl)ammonium perchlorate (IVb) was synthesized in a similar way in the presence of 40 mmol of triethylamine. The crude product was recrystallized from ethanol. Yield 68%, yellow crystals, mp 201–202°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.59 t and 1.64 t (6H, CH_3, J = 7 Hz), 4.29 q and 4.33 q (4H, NCH_2, J = 7 Hz), 4.84 m and 6.02 m (2H, N**C**$\mathbf{H}_2$Ph, J = 14 Hz), 5.84 d (1H, 4-H, J = 7.7 Hz), 7.28 d.d (1H, 5-H), 7.71 d.d (1H, 6-H), 8.08 d (1H, 7-H, J = 7.7 Hz), 7.10–7.75 m (14H, H_{arom}). Found, %: N 7.45. $C_{25}H_{25}BrClN_3O_4$. Calculated, %: N 7.68.

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