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NMR STUDY OF MOLECULAR COMPLEXES OF 1 2- AND 3-SUBSTITUTED INDOLE DONORS WITH POLYNITROAROMATIC ACCEPTORS†

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Abstract—The stability of electron donor-acceptor complexes formed, in $CDCl_3$ solutions, between differently-substituted indoles (1-, 2- and 3-Me, Et, i.Pr, t.Bu, OMe, SMe, COOEt) and 1,3,5-trinitrobenzene, 1,3-dinitrobenzene and their derivatives was investigated by NMR of the acceptor's protons. From magnetically non-equivalent protons of the acceptor, different association constants K for one complex formation could be measured in many cases, but only aromatic protons led to reliable K values.

Many papers have dealt with the formation, in solutions, of molecular complexes between indole donors and organic π-acceptors,[1-4] particularly polynitroaromatic compounds.[5,6] We have previously studied charge-transfer (CT) complex formation between a large series of indole derivatives and chloranil as electron acceptor, and evaluated their association constants solely by electronic spectroscopy from CT bands in the visible range.[7] When the acceptor molecule possesses hydrogen atoms, complex formation with a donor can easily be investigated using the NMR method.[8] We have used this method in the present work to determine, in $CDCl_3$ solution, the stabilities of electron donor-acceptor complexes formed between 1-, 2- and 3-substituted indoles[7] (A) and several polynitroaromatic acceptor compounds, i.e. 1,3,5-trinitrobenzene (TNB), 2,4,6-trinitroanisol (TNA) and 2,4,6-trinitrotoluene (TNT). We have also investigated complex formation with 2-methylindole as electron donor and 1,3-dinitrobenzene or its 5-substituted derivatives (5-OMe, 5-CN, 5-COOMe) (B) as electron π-acceptors. As all the acceptor molecules, except TNB, bear magnetically non-equivalent protons, the NMR method could be used for distinct measurements of the association constants.

Association constants K were determined for 1:1 complex formation according to the equilibrium: $D + A \overset{K}{\rightleftharpoons} DA$. Thus, for a series of solutions containing the acceptor A at a fixed concentration $(A)_0$ and the donor D at various concentrations $(D)_0$ (with $(D)_0 \gg (A)_0$), we measured the chemical shifts δ of one species of acceptor's protons. Then we could determine K and Δ_0 of the relation 1, by plotting the observed values of $\Delta/(D)_0$ against Δ[9].

$$\frac{\Delta}{(D)_0} = -K.\Delta + K.\Delta_0 \qquad (1)$$

where $\Delta = \delta_A - \delta$, and $\Delta_0 = \delta_A - \delta_{DA}$. δ_A and δ_{DA} are the chemical shifts of the acceptor's proton, in free acceptor and complex respectively.

†Preliminary results of this study were presented in a note (Ref. 6).

RESULTS AND DISCUSSION

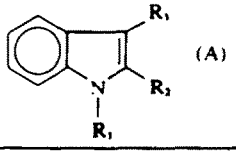
Indole-TNB complexes

Foster and Fyfe[5] made the first determinations, by NMR spectroscopy, of association constants for complex formation between indole or its derivatives and TNB. It was interesting to extend this study to a larger series of indole derivatives (A), i.e. substituted in -1, -2 and -3 position by alkyl, OMe, SMe and COOEt groups, in order to investigate the electronic and steric factors affecting stability of the complexes.

As shown in Table 1, K_{TNB} values for equilibria involving the indole-TNB complexes are very dependent on the indole's substituent and the position of the latter on the indole nucleus. Particularly, the large effect observed upon varying the position of a substituent in -1, -2 or -3 of the heterocycle seems to be consistent with the localization of the acceptor molecule next to the C(2)–C(3) bond of the donor.[1,3] However, as anticipated from donor-acceptor interaction energies, an electrodonor substituent always increases the stability of the complex and an electroattractor lowers it. This clearly appears from the K_{TNB} values obtained for methylindole and ethoxycarbonylindole complexes respectively, as compared to the indole complex. The K_{TNB} values (Table 1) for indole, 2-methylindole and 3-methylindole-TNB complexes, at 27°, compare well with those reported,[5] at 33.5° in $CDCl_3$ solutions. Moreover, when the size of the electrodonor substituent increases from Me to *t*-Bu, the stability of complexes generally decreases, although this steric effect can be minimized by larger electrodonor ability, as observed for i-Pr substituent. Big substituents on the indole donor, keeping the TNB acceptor molecule at a distance, can obviously lower the stability of the complexes. Specific interactions between the donor's substituent and the acceptor can also contribute to the stability of the complex: e.g. OMe and SMe groups can interact with electron acceptors by their lone electron pairs.[10-12] On the whole, as K_{TNB} values of Table 1 are not easily related to the structure of the indole donor, we shall only compare indole derivatives substituted at the same position.

(i) Substitution of indole at the 1-position gives the K_{TNB} values order: COOEt < Et < H < Me. Actually, the stabilities of indole and 1-alkylated indole-TNB complexes are very similar, and the substitution effect is

Table 1. Association constants K_{TNB} (mole $^{-1}$l) and $\Delta_{\sigma TNB}$ (Hz) (relation 1) for the complexes of indoles (A) with TNB, in $CDCl_3$ at 27°



R_1, R_2 or R_3 of (A)	$R_2 = R_3 = H$ R_1		$R_1 = R_3 = H$ R_2		$R_1 = R_2 = H$ R_3	
	K_{TNB}	$\Delta_{\sigma TNB}$	K_{TNB}	$\Delta_{\sigma TNB}$	K_{TNB}	$\Delta_{\sigma TNB}$
H	**1**: 1.40	98				
CH_3	**2**: 1.45	101	**5**: 1.75	120	**11**: 1.90	130
C_2H_5	**3**: 1.36	97	**6**: 1.25	95	**12**: 1.46	102
$CH(CH_3)_2$			**7**: 1.67	90	**13**: 1.12	113
$C(CH_3)_3$			**8**: 1.14	89	**14**: 0.71	97
$COOC_2H_5$	**4**: 0.85	94	**9**: 0.58	72		
OCH_3					**15**: 1.20	82
SCH_3			**10**: 1.01	85	**16**: 0.94	67

significant for the highly electroattractor COOEt group only.

(ii) Substitution at the 2-position of indole leads to the K_{TNB} values order: COOEt < SMe < t-Bu < Et < H < i-Pr < Me. The weaker stability of the ethyl 2-indolecarboxylate-TNB complex is consistent with the low electron density at the C(2)–C(3) bond of the indole conjugated with 2-COOEt group. The 2-SMe group on the indole donor also hinders complex formation, mainly by steric effect. The order of stabilities of the indole and 2-alkylated indole-TNB complexes shows the combined effect arising from both electrodonor capacity and steric interaction of alkyl substituents; the former seems to be prevailing with Me and i-Pr groups, and the latter with t-Bu and Et groups. However, the stability of the 2-ethyl indole-TNB complex is surprisingly low, so that the order of our K_{TNB} values differs for instance from that reported for alkylbenzene-TNB complexes:[13] t-Bu < H < i-Pr < Me ≃ Et.

(iii) Substitution of the indole at position -3 gives the following K_{TNB} values order: t-Bu < SMe < i-Pr < OMe < H < Et < Me. This shows especially predominant steric effect of the 3-alkyl substituent within the 3-alkylated indoles' series.

The variable influence of an indole substituent, according to its nuclear position, upon the stability of indole-acceptor complexes was known before.[5,7] Thus, constants of association of 5-methoxyindole and its 1- or 2-alkylated (Me, Et) derivatives with TNB have been reported by Sung and Parker.[14] The K_{TNB}^{5OMe} values of these authors are linearly connected to our K_{TNB} values for indole and 1- or 2-methyl(ethyl)indole-TNB complexes (Fig. 1). This good correlation leads us to suppose that the 5-OMe indole substituent does not act sterically or specifically with TNB (this is consistent with an acceptor's localization near the C(2)–C(3) bond of indole), but increases the stability of all indole-TNB complexes by the same +M electronic effect transmitted through the benzene nucleus of the donor. Moreover, Green and Malrieu[15] computed, in different ways, the indoles' ability to form donor-acceptor molecular complexes, and could connect this property with electronic superdelocalizability at C-3 from an inductive model of the indole. The order of stabilities of the methyl-indoles CT complexes found by calculation[15] (H < 1-Me < 3-Me < 2-Me) does not agree fully with our K_{TNB} values

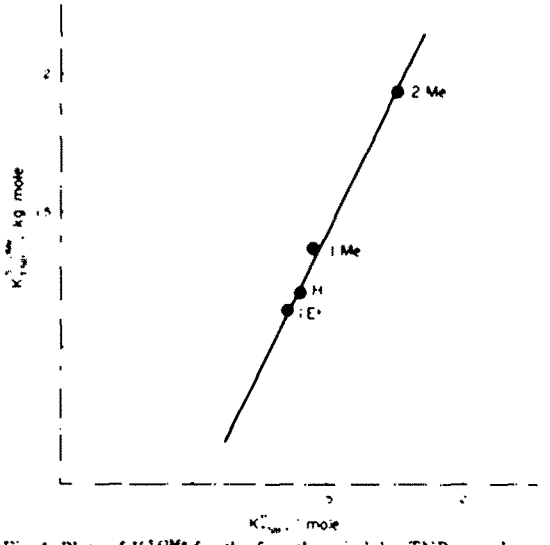


Fig. 1. Plots of K_{TNB}^{5OMe} for the 5-methoxyindoles-TNB complexes vs K_{TNB}^{H} for the corresponding indoles-TNB complexes, in $CDCl_3$ at 27°.

(H < 1-Me < 2-Me < 3-Me) nor with those reported by Foster and Fyfe.[5]

Study of the indole-TNB complexes by spectroscopy in the visible range would have been very useful to confirm their association constants. The two methods, NMR and electronic spectroscopy, sometimes have led to distinct constants' values.[16] Unfortunately, CT bands for our indole-TNB complexes in $CHCl_3$ are largely masked by absorption bands of the acceptor. However, from the CT band of 2-methylindole-TNB complex (λ_{max} = 390 nm, ϵ = 820) we calculated: K = 1.80 ± 0.1 mol $^{-1}$l, as compared to: K = 1.75 mol $^{-1}$l, using the NMR method.

Indole-TNA complexes

Magnetically non-equivalent protons of the TNA acceptor allow distinct determinations of association constants for the indole-TNA complexes. The two types of values, determined from aromatic protons (K_{TNA}^{Ar}) or from protons of the OMe group (K_{TNA}^{Me}), are reported on Table 2; they generally differ. Multiplicity of association

Table 2. Association constants K_{TNA} (mole $^{-1}$ l) and Δ_{OTNA} (Hz) (relation 1) for the complexes of indoles (A) with TNA, in $CDCl_3$ at 27°, evaluated from aromatic (Ar) and OCH_3 (Me) protons of TNA

Substituant	$R_2 = R_3 = H$, R_1				$R_1 = R_3 = H$, R_2				$R_1 = R_2 = H$, R_3			
	K^{Ar}_{TNA}	Δ^{Ar}_{OTNA}	K^{Me}_{TNA}	Δ^{Me}_{OTNA}	K^{Ar}_{TNA}	Δ^{Ar}_{OTNA}	K^{Me}_{TNA}	Δ^{Me}_{OTNA}	K^{Ar}_{TNA}	Δ^{Ar}_{OTNA}	K^{Me}_{TNA}	Δ^{Me}_{OTNA}
H	0.60	100	0.68	69								
CH_3	0.63	116	0.22	73	0.73	82	0.36	46	0.75	100	0.40	67
C_2H_5	0.46	110	0.20	72	0.53	90	0.20	54	0.46	118	0.20	87
$CH(CH_3)_2$					0.67	111	0.30	96	0.48	100	0.20	73
$C(CH_3)_3$					0.51	90	0.30	66	0.28	127	0.24	80
$COOC_2H_5$	0.35	98	0.18	56	0.30	125	0.17	91				
OCH_3									0.53	112	0.28	85
SCH_3					0.40	96	0.40	57	0.48	81	0.26	60

constants' values, arising from magnetically different protons of the acceptor, was reported before,[17-20] and received several explanations. Klinck and Stothers,[21] Orgel and Mulliken,[22] supposed that several isomeric 1:1 complexes may be formed at once. Dodson and Foster,[19] on the other hand, accounted for the multiplicity of association constants by suggesting the formation of some 2:1 complex together with the 1:1 complex. Foster *et al.*,[23] more recently, confirmed this, and questioned many previous determinations of complexes' association constants.

If we consider (when (D) ≫ (A)) the two equilibria leading to 1:1 (DA) and 2:1 (D_2A) complexes: $D + A \overset{K_1}{\rightleftharpoons} DA$, and $2D + A \overset{K_2}{\rightleftharpoons} D_2A$, the NMR method leads to only one apparent constant K value, different both from K_1 and K_2; it is generally dependent on the concentration ranges. For this reason, Foster and Fyfe[5] have proposed to invert the donor and acceptor parts in the NMR method, i.e. to measure the chemical shifts of a proton of the donor at one low concentration, for different high concentrations of the acceptor. However, with indole donors, difficulties could arise from the complexity of their NMR spectra. Therefore we measured the stability of the 2-methylindole-TNA complex, in $CDCl_3$ solutions: the chemical shifts of the 3-H of indole nucleus led to the association constant: $K^{D}_{TNA} = 0.65 \pm 0.05$ mol $^{-1}$ l ($r = 0.988$). This value is reasonably near to that previously determined: $K^{Ar}_{TNA} = 0.73$ mol $^{-1}$ l from the aromatic protons of TNA, but is clearly different from that determined from the protons of OMe group of this acceptor: $K^{Me}_{TNA} = 0.36$ mol $^{-1}$ l. We can infer thereform that, at least in that case, only a 1:1 complex is formed, at all concentrations of donor and acceptor. We also observe that only measurements of the shifts of the aromatic protons of the acceptor give reliable values for the association constant. Craenen, Verhoeven and de Boer[18] already commented within, after evaluating, both by NMR and electronic spectroscopy, the stabilities of some complexes formed with methyl 2,4,6-trinitrobenzoate as acceptor. Using the NMR method, association constants determined from the aromatic protons of the acceptor only proved to be in agreement with values obtained by electronic spectroscopy, whereas those evaluated from protons of the COOMe group were not. These authors concluded that the reference protons ought to be close to the centre of the molecular complex. Similarly, for the indole-TNA complexes, comparison between Δ^{Ar}_{OTNA} and Δ^{Me}_{OTNA} shows (Table 2) that the aromatic protons of the acceptor are closer to the centre of the complex than the protons of the OMe group, and we can expect that the K^{Ar}_{TNA} values of Table 2 are the most significant ones. This was ascertained by plotting K^{Ar}_{TNA} and K^{Me}_{TNA} values against K_{TNB} values: only the former were connected linearly with K_{TNB} (Fig. 2), according to relation 2. The lesser stability of the indole-TNA complexes as compared with the indole-TNB complexes may be explained by the smaller charge of the benzene nucleus for TNA.[24]

$$K^{Ar}_{TNA} = 0.40 \cdot K_{TNB} \qquad (2)$$

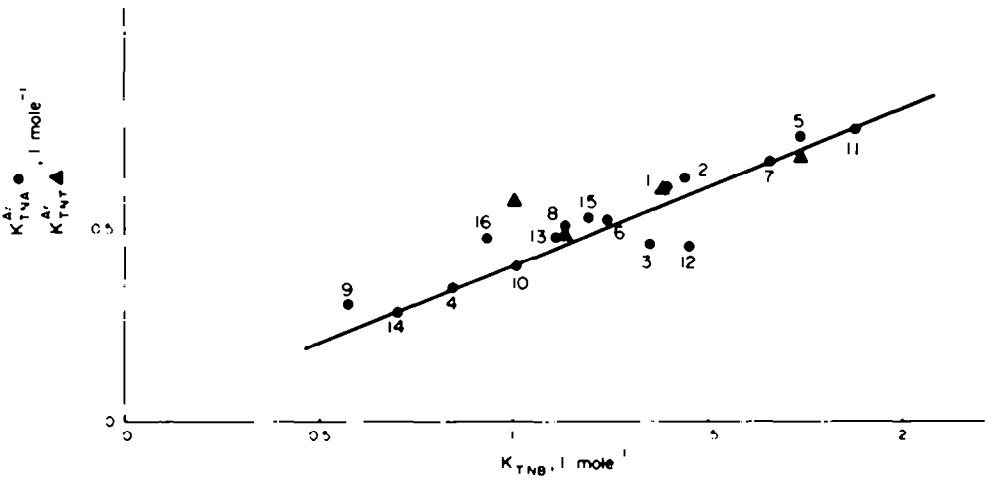


Fig. 2. Plots of K^{Ar}_{TNA} and K^{Ar}_{TNT} for the complexes of indoles (A) with TNA or TNT, respectively, vs K_{TNB} for the corresponding indoles-TNB complexes, in $CDCl_3$ at 27°.

Indole-TNT complexes

The association constants of some indole-TNT complexes were determined both from aromatic protons and protons of the Me group of the acceptor (Table 3). The values K_{TNT}^{Ar} and K_{TNT}^{Me} show the same discrepancy as that noted previously for the indole-TNA complexes. However, plotting of K_{TNT}^{Ar} and K_{TNT}^{Me} against K_{TNB} (Fig. 2) shows that only the former may be significant. Moreover, the K_{TNT}^{Ar} values fit well with relation 2 for the indole-TNA complexes, and we can infer therefrom that TNT and TNA have the same ability to form CT complexes with indole and its derivatives. However, this result cannot be considered as general; hexamethylbenzene, for instance, gives, with TNT and TNA, complexes of quite different stabilities.[25] Perhaps, specific interactions of the Me or OMe group of the acceptor with some donors account for the discrepancy. This could be the case for 2-methylthioindole, whose complexes with TNT and TNA have slightly different stabilities.

Table 3. Association constants K_{TNT} (mole $^{-1}$ l) and $\Delta_{\sigma TNT}$ (Hz) (relation 1) for the complexes of indoles (A) with TNT, in $CDCl_3$ at 27°, evaluated from aromatic (Ar) and CH_3(Me) protons of TNT

$R_1 = R_3 = H$ R_2	K_{TNT}^{Ar}	$\Delta_{\sigma TNT}^{Ar}$	K_{TNT}^{Me}	$\Delta_{\sigma TNT}^{Me}$
H	0.60	98	0.33	62
CH_3	0.68	68	0.36	39
$C(CH_3)_3$	0.49	104	0.31	70
SCH_3	0.57	78	•	•

•Signal masked.

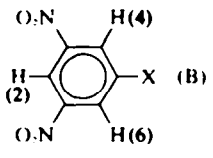
Complexes of 2-methylindole with 1,3-dinitrobenzene and its derivatives

It proved to be interesting to compare 1,3-dinitrobenzene (DNB) and its 5-X substituted derivatives (X = OMe, CN, COOMe) (B) with the trinitroaromatic acceptors. Comparison was made only with the good electron donor, 2-methylindole, and the association constants of the complexes were determined both from the magnetically non-equivalent aromatic protons H-2 and H-5 (Table 4). It appeared that these constants, K_X^{H2} and K_X^{H4}, were not dependent of the reference aromatic proton of the acceptor, contrary to our previous evaluations from aromatic and non-aromatic protons of TNA and TNB. This result is not surprising, since the H-2 and H-4 of the dinitroaromatic acceptors (B) are, very likely, equally close to the centre of the complexes.

Moreover, when changing the 5-X substituent on the DNB acceptor, stability of these complexes increases according to the order: X = H ≃ OMe < COOMe < CN < NO_2 which is the same as noted before for analogous complexes of hexamethylbenzene;[26] the association constants K_X can be connected to the Hammett's σ_m values of the 5-X substituent (Fig. 3).

The above results make it clear that the NMR method can give reliable determinations of the association constants of the 1:1 donor-acceptor complexes formed between very different indoles and several 1,3-dinitro- and 1,3,5-trinitrobenzene derivatives, provided that the aromatic protons of the acceptor are used as reference. Generally speaking, the stability of these complexes appears more related to the electron-withdrawing power of the acceptor than to the nature of the substituents in -1, -2 or -3 position of the indole donor. Moreover, the lack of correlation between the association constants of these complexes and those previously determined[7] for the analogous indole-chloranil complexes indicates that the stability of such molecular complexes cannot be simply connected with the respective electrodonor and electroacceptor abilities of the two components.

Table 4. Association constants K_x (mol $^{-1}$ l) and Δ_o (Hz) (relation 1) for the complexes of 2-methylindole with DNB and its 5-X substituted derivatives (B), in $CDCl_3$ at 27°, evaluated from H-2 and H-4 of the acceptor



X	K_X^{H2}	Δ_o^{H2}	K_X^{H4}	Δ_o^{H4}
H	0.23	104	0.24	115
OCH_3*	0.23	88	0.23	110
$COOCH_3$	0.54	89	0.54[b]	89[b]
CN	1.14	102	1.12	110

*From H of OCH_3 as reference protons, were obtained: K = 0.23 mole $^{-1}$ l, Δ_o = 100.

[b]The three aromatic protons are magnetically equivalent both in the acceptor and the complex.

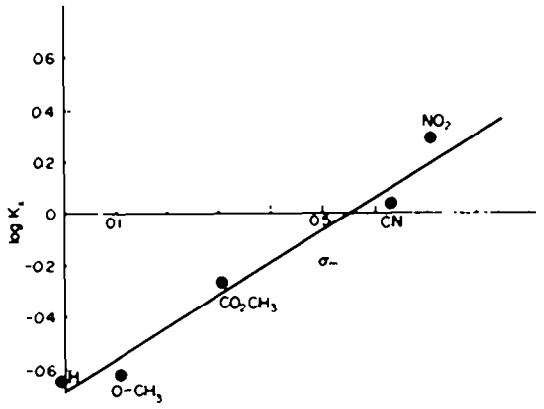


Fig. 3. Plot of $\log_{10} K_X$ for the complexes of 2-methylindole with 1,3-dinitrobenzene and its 5-X substituted derivatives (B) vs the Hammett σ_m constants for the X substituent, in $CDCl_3$ at 27°.

$$\log_{10} K_X = 0.69 + 1.24 . \sigma_m ; r = 0.988.$$

EXPERIMENTAL

Commercially not available substances were prepared according to published procedures: indoles: **2**;[27] **3**;[28] **6**;[29] **7**;[30] **8**;[30] **10**;[31] **12**;[32] **13**;[33] **14**;[34] **15**;[35] **16**.[36] 1,3-dinitro-5-methoxybenzene.[37] All the indoles were purified[7] just before use, and the nitroaromatic compounds were recrystallised twice.

Mixed solutions of the donor and the acceptor were prepared in pure (99.8%) deuteriochloroform (Uvasol Merck), immediately before NMR measurements. For the determination of each association constant, eight different concentrations of the donor (0.1–2 mol/l) and a fixed concentration of the acceptor, according to the number of equivalent aromatic protons (0.02 (3H), 0.03 (2H) and 0.04 mol/l (1H)), were used. Proton NMR spectra were recorded at 60 MHz on a Jeol C60 instrument, operating at 27 ± 1°, and using TMS as internal standard. Signal frequencies of the reference protons were determined, with a 0.2 Hz accuracy, by the frequency sweep method by means of a frequencemeter

instrument. The K and Δ_o values of relation 1 and parameters of the other relations were obtained in the usual manner by a linear least-squares analysis using a Hewlett-Packard HP25 computer; $r > 0.99$ for the relation 1 in all cases.

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