295. Crystal Structure of *cis*-(4'-Methyl-N,N,O)-azoxybenzene

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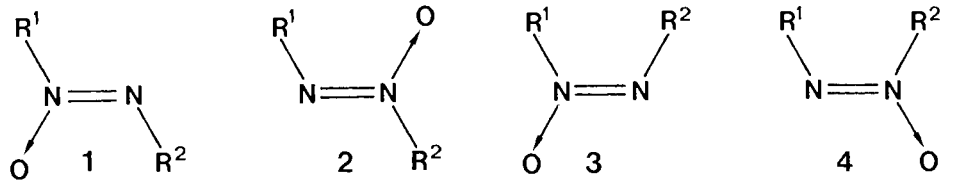
Kristallstruktur von *cis*-(4'-Methyl-N,N,O)-azoxybenzol

Zusammenfassung

Durch *Röntgen*-Strukturanalyse der Titelverbindung **3d** konnte die Stellung des Sauerstoffatoms eindeutig festgelegt werden. Dies impliziert zugleich eine sichere Strukturzuordnung für die stellungsisomere *cis*-Azoxyverbindung **4d**. Frühere Strukturzuordnungen [8] für **3d** und **4d** werden damit zwar bestätigt, doch zeigt ein Vergleich der ^{1}H-NMR.-Spektren aller vier isomeren 4-Methyl-azoxybenzole **1d** bis **4d** in Deuteriotrichlormethan, dass die früheren Zuordnungsargumente aufgrund der relativen Lage der Methylsignale in den ^{1}H-NMR.-Spektren in Benzol unzureichend waren. Auch Verwendung von Tris(1,1,1,2,2,3,3-heptafluoro-7,7-dimethyl-4,6-octandionato)europium (Eu(fod)$_3$) als Verschiebungsreagens für die ^{1}H-NMR.-Spektren von Gemischen von **3d** und **4d** erlaubt, im Unterschied zu der Situation bei Gemischen der stellungsisomeren *trans*-4-Methyl-azoxybenzole **1d** und **2d** [18], keine eindeutige Zuordnung der Signale beider *cis*-Stellungsisomeren. Dagegen lässt sich das ^{1}H-NMR.-Spektrum von reinem **3d** in Deuteriotrichlormethan nach Zusatz von Eu(fod)$_3$ im Einklang mit dem Ergebnis der *Röntgen*-Strukturanalyse interpretieren.

Die *Röntgen*-Strukturanalyse von **3d** ist die erste einer unsymmetrisch substituierten und zugleich die erste einer *cis*-konfigurierten aromatischen Azoxyverbindung. Das Resultat der Analyse ist in den *Fig. 1*, *2* und *3* dargestellt. Bindungslängen und Winkel der Azoxygruppierung und entsprechende Werte anderer aromatisch substituierter Azo- und Azoxystrukturen, für die *Röntgen*-Strukturanalysen bekannt sind, finden sich in *Tabelle 2* zu Vergleichszwecken.

1. Introduction. – Unsymmetrically substituted azoxy compounds can exist as four isomers with respect to the arrangement of substituents R^1 and R^2 on the N,N,O-function, namely as two regioisomeric pairs of *trans*- (**1** and **2**) and *cis*-azoxy compounds (**3** and **4**). Only a few cases of unsymmetrically substituted azoxy



	a	b	c	d
R^1	C_6H_{11}	C_6H_5	C_6H_5	C_6H_5
R^2	CH_3	CH_3	C_2H_5	p-$CH_3C_6H_4$

compounds have been reported for which all possible four isomers (**1** to **4**) are known[1]), namely **1a** to **4a** [6], **1b** to **4b** and **1c** to **4c** [7], as well as **1d** to **4d** [8].

In the dialkyl case **1a** to **4a** [6] and in both aryl-alkyl cases **1b** to **4b** and **1c** to **4c** [7] the chemical structures of all four isomers have been established: for the *trans*-isomers **1a–c** and **2a–c** by regiospecific synthesis [9] [10] and for the *cis*-isomers **3a–c** and **4a–c** by spectroscopic considerations [6] [7] with confirmation by X-ray analysis [6] of the two *cis*-isomers **3a** and **4a**[2]).

In the diaryl case the constitutions of the *trans*-isomers **1d** and **2d** were deduced [11] from the difference of reactivity of the aromatic rings, one connected to N(O) and the other to N, as well as from the regiospecific synthesis of one isomer, namely **1d** [10]. As far as the structure of the *cis*-isomers **3d** and **4d** is concerned, the *cis*-configuration followed from their formation by peracid oxidation of *cis*-4-methyl-azobenzene and from their UV. spectra [8]. The constitutions of the two *cis*-isomers **3d** and **4d** were assigned [8] on the basis of ^{1}H-NMR. arguments. These arguments will be discussed critically in chapter 2 and unambiguous structural proof for one of the isomers, namely **3d**, by X-ray analysis will be reported in chapter 3.

2. ^{1}H-NMR. spectra of the isomers 1d to 4d. – The position of the ^{1}H-NMR. methyl signals of the 4-methyl-azoxybenzene isomers **1d–4d** in benzene and in trichloromethane solution could be derived from the observations during thermal isomerization of **3d** and **4d** (see Exper. Part and [8]). The chemical shifts are given

Table 1. *^{1}H-NMR. signals of methyl groups in* **1d–4d**

Compound	δ-Values in ppm at 60 MHz	
	in benzene [8]	in $CDCl_3$[a])
trans-4-methyl-azobenzene	2.08	2.40
trans-(4′-methyl-N,N,O)-azoxybenzene (**1d**)	2.08	2.45
trans-(4′-methyl-O,N,N)-azoxybenzene (**2d**)	1.96	2.45
cis-4-methyl-azobenzene	1.93	2.28
cis-(4′-methyl-N,N,O)-azoxybenzene (**3d**)	1.88	2.27
cis-(4′-methyl-O,N,N)-azoxybenzene (**4d**)	1.76	2.31

[a]) This work.

[1]) Of other unsymmetrically substituted azoxy compounds only one or both *trans*-isomers have been described. Of special interest among them are a few natural products with high physiological activity, *e.g.* macrozamin [1], cycasin [2], elaiomycin [3], and LL-BH872a [4] as well as a recently isolated aromatic azoxy compound [5].

[2]) Details not yet published.

in *Table 1* together with the corresponding signals of *trans*- and *cis*-4-methyl-azobenzene for comparison.

Webb et al. [8] arrived at their structural assignments for the *cis*-isomers **3d** and **4d** from the observation of a shift of ^{1}H-NMR. methyl signals in benzene solution when going from the azo to the azoxy compounds. In each series of configurationally equivalent azoxy compounds only one of the regioisomers shows a considerable upfield shift of its methyl signal when compared with the respective azo compound (see *Table 1*).

It was known [11] that the *p*-tolyl substituent in the *trans*-isomer **2d** is located at the same nitrogen atom as the oxygen atom. Thus the relative upfield shift in the ^{1}H-NMR. methyl signal of **2d** in benzene was ascribed to a field effect of the azoxy function influencing mainly the substituent at the oxidized nitrogen atom. The same effect was assumed to operate in the *cis*-series and hence the stronger upfield shifted methyl signal at 1.76 ppm (in benzene solution) was ascribed to the isomer **4d**.

We have found that similar shifts of the methyl signals are not observed in the ^{1}H-NMR. spectra in trichloromethane solution (see *Table 1*). Here, the methyl signals of both *trans*-azoxy isomers **1d** and **2d** are shifted downfield when compared with *trans*-4-methyl-azobenzene. Only one *cis*-azoxy regioisomer, namely **3d** (with the *p*-tolyl substituent at the non-oxidized nitrogen atom), shows a slight upfield shift of its methyl signal in comparison with *cis*-4-methyl-azobenzene.

It is obvious from these results that the benzene induced upfield shift of the methyl signal in **2d** and **4d**, which is at the base of the structural arguments by *Webb et al.* [8], is, in fact, a solvent effect. In this connection it is of interest that *Rae & Dyall* [12] found the resonance signals of the *N*-methyl protons in a series of *para*-substituted *N*,*N*-dimethyl-anilines in benzene solution to be shifted upfield by strongly electron-withdrawing substituents. Since this effect was not observed in trichloromethane solution it was attributed to specific solvation by benzene. The same type of combined benzene solvent/electron-withdrawing substituent effect was evoked [13] as a rationalization for the upfield shifts of the methyl signals of **2d** and **4d** by comparison with **1d** and **3d** in benzene solution, taking into account the greater electron-withdrawing power of the phenyl-N,N,O- as compared with the *p*-tolyl-N,N,O-azoxy group.

However, if such an effect were responsible for the observed shifts of the methyl signal of **2d** as compared with **1d**, or **4d** as compared with **3d**, it would not necessarily operate in the same direction for both pairs of stereoisomers (**1d/3d** and **2d/4d**), considering the difference in molecular geometry and the correspondingly different arrangements of benzene solvent molecules around the substrate molecules. X-ray analysis (see chapter 3) shows a considerable rotation of the two aromatic rings out of the plane of the N,N,O-function in the crystalline state for the *cis*-isomer **3d**. A similar distortion would be expected for *cis*-azoxybenzenes in solution and this, in fact, expresses itself by a strong reduction of the extinction of the UV. absorption at long wavelengths as compared with the aromatic *trans*-azoxy compounds [14], which may be essentially coplanar [15] [16]. We conclude, therefore, that no simple rationale is at hand for the benzene induced upfield shift of the ^{1}H-NMR. methyl signals of **2d** and **4d** as compared with **1d** and **3d**, so that chemical shift observations – at least from signals of *para*-substituents – cannot be taken as

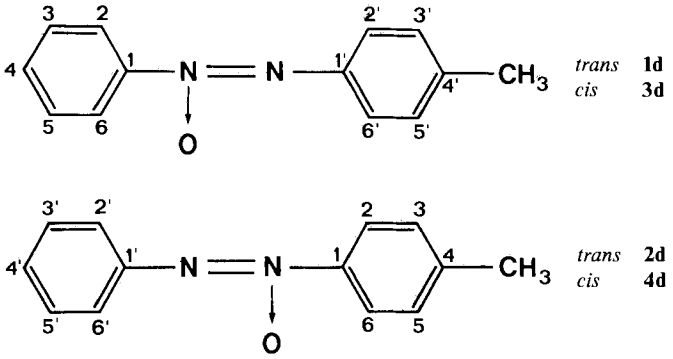
the basis of a structural assignment of regioisomeric unsymmetrically substituted aromatic azoxy compounds. Even for aliphatic azoxy compounds where α-protons should act as a much more sensitive probe of the influence of the oxygen atom on its geminal *vs.* vicinal substituent, it has been stressed that chemical shift arguments can be applied only with caution [6] [17], at least for the *cis*-isomers.

We therefore looked for another spectroscopic method for the structural assignment of the two *cis*-4-methyl-azoxybenzenes **3d** and **4d**. *Rondeau et al.* [18] have shown that the ^{1}H-NMR. spectra of regioisomer mixtures of unsymmetrically substituted azoxybenzenes with *trans*-configuration, including compounds **1d** and **2d**, become first order for the aromatic protons of each isomer in the mixture upon addition of 0.4 molar equivalents of tris(1,1,1,2,2,3,3-heptafluoro-7,7-dimethyl-4,6-octanedionato)europium (Eu(fod)$_3$). In particular, the *ortho*-protons exhibit different Eu(fod)$_3$ shift effects so that separate first order signals can be observed in the mixtures of *trans*-azoxy regioisomers.

We have tried to use the same ^{1}H-NMR. shift reagent to solve the assignment problem of the *cis*-isomers **3d** and **4d**. However, effects analogous to those with the *trans*-isomers **1d** and **2d** were not observed in the ^{1}H-NMR. spectra of mixtures of the *cis*-4-methyl-azoxybenzenes **3d** and **4d** upon addition of up to as much as 0.8 molar equivalents of Eu(fod)$_3$ to the solutions in trichloro- or tetrachloromethane. In these systems the shift reagent generated four complex multiplets for the aromatic protons. The multiplets could be assigned (see below) only by comparison with the Eu(fod)$_3$ shifted ^{1}H-NMR. spectrum of the pure *cis*-isomer **3d**, which will now be described: With 0.7 molar equivalents of Eu(fod)$_3$ in trichloromethane solution the *ortho*-protons of the phenyl ring (H–C(2) and H–C(6), for numbering see formulae at p.3019) of **3d** appeared at lowest field (11.83 ppm) as a double doublet (J=8 and 2). The next signal going upfield was a doublet (J=8) for the *ortho*-protons of the *p*-tolyl ring (H–C(2′) and H–C(6′)) at 9.85 ppm, followed by a three proton multiplet at 9.3–8.6 ppm for H–C(3), H–C(4) and H–C(5) of the phenyl group. Finally, the remaining two *meta*-protons of the *p*-tolyl ring were registered as a doublet (J=8) at 7.70 ppm. The methyl signal appeared at 2.52 ppm. The observed shifts are in agreement with the assumption of a linear N–O–Eu complex which influences the chemical shifts of the various protons by a pseudocontact interaction through space [18]. Thus it was possible to assign the correct structure to one *cis*-isomer, namely **3d**, in agreement with the result of the X-ray analysis to be reported in chapter 3.

When the ^{1}H-NMR. spectrum of pure **3d** was compared with the ^{1}H-NMR. spectrum of a (62:38)-mixture of **3d** and **4d**, both shifted by the presence of 0.7 molar equivalents of Eu(fod)$_3$, the relative intensities of the four multiplets showed that protons in equivalent positions with respect to the N(O)-function are subjected to nearly identical shift effects in both regioisomers (see Exper. Part). The two methyl signals at 3.44 and 2.52 ppm in a ratio of 38:62 had to be assigned to **4d** and **3d**, respectively.

These assignments of the methyl signals and of the aromatic proton multiplets (see Exper. Part) were confirmed by monitoring the changes of the ^{1}H-NMR. spectrum of the (62:38)-mixture of **3d** and **4d** in presence of Eu(fod)$_3$ at 25°: In the methyl signal region the singlet at 3.44 ppm (CH_3 of **4d**) disappeared more rapidly



than the one at 2.52 ppm (CH_3 of **3d**) while two new singlets at 2.12 ppm and at 2.62 ppm (CH_3 of **1d** and of **2d**, see also [18]) appeared, the latter increasing more rapidly than the former. The (62:38)-ratio of the sum of the intensities of the two signals assigned to **1d** and **3d** relative to the intensity of those assigned to **2d** and **4d** remained constant until complete disappearance of the original two signals at 2.52 ppm and 3.44 ppm of the *cis*-regioisomers. Parallel to these changes in the methyl signal region of the ^{1}H-NMR. spectrum, the signals of the aromatic protons could be recognized as superimpositions of the four multiplets generated by **3d** and **4d** and the more clearly resolved signals of **1d** and **2d** [18] during the thermal *cis* → *trans* isomerization process.

Our results confirm the contention by *Webb et al.* [8] that the mode of isomerization of **3d** and **4d** is a pure stereoisomerization, *i.e.* **3d** isomerizes only into **1d** and **4d** only into **2d**. Without the definite structural assignments for **3d** and **4d** a simultaneous stereo- and regioisomerization mechanism which would transform **3d** into **2d** and **4d** into **1d** could not have been rigorously excluded[3]).

3. X-ray analysis of 3d. – *Crystal data. cis*-(4′-Methyl-N,N,O)-azoxybenzene (**3d**), $C_{13}H_{12}N_2O$, $M = 212.25$, crystallized from pentane/ether forms yellow prismatic crystals, monoclinic, space group $P2_1/c$, $a = 7.635(2)$, $b = 7.671(2)$, $c = 19.336(5)$ Å, $\beta = 98.30(2)°$, $V = 1121$ Å^3, $Z = 4$, $d_{calc} = 1.257$ g cm^{-3}. Linear absorption coefficient $\mu = 6.1$ cm^{-1} (Cu$K\alpha$).

Intensity Data. Cu$K\alpha$-radiation ($\bar{\lambda} = 1.542$ Å, graphite monochromator) was used to measure intensity profiles of reflexions on a CAD-4F diffractometer from a crystal of approximate dimensions $0.1 \times 0.2 \times 0.3$ mm by ω: 2 θ-scan, variable scan width $\Delta\omega = 1° + 0.14$ tg θ, scan speed adjusted to achieve a ratio $\sigma(I)/I \approx 0.02$ ($t_{max} = 120$ s). Periodic intensity and orientation control indicated no deterioration of the crystal during data collection. The net intensities of reflexions were evaluated by profile analysis [20] and standard deviations calculated as $\sigma(I) = \{<I> + c^2I^2\}^{1/2}$, where $<I>$ is the variance of a measurement assuming *Poisson*-distribution of counts, and c^2I^2 a term accounting for experimental errors ($c = 0.02$). Of 1654 unique reflexions within the limiting sphere of $\theta \leqslant 60°$, 1543 reflexions were found to have significant intensity, $I \geqslant 3\sigma(I)$. Data reduction [21] resulted in $\bar{B} = 3.5$ Å^2, $<|E|> = 0.780$, $<|E^2 - 1|> = 1.055$, $<|E^2|> = 1.030$. No absorption corrections were applied (max. error in intensity was estimated to be less than 6.5%).

Structure solution and refinement. The structure was solved by application of an automated symbolic addition procedure [22] and refined by minimisation of

$$\Phi = \sum_{\underline{h}} \omega_{\underline{h}} (|F_o| - kG|F_c|)^2$$

[3]) The same reasoning applies to the photochemical transformation of **1d** into **3d** and **2d** into **4d** [19].

by block-diagonal LS approximation (k = scale factor, G = isotropic extinction coefficient [23]). The structure factor F_c was calculated on the basis of anisotropically vibrating C-, N-, and O-atoms, isotropic H-atoms[4]) using form factors taken from International Tables III (1962). The weighting function applied was

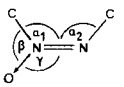
$$\omega_h = (1/\sigma_F^2) \exp. \left\{ \frac{8\pi^2 q}{p(q+p)} \sin^2 \theta/\lambda^2 \right\}$$

with $q = 7$ Å^{-2}, $p = 5$ Å^{-2} [24]. Convergence was reached at $R = 0.045$ including all significant data.

Results. A list of atomic coordinates with LS-computed standard deviations is given in *Table 3* (atom numbering see *Fig. 2*). Mean radial e.s.d.'s of atomic positions are σ(C) = 0.002, σ(N, O) = 0.0015, σ(H) = 0.04 Å. A complete list of structure factors and atomic parameters can be obtained from the second author (*H. P. W.*).

The structure of **3d** is influenced by two factors, namely by the tendency to reduce the steric strain imposed by the interaction of the two *cis*-oriented aryl groups and by the electron-donating effect of the *p*-tolyl substituent at N(2) on the N, N, O-function.

Table 2. *Bond lengths and angles in various azo compounds*



	C–N(O)	C–N	N–N	N–O	α_1	β	γ	α_2	Ref.
Ph, Tol, O	1.470(2)	1.427(3)	1.265(2)	1.264(2)	125.0(5)	114.3(5)	120.5(5)	119.2(5)	(this work)[a])
Ph, Ph, O, O	1.454(5) 1.463(5)	–	1.321(5)	1.268(4) 1.261(4)	118.7(3)	120.4(3) 120.0(3)	119.5(3) 120.8(3)	119.7(3)	[25][a])
A, O, A	1.570(7) 1.496(5)	1.559(7) 1.496(6)	1.155(6) 1.218(5)	1.291(6) 1.279(4)	109.1(5) 111.8(3)	116.2(4) 117.9(3)	134.7(6) 130.3(4)	113.5(5) 114.7(3)	[15][b]) [16][c])
Ph, Ph	–	1.443(5)	1.251(4)	–	121.9	–	–	(121.9)	[26][a])
Ph, Ph	–	1.434(3)	1.243(5)	–	113.8	–	–	(113.8)	[27][a])

[a]) Ph = phenyl; Tol = *p*-tolyl;
[b]) A = *p*-ethoxycarbonyl-phenyl
[c]) A = *p*-methoxy-phenyl

The strain effect can be seen in: (1) the rotation of the two aromatic planes by 55(1)° about the C–N bonds, (2) the C–N=N–C torsional angle of 14(1)°, and (3) the significant out-of-plane deformation of the two sp^2-atoms C(11) and C(21) to bring N(1) and N(2) out of the aromatic planes by 0.114(6) Å and 0.171(6) Å,

[4]) *H*-positions from F-*Fourier* maps.

Table 3. *Atomic coordinates* $\times 10^5$ *for C, N, and O-atoms,* $\times 10^4$ *for H-atoms with e.s.d.'s.*

N(1)	12541(16)	55042(19)	33244(6)
N(2)	6129(17)	48421(22)	38318(7)
O(1)	4780(17)	67534(20)	29809(7)
C(11)	29590(18)	50164(18)	31102(7)
C(12)	30025(22)	46419(26)	24158(8)
C(13)	46280(26)	43061(28)	22092(9)
C(14)	61570(22)	43819(25)	26839(10)
C(15)	60762(21)	47739(26)	33748(9)
C(16)	44634(20)	50872(24)	35941(8)
C(21)	13527(18)	32652(22)	41382(7)
C(22)	15187(25)	17522(25)	37599(8)
C(23)	20261(29)	2323(25)	41085(10)
C(24)	23726(23)	1389(25)	48316(10)
C(25)	21796(24)	16666(28)	52009(8)
C(26)	16649(22)	32076(25)	48654(8)
C(24A)	29044(32)	−15325(31)	52086(14)
H(12)	1963(36)	4580(35)	2105(14)
H(14)	7295(35)	4109(38)	2531(13)
H(13)	4721(37)	4183(37)	1699(14)
H(15)	7084(41)	4872(39)	3680(16)
H(16)	4388(31)	5314(30)	4043(12)
H(22)	1226(35)	1798(34)	3246(13)
H(23)	2160(36)	−833(38)	3854(13)
H(25)	2381(36)	1592(35)	5699(14)
H(26)	1513(26)	4258(28)	5090(10)
H(24A1)	2682(67)	−2539(64)	4978(25)
H(24A2)	4211(74)	−1662(71)	5361(29)
H(24A3)	2177(57)	−1680(52)	5618(22)

respectively. The bending is such as to bring the atoms C(14) and C(24) further apart. Similar deformations have been observed in *cis*-azobenzene [26] and in the *cis*-dimer of nitrosobenzene [25].

In addition to these distortions the unsymmetrical substitution pattern of the azoxy function with the electron-donating *p*-tolyl substituent at N(2) reflects itself in the bond lengths and angles: (1) The N(2)–C(21) bond is 0.043 Å shorter than the N(1)–C(21) bond, whereas the corresponding bonds in symmetrically substituted diaryl azo compounds, *i.e. cis*-dimer of nitrosobenzene [25] and *cis*- and

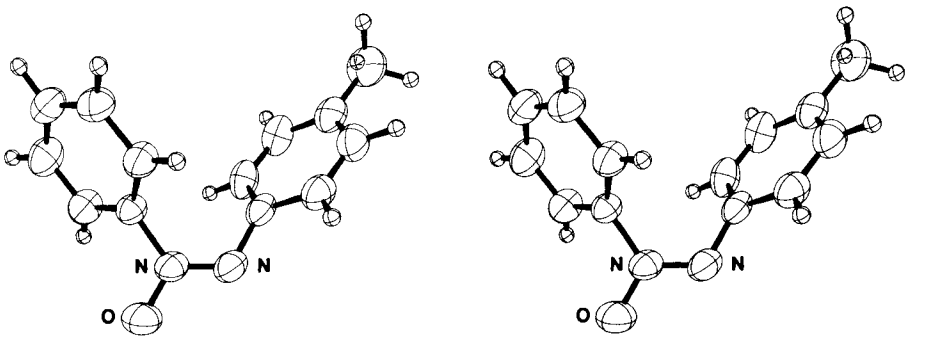


Fig. 1. *Stereoscopic view of the molecule.* The 50% probability ellipsoids of vibration are drawn for C, N, and O-atoms. H-atoms have been given a unique isotropic B = 1 Å^2.

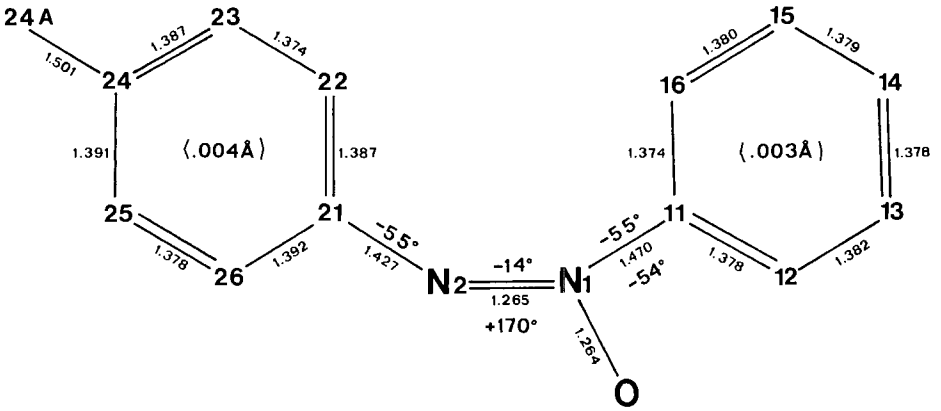


Fig. 2. *Numbering scheme of atoms.* Bond lengths ($\sigma_{av} \approx 0.004$ Å) and some torsions angles ($\sigma_{av} \approx 1°$) are given. The two numbers in the aromatic rings are the mean deviations of the 6 ring atoms form their respective LS-planes.

trans-azobenzene [26] [27], are of equal length (see *Table 2*). The N–N bond is significantly shorter than in the *cis*-dimer of nitrosobenzene, but only slightly longer than in *cis*- and *trans*-azobenzene. Quite different bond lengths, however, have been reported for two symmetrically substituted *trans*-azoxybenzenes [15] [16], for which we have no explanation. (2) The bond angles α_2 and γ (see *Table 2*) are both nearly 120°, but α_1 is increased by about 5° while β is correspondingly reduced. These deformations can be rationalized qualitatively in terms of the VSEPR-theory [28] as a consequence of the different electron-releasing power of the ligands around the N–N bridge.

The packing diagram is shown in *Fig. 3*. There are no unusually short intermolecular distances.

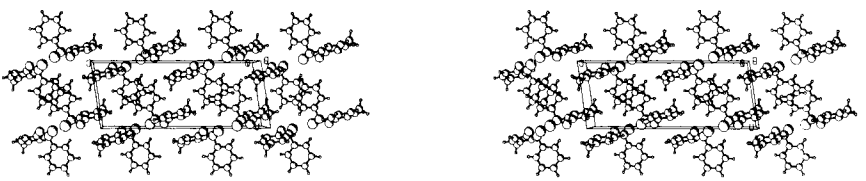


Fig. 3. *Packing diagram in projection along* b.

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Experimental Part

1. General. – Melting points were taken on a *Mettler* FP 5 apparatus with a *Kofler* heating block; the temperatures are not corrected. The *electronic spectra* were measured on a *Beckmann*-spectrophotometer ACTA III. They are described as follows: UV. (solvent): maxima in nm (extinction ε). The *proton resonance spectra* were measured on a *Varian* EM-360 instrument at 60 MHz. They are recorded as follows: ^{1}H-NMR. (solvent): chemical shifts in ppm on the δ-scala (TMS internal = 0)/ multiplicity with s = singlet, d = doublet, m = multiplet, splitting J in Hz, relative integration in H units (interpretation). The *mass spectrum* was measured on a *CEC* 21-110B instrument at 70 eV. It is described as follows: MS.: molecular ion (M) and fragment ions in m/e / intensities relative to the base peak in % (interpretation). Reported are all peaks with a relative intensity > 5%.

We thank the MS.-laboratory of the Organisch-chemisches Institut der Universität Zürich (direction Prof. *M. Hesse*) for the mass spectrum.

2. Oxidation of *cis*-4-Methyl-azobenzene. – A modification of the procedure of *Webb et al.* [8] was used: A solution of 403 mg (2.1 mmol) *m*-chloroperbenzoic acid (90% purity) in 20 ml CH_2Cl_2 was cooled to $-3°$ and then added to a solution of 392 mg (2.0 mmol) *cis*-4-methyl-azobenzene in 15 ml CH_2Cl_2 at $-3°$ under exclusion of light. After standing for 4 h in the cold and dark the reaction mixture was evaporated to dryness at 0° and the residue chromatographed on 30 g silica (*Merck* silica gel 60) with CH_2Cl_2 at $+1°$. After elution of a first orange fraction (34 mg) which consisted of a mixture of trans-*4-methyl-azobenzene* and the regioisomeric trans-*4-methyl-azoxybenzenes* (**1d** and **2d**) (^{1}H-NMR. in benzene solution, see [8]) a light yellow main fraction was obtained. After its evaporation to dryness at 0° and treatment of the remaining oil with 5 ml pentane at $-20°$ for 24 h 371 mg (87%) of a (62:38)-mixture (ratio determined by ^{1}H-NMR., see below) of cis-*(4'-methyl-N,N,O)-azoxybenzene* (**3d**) and cis-*(4'-methyl-O,N,N)-azoxybenzene* (**4d**) crystallized as yellow needles, m.p. 61–64°. This material was ground thoroughly to ensure homogeneous composition before measuring the spectra. – UV. (C_2H_5OH): 338 (3900); 241 (13010). – ^{1}H-NMR. (C_6D_6): 7.4–6.3/*m*, 9H (aryl-H); 1.88/*s* (CH_3 of **3d**) and 1.76/*s* (CH_3 of **4d**), together 3H in a ratio of 62:38. – ^{1}H-NMR. ($CDCl_3$): 7.7–6.6/*m*, 9H (aryl-H); 2.31/*s* (CH_3 of **4d**) and 2.27/*s* (CH_3 of **3d**), together 3H[5]). – ^{1}H-NMR. (CCl_4): almost identical with the spectrum in $CDCl_3$ solution. – Addition of increasing amounts of tris(1,1,1,2,2,3,3-heptafluoro-7,7-dimethyl-4,6-octanedionato) europium ($Eu(fod)_3$) to the $CDCl_3$ or CCl_4 solutions generated in the ^{1}H-NMR. spectra a sequence of 4 multiplets for the aromatic protons. Clear separation of them started on addition of approximately 0.4 molar equivalents of the shift reagent. From addition of 0.6 to 0.8 molar equivalents of $Eu(fod)_3$ no change of the complex line pattern within the 4 multiplets was observed. The two methyl signals were separated already after addition of 0.15 molar equivalents of $Eu(fod)_3$ to such an extent that their relative intensities could be determined by integration. For example, the ^{1}H-NMR. ($CDCl_3$, with 0.7 molar equivalents of $Eu(fod)_3$): 12.0–11.7/doubletoid *m*, 2H (H–C(2) and H–C(6)[6]) of **3d** and **4d**); 10.3–9.7/*m*, 2H (H–C(2') and H–C(6') of **3d** and **4d**); 9.3–8.6/*m*, 2.6H (H–C(3), H–C(4) and H–C(5) of **3d** and H–C(3) and H–C(5) of **4d**); 8.1–7.4/*m*, 2.4H (H–C(3') and H–C(5') of **3d** and H–C(3'), H–C(4') and H–C(5') of **4d**); 3.44/*s* (CH_3 of **4d**) and 2.52/*s* (CH_3 of **3d**), together 3H in a ratio of 38:62.

3. Thermal Isomerization of 3d and 4d. – Solutions of the (62:38)-mixture of **3d** and **4d** (see Exper. 2) in C_6D_6 and in $CDCl_3$ were kept at 25° with exclusion of light and their ^{1}H-NMR. spectra monitored. With respect to the solution in C_6D_6 the observations of *Webb et al.* [8] were confirmed. – With respect to the $CDCl_3$ solution the methyl signal at 2.31 ppm (CH_3 of **4d**) disappeared more rapidly than the one at 2.27 ppm (CH_3 of **3d**) while a new signal at 2.45 ppm (CH_3 of **3d** and **4d**) appeared. In the $CDCl_3$ solution with 0.7 molar equivalents of $Eu(fod)_3$ the signal at 3.44 ppm (CH_3 of **4d**) disappeared more rapidly than the one at 2.52 ppm (CH_3 of **3d**) with simultaneous generation of two new methyl signals at 2.12 ppm (CH_3 of **1d**) and at 2.62 ppm (CH_3 of **2d**), the latter increasing more rapidly than the former. Finally, only these two methyl signals were present in a ratio of 62:38. This ratio was also observed for the signals of H–C(2), H–C(6), H–C(2'), and H–C(6') of **1d** (at lowest field) relative to the signals of the same protons of **2d** (at slightly higher field) [18] after complete isomerization of **3d** and **4d** into **1d** and **2d**.

4. Isolation of *cis*-(4'-Methyl-N,N,O)-azoxybenzene (3d). – A solution of 58.2 mg (0.27 mmol) of the (62:38)-mixture of **3d** and **4d** (see Exper. 2) in 0.4 ml $CDCl_3$ was kept in the dark at 25° for 17 h until the ^{1}H-NMR. spectrum showed complete disappearance of the signal at 2.31 ppm (CH_3 of **4d**). Evaporation at 0° and prep. TLC. (*Merck* PLC. plates silica gel 60 F_{254}) of the residue with CH_2Cl_2 at $+1°$ gave two fractions: a) From an orange zone at Rf = 0.5–0.6 34,0 mg (59%) of a (58:42)-mixture of trans-*4-methyl-azoxybenzenes* **1d** and **2d** (ratio determined by ^{1}H-NMR. in C_6D_6 solution [8]) was obtained. b) From a yellow zone at Rf = 0.2–0.3 18.0 mg (31%) of **3d** was isolated as a yellow oil after elution with $CHCl_3$ and evaporation of the solvent at 0°. – ^{1}H-NMR. (C_6D_6): 7.1–6.6/*m*, 9H

[5]) Relative amounts of **3d** and **4d** could not be deduced from the ^{1}H-NMR. spectra of mixtures of **3d** and **4d** in $CDCl_3$ or in CCl_4 solution due to poor separation of the methyl signals unless $Eu(fod)_3$ was added to the solutions.

[6]) For numbering see formulae in chapter 2 of the theoretical part.

(aryl-H); 1.88/*s*, 3H (CH_3–C(4′)). – ^{1}H-NMR. ($CDCl_3$): 7.4–6.7/*m*, 9H (aryl-H); 2.27/*s*, 3H (CH_3–C(4′)). – ^{1}H-NMR. ($CDCl_3$ with 0.7 molar equivalents Eu(fod)$_3$): 11.83/*d*×*d*, *J* = 8 and 2, 2H (H–C(2) and H–C(6)); 9.85/*d*, *J* = 8, 2H (H–C(2′) and H–C(6′)); 9.3–8.6/*m*, 3H (H–C(3), H–C(4), and H–C(5)); 7.70/*d*, *J* = 8, 2H (H–C(3′) and H–C(5′)); 2.52/*s*, 3H (CH_3–C(4′)). – Crystallization of this oil from pentane/ether at −3° afforded 14.0 mg (24%) **3d** as yellow prismatic crystals, m.p. 85° (mp. of one *cis*-4-methyl-azoxybenzene isomer with non-localized NO-bond was reported [8] as 83.5–84.5°). – UV. (C_2H_5OH): identical with the spectrum reported [8] for the unidentified isomer, m.p. 83.5–84.5°. – MS.: 212/17 (*M*); 183/8; 141/5; 105/15 (C_7H_7N or $C_6H_5N_2$); 104/11; 91/24 (C_7H_7 or C_6H_5N); 77/100 (C_6H_5). – X-ray analysis see chapter 3.

REFERENCES

[1] *B. Lythgoe & N. V. Riggs*, J. chem. Soc. *1949*, 2716; *B. W. Langley, B. Lythgoe & N. V. Riggs*, Chemistry & Ind. *1951*, 75; *B. W. Langley, B. Lythgoe & N. V. Riggs*, J. chem. Soc. *1951*, 2309; *B. W. Langley, B. Lythgoe & L. S. Rayner*, ibid. *1952*, 4191.

[2] *K. Nishida, A. Kobayashi & T. Nagahama*, Bull. agr. chem. Soc. Japan *17*, 77 (1955); *N. V. Riggs*, Chemistry & Ind. *1956*, 926; *B. Korsch & N. V. Riggs*, Tetrahedron Letters *1964*, 523; *H. Matsumoto, T. Nagahama & H. O. Larson*, Biochem. J. *95*, 13c (1965); *M. Spatz*, Ann. N.Y. Acad. Science *163*, 697 (1969).

[3] *T. H. Haskell, A. Ryder & Q. R. Bartz*, Antibiot. Chemother. *4*, 141 (1954); *C. L. Stevens, B. T. Gillis, J. C. French & T. H. Haskell*, J. Amer. chem. Soc. *78*, 3229 (1956); *iidem*, ibid. *80*, 6088 (1958); *C. L. Stevens, B. T. Gillis & T. H. Haskell*, ibid. *81*, 1435 (1959).

[4] *W. J. McGahren & M. P. Kunstmann*, J. Amer. chem. Soc. *91*, 2808 (1969); *iidem*, ibid. *92*, 1587 (1970); *iidem*, J. org. Chemistry *37*, 902 (1972).

[5] *A. Gasco, A. Serafino, V. Mortarini, E. Menziani, M. A. Bianco & J. C. Scurti*, Tetrahedron Letters *1974*, 3431.

[6] *K. G. Taylor, S. R. Isaac & J. L. Swigert*, J. org. Chemistry *41*, 1146 (1976).

[7] *K. G. Taylor & T. Riehl*, J. Amer. chem. Soc. *94*, 250 (1972).

[8] *D. L. Webb & H. H. Jaffé, ibid. 86*, 2419 (1964).

[9] *J. P. Freeman*, J. org. Chemistry *28*, 2508 (1963); *K. G. Taylor, S. R. Isaac & M. S. Clark*, ibid. *41*, 1135 (1976).

[10] *T. E. Stevens*, J. org. Chemistry *29*, 311 (1964).

[11] *D. Bigiavi & V. Sabatelli*, Gazz. chim. ital. *57*, 557 (1927).

[12] *I. D. Rae & L. K. Dyall*, unpublished results from [13].

[13] *D. A. R. Happer & J. Vaughan*, in S. Patai (ed.), 'The Chemistry of the Hydrazo, Azo and Azoxy Group', p. 253, J. Wiley & Sons, London–New York–Sydney–Toronto 1975.

[14] *H. H. Jaffé & M. Orchin*, 'Theory and Applications of UV-Spectroscopy', p. 276–286 and 424–434, J. Wiley & Sons, New York–London 1962.

[15] *W. R. Krigbaum & P. G. Barber*, Acta crystallogr. *B27*, 1884 (1971).

[16] *W. R. Krigbaum, Y. Chatani & P. G. Barber, ibid. B26*, 97 (1970).

[17] *J. P. Snyder, V. T. Bandurco, F. Darack & H. Olsen*, J. Amer. chem. Soc. *96*, 5158 (1974).

[18] *R. E. Rondeau, M. A. Berwick, R. N. Steppel & M. P. Servé*, J. Amer. chem. Soc. *94*, 1096 (1972).

[19] *D. L. Webb & H. H. Jaffé*, Tetrahedron Letters *1964*, 1875.

[20] *R. Diamond*, Acta crystallogr. *A25*, 43 (1969).

[21] *A. J. C. Wilson*, Nature *151*, 150 (1942).

[22] *J. Karle & I. L. Karle*, Acta crystallogr. *21*, 849 (1966).

[23] *P. Coppens & W. C. Hamilton*, Acta crystallogr. *A26*, 71 (1971).

[24] *J. D. Dunitz & P. Seiler*, Acta crystallogr. *B29*, 589 (1973).

[25] *D. A. Dietrich, I. C. Paul & D. Y. Courtin*, J. Amer. chem. Soc. *96*, 6372 (1974).

[26] *A. Mostad & C. Rømming*, Acta chem. scand. *25*, 3561 (1971).

[27] *C. J. Brown*, Acta crystallogr. *21*, 146 (1966).

[28] *R. J. Gillespie*, «Molekülgeometrie», Verlag Chemie, Weinheim 1975.