The Conformers of a Nitrosamine and a Carboxamide: Comparison of NMR Line Shape and Equilibration Methods¹

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Activation parameters for the interconversion of conformers IA and IB of neopentylbenzylnitrosamine and of rotamers IIA and IIB of N, 2, 4, 6-tetramethyl-N-benzylbenzamide were determined by two techniques: Equilibration of pure IB (or IIA, respectively) and subsequent measurement of ¹H-NMR line shapes with the same sample. E_{a^-} and k_0 -values obtained by the two methods agree well within error limits, thus confirming the accuracy of rate determinations using NMR line shapes. Chemical shifts $\Delta \nu$, line widths b_E , and equilibrium constants K were extrapolated to those temperatures at which they could not be measured directly. Line shape parameters were used for the evaluation of spectra. This method is shown to be preferable to the complete line shape analysis if the line broadening by field inhomogeneities is not taken into account by a convolution.

INTRODUCTION

Kinetic results obtained by high-resolution NMR line shape analysis are subject to serious systematic errors (1-3). This method can be tested by comparing activation parameters measured by line shapes with those from spin-echo (4), double-resonance (5, 6) or equilibration, i.e. the direct observation of a timedependent property of the system under study (7, 8). Such properties used in chemical kinetics include optical rotation and the intensity of UV, visible, IR, and NMR absorptions. This paper deals with the comparison of results obtained by line shapes and equilibrations. Only a limited number of compounds will permit the application of both methods to the same process, because rate constants of fixed magnitudes (approximately 1 to $10^4 \sec^{-1}$ for line shape analyses and less than $10^{-3} \sec^{-1}$ for equilibrations) must occur under conditions suitable for measurement. A second restriction for the investigation of intramolecular

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processes originates in the limited availability of separate isomers which equilibrate in solution.

One class of compounds ideally suited for the desired test of the line shape procedure are nitrosamines, since the separation and equilibration of their conformers has recently been achieved (7, 9-11). Almost the same situation exists for 2,4,6trimethylbenzamides (7, 12) and for some formamides subsequently separated into more or less pure rotamers (8, 10, 13, 14). This papers deals with conformers IA and IB of neopentylbenzylnitrosamine and with rotamers IIA and IIB of N, 2, 4, 6-tetramethyl-N-benzylbenzamide. The pure crystalline nitrosamine IB (or IIA in the case of the benzamide) equilibrates in solution, generating a certain amount of IA (or IIB, respectively) which was determined as a function of time at several temperatures by ¹H-NMR signal intensities. After the equilibration, a detailed line shape analysis of the same mixture in the same sample tube was carried out in order to test the accuracy of the line shape method as rigorously as possible.



SCHEME 1

EXPERIMENTAL

Conformer IB was prepared in the following way: 3.0 g (0.029 mole) of neopentylamine, 5.0 g of NaHCO₂, 4 cm³ of water, and 3.7 g (0.03 mole) of benzylchloride were refluxed. After the addition of an excess of NaOH, neopentylbenzylamine was extracted with ether and twice distilled: 4.2 g (72%), bp 108°C (13 mm), $n_D^{23} = 1.4909$. Calculated for C₁₂H₁₉N: C, 81.29; H, 10.81; N, 7.90. Found: C, S1.30; H, 10.69; N, 8.14. 17.2 g (0.25 mole) of NaNO₂ in 200 cm³ of water were added to 8.8 g (0.05 mole) of the amine in 50 cm³ of water and 27.0 g (0.25 mole) of conc. HCl at -10° C. After extraction of the mixture with ether the extract was evaporated. The residue crystallized from petroleum ether (bp 40–60°C) at -25° C. The filtrate was refluxed for 30 min in order to equilibrate IA and again cooled to -25° C. The overall yield of 3 such crystallizations was

8.5 g (82%) of pale-yellow IB, mp 42–44°C. Calculated for C₁₂H₁₈N₂O:C, 69.85; H, 8.80; N, 13.58. Found: C, 69.97; H, 8.55; N, 13.67. The ¹H-NMR spectra in hexachlorobutadiene solution showed 2% \pm 2% of conformer IA to be present in these crystals. (A more complete separation of the conformers can be attained (10).) However, it can be proved that the kinetic expression (7, 12) used for the equilibrations is valid irrespective of the conformer ratio at the beginning of the experiment. The concentrations for the measurements were 0.6 mole liter⁻¹ in hexachlorobutadiene. One drop of octamethylcyclotetrasiloxane (7) served as an internal standard (τ (Me) = 9.92).

The synthesis of rotamer IIA as well as the preparation and the spectra of its solutions (0.6 mole liter⁻¹ in a mixture of 1-chloronaphthalene and benzotrichloride, 1:1, v:v) have been published (7).

The equilibrations of IIA and IIB have already been described (7). For IA and IB a Varian A-60 spectrometer equipped with a variable temperature system was used. These equilibrations could be measured during 1.5 half-lives of the process, using the $C\underline{H}_2C_6H_5$ protons (Fig. 1). The sweep rate was 5 cps². It was necessary to use different procedures for the following temperatures:

28.9 and 31.9°C: Equilibrations in the probe without using the variable temperature system. The probe temperature was determined by insertion of a calibrated thermometer instead of the sample tube; the maximum error ΔT was ± 0.2 °C.

15.5, 36.3, 40.3, and 44.7°C: Equilibrations in the probe using the variable temperature system. The temperatures were determined according to the manu-



FIG. 1. Conformers IA and IB in hexachlorobutadiene at 5°C. The spectrometer amplitude was reduced when the methyl signals were recorded. τ : chemical shifts, referred to tetramethylsilane. Upper spectrum: 5 min after dissolving crystalline IB. Lower spectrum: same solution after equilibration.

facturer's instructions ($\Delta T = \pm 2^{\circ}$ C). These equilibrations (and those at 28.9 and 31.9°C) consisted of 25–70 integrations at different times.

5.7 and 23.1°C: Equilibrations in a bath of solid-liquid benzene or *tert*-butanol, respectively. At intervals of 10 min the sample tube was withdrawn from the bath for one rapid integration in the spectrometer probe, the temperature of which was kept at 5.7 or 23.1°C. Any change in temperature by handling the tube was carefully avoided. The temperatures were determined by a calibrated thermometer; the maximum error ΔT was $\pm 0.2^{\circ}$ C.

Line shapes were measured with the equilibrated samples using a Varian HA-100 spectrometer equipped with a variable temperature system. Temperatures were determined in the usual way with the ethylene–glycol sample. The temperature-dependence of the glycol shift was calibrated using the clearing-points of cristalline liquids. The systematic error of this calibration does not exceed $\pm 0.5^{\circ}$. For IA/IB the signals of the CH₂C₆H₅, CH₂C(CH₃)₃, and CH₃ protons could be used (Fig. 1), whereas for IIA/IIB only the CH₂ absorptions were recorded. Each signal was run from 2 to 6 times at a given temperature with a sweep rate of 0.2 to 1.0 cps². Above 170°C the samples of IA/IB turned brown; no additional signals appeared in the spectrum. 8–30 integrations of the CH₂C₆H₅ signals were used to compute average equilibrium constants K for conformers IA/IB and IIA/IIB at different temperatures. The sweep rate was 5 cps².

The numerical calculations were carried out with an IBM-7040 computer. The programs are written in Fortran IV.

RESULTS OBTAINED BY THE LINE SHAPE METHOD

(a) General. The ⁴H-NMR spectrum of the equilibrium mixture of the neopentylbenzylnitrosamines IA and IB in hexachlorobutadiene at 5°C is given in Fig. 1. The observed signals were correlated with the protons of IA and IB by means of the literature data (15). Above 100°C the line widths increase; at still higher temperatures corresponding signals of the two conformers coalesce. The same situation exists for the N, 2, 4, 6-tetramethyl-N-benzylbenzamides IIA and IIB, the spectrum of which has been discussed (7, 12).

Gutowsky and Holm (16) have given a theory describing the dependence of an NMR spectrum upon the rate constant k_A (or k_B) of the process

$$A \xrightarrow[]{k_A}{k_B} B$$

Scheme 2

Furthermore, the line shapes depend upon Δv , $b_{\rm E}$, and $K: \Delta v = |v_A - v_B|$ is the chemical shift difference of corresponding signals due to conformers A and B. $b_{\rm E} = b - b_{\rm EX}$ represents the measured line width b minus the contribution of conformational broadening $b_{\rm EX}$. K is the equilibrium constant of A and

 $B:K = [B]/[A] = k_A/k_{B\cdot\Delta_F}$, b_E , and K must be known for the evaluation of spectra, but can be measured only *outside* the temperature range which yields k_{A^-} and k_{B^-} values. Therefore, they must be extrapolated or interpolated to those temperatures. This will be done in sections (b), (c), and (d) for the CH₃ protons



FIG. 2. Extrapolation of chemical shift difference $\Delta \nu$ at 100 Mcps for methyl signals of neopentylbenzylnitrosamines IA and IB in hexachlorobutadiene.

TABLE I

Spectral Results for IA/IB (in Hexachlorobutadiene) and IIA/IIB (in 1-Chloronaphthalene/Benzotrichloride, 1:1)^a

^	C'	$ au_{\rm A}$	$\tau_{\rm B}$	Δγ (α	cps)	<i>K</i>		T (90)
	Signals used	30°C	30°C	50°C 1	50°C	50°C 1	50°C	$T_{\rm c}({\rm °C})$
CH ₂ C ₆ H ₅	CH3	9.15	9.04	11.2	11.5 ^b	_		138
O=N-N CH ₂ C(CH ₃) ₃	$\mathrm{C}\underline{\mathrm{H}}_2(\mathrm{C}\mathrm{H}_{\mathfrak{z}})_{\mathfrak{z}}$	6.88	6.25	59.9	56.9^{b}	1 22	1 40b	
IA and IB	$CH_2C_6H_5$	4.68	5.22	52.6	53.8^{b}) 1.55	1.49-	
CH ₃ C ₉ H ₁₁ CO-N CH ₂ C ₆ H ₅	CH_2	5.31	5.99	62.2	56.2 ^b	0.41	0.44 ^b	$\sim \! 175$
IIA and IIB								

• τ_A , τ_B : chemical shifts for conformers A and B, referred to tetramethylsilane; $\Delta \nu$: chemical shift difference of the signals for A and B, at 100 Mcps; K = [B]/[A]: equilibrium constant; T_c : coalescence temperature, at 100 Mcps.

^b Extrapolated values.

of IA and IB. Sections (e) to (h) will describe and compare the different procedures for determining k_A from line shapes. Section (i) deals with the errors involved.

(b) Extrapolation of $\Delta \nu$. For all pairs of sharp lines in the spectra of IA/IB and IIA/IIB the chemical shift depends linearly upon the temperature (e.g. Fig. 2). The same behavior is supposed for higher temperatures, for which $\Delta \nu$ -values were therefore obtained by extrapolation (Fig. 2 and Table I).

(c) Determination of $b_{\rm E}$. For high $(k_A > 10^4 \, {\rm sec}^{-1})$ and low rates $(k_A < 1 \, {\rm sec}^{-1})$ $b_{\rm E}$ equals the measured width b, since $b_{\rm EX}$ is zero. The interpolation for the medium range of k_A -values should take account of all contributions (1) to $b_{\rm E} = b_{\rm I} + b_{\rm C} + b_{\rm R}$. $b_{\rm I}$ is due to field inhomogeneities and is nearly independent of T. $b_{\rm I}$ was measured with the signals of acetaldehyde; we found 0.3 to 0.5 cps, depending upon the spectrometer conditions. $b_{\rm C}$ is the result of unresolved longrange couplings and was determined by double-resonance. $b_{\rm C}$ was 0.3 cps or less for IA/IB and IIA/IIB. $b_{\rm R}$ represents the contribution of relaxation to $b_{\rm E}$. Its temperature dependence (1) is given by

$$\log_{10} (Tb_{\rm R}) = \text{Const.} + W/RT \tag{1}$$

where W is an energy of interaction. As the signals of both compounds investigated are still somewhat broadened by $b_{\rm EX}$ at 200°C, the upper temperature limit of our spectrometer, $b_{\rm E}$ has to be *extra*polated (Fig. 3) from the low-temperature values according to Eq. (1).

(d) Extrapolation of K. From the relative intensities of all pairs of lines origi-



FIG. 3. Extrapolation of $b_{\rm R}$, the relaxation contribution to the line width, for methyl signals of neopentylbenzylnitrosamines IA and IB in hexachlorobutadiene. The extrapolation applies for both conformers, as IA (O) and IB (\bigoplus) show the same $b_{\rm R}$ at lower temperatures.

TABLE II

Equilibrium Parameters for *IA/IB* (in Hexachlorobutadiene) and *IIA/IIB* (in 1-Chloronaphthalene/Benzotrichloride, 1:1): Statistical Errors are Given

		ΔH (cal mole ⁻¹) n	ΔG (cal nole ⁻¹) 100°C	ΔS (e.u.) 100°C
$ \begin{array}{c} \begin{array}{c} \begin{array}{c} \begin{array}{c} \begin{array}{c} \begin{array}{c} \begin{array}{c} \begin{array}{c}$	CH ₂ C(CH I-N CH ₂ C ₆ H ₅ IB	,3)3 +272 ±22	-250 ± 49	$^{+1.4}_{\pm 0.1}$
$\begin{array}{c} C_{9}H_{11} \\ C - N \\ O \\ CH_{2}C_{6}H_{5} \\ \hline \\ IIA \end{array}$	CH ₂ C ₆ H ₅ CH ₃ IIB	+204 ± 10	+634 ± 20	-1.2 ± 0.1

nating from the two conformers, K can be measured below 120°C. Its temperature dependence is given by

$$\ln K = -\Delta H/RT + \Delta S/R \tag{2}$$

Assuming that the enthalpy and entropy differences (Table II) are independent of T, $\ln K$ was extrapolated (Fig. 4 and Table I) according to Eq. (2).

(e) Use of the coalescence temperature. The k_A -value at the coalescence temperature T_c is obtained from the diagram of Fig. 5. On heating the sample one reaches T_c when the minimum between the coalescing absorptions begins to disappear. Fig. 6 contains one point determined in this manner by the coalescence of methyl signals in IA and IB.

(f) Approximations for fast and slow interconversion. Further k_A -values may be obtained from line widths at high and low temperatures, where $b_{\rm E} < b_{\rm EX} \ll \Delta \nu$. Small rate constants are given by (17)

$$k_A = \pi b_{\rm EX} \tag{3}$$

 b_{EX} being the conformational broadening of signal A. (Similarly, the k_B -value results from signal B.) Eq. (3) is valid as far as the two absorptions do not overlap significantly. Large rate constants are given by (17)

$$k_{A} = \frac{4\pi\Delta\nu^{2}K}{b_{\rm EX}(1+K)^{3}}$$
(4)

 k_A determined by Eq. (4) does not deviate from the true value by more than 10% when it amounts to at least three times the value at T_c .



FIG. 4. Extrapolation of the equilibrium constant K = [B]/[A] for neopentylbenzylnitrosamines IA and IB in hexachlorobutadiene, obtained from 8-30 integrals of the 4 methylene signals. Error intervals represent standard deviations.

Preliminary Arrhenius diagrams for IA/IB and IIA/IIB were already obtained from the information according to sections (e) and (f).

(g) Determination of k_A by line shape parameters. This procedure yields k_A -values for the whole range of temperatures³ at which $b_{EX} \neq 0$. Characteristic parameters for the line shape (1) are used, the most important of which is the line width b. Below T_c further parameters are $\Delta \nu_m$, the frequency difference between the absorption maxima corresponding to A and B, and I_m/I_o , the ratio of the intensities in the absorption maximum and in the minimum between the absorptions of A and B. Initially, b, $\Delta \nu_m$, and I_m/I_o were computed according to Gutowsky and Holm (16) as functions of k_A , b_B , $\Delta \nu$ and K. Secondly, diagrams were drawn from which we were able to read the k_A -values of IA/IB and IIA/IIB (Table III) corresponding to the measured parameters b, $\Delta \nu_m$, or I_m/I_o .

(h) Determination of k_A by numerical adaption of complete shapes. This timeconsuming procedure evaluates the rate constant by comparing the experimental line shape with that according to Ref. (16). Extrapolation of $\Delta\nu$, b_E , and K is necessary as above. The calculated shape is adapted to the experimental one by variation of k_A . As an indication of their agreement we tried the sum of square deviations and the sum of χ^2 -values (19). χ represents the difference between the experimental intensity I and the calculated one, divided by \sqrt{I} . The adaption

³ It must be pointed out that each line shape parameter yields accurate k_A -values only in a fixed temperature range: For b this range is outside the region of coalescence; for $\Delta \nu_m$ and I_m/I_o only a small range below T_c is favourable. The use of the parameters outside these ranges may result in large errors of k_A (18). Therefore, all parameters should be used for the determination of activation energies (3).



FIG. 5. Diagram for the determination of the rate constant k_A at the coalescence temperature T_c . K: equilibrium constant; $b_E = b - b_{EX}$: line width b minus contribution of conformational broadening b_{EX} ; $\Delta \nu$: chemical shift difference between two corresponding signals. When K > 1, 1/K is to be used as the parameter of the diagram; in this case k_B is obtained instead of k_A . The data were computed using the equations of Reference (16).

according to χ^2 results in good agreement near the base line of the signals; however, our results in Table IV (cf. section (i)) show that this method is unfavorable in our cases. On the other hand, the adaption according to square deviations results in good agreement at the top of the signals; we used this method for some results of Table IV and for a check of some k_A -values of IIA/IIB in Table III. We did not try mere inspection of spectra, as this seems to us to be an ill-defined indication of agreement.

(i) Calculation of the line shape and comparison of the different evaluation pro-

TABLE III

RATE CONSTANTS⁸ k_A for Processes IA \rightarrow IB of Neopentylbenzylnitrosamine in Hexachlorobutadiene and IIA \rightarrow IIB of N,2,4,6-Tetramethyl-N-Benzylbenzamide in 1-Chloronaphthalene/Benzotrichloride (1:1), Obtained by Line Shapes

$IA \rightarrow I$	ſB	$IIA \rightarrow IIB$		
T (°C)	$k_A \;(\mathrm{sec}^{-1})$	T (°C)	$k_A (\text{sec}^{-1})$	
112.0	2.65	122.2	1.14	
120.9	5.82	131.1	1.76	
129.6	11.8	140.0	3.64	
$T_c = 138.0$	21.6	148.9	7.50	
138.6	24.3	157.8	11.0	
147.3	42.2	166.8	27.7	
156.1	81.9	175.8	46.0	
165.0	149	193.6	116	
174.0	285			
182.8	378			

^a The k_A -values are averaged from up to 12 measurements from different signals.

TABLE IV

Test of Field Distribution Functions $g(\nu)$ and Evaluation Procedures⁴

		Lorentzian field Gaussian field distribution function		Triangle field distribution function			
		CLS ^b	LSP	CLS ^b	LSP	CLS ^b	LSP
$k(\sec^{-1})$	5.0	4.7(4.2)	5.0	3.2(2.9)	3.4	3.2(2.9)	3.4
	20.0	19.0	18.6	18.2	17.6	18.2	17.6
	40.0	40.2	44.4 62.6	40.2 62.4	40.4	40.2 62.4	40.2
	330	354 (401)	331	492(537)	448	496(541)	455
E_a (kcal mole ⁻¹)	20.0	20.7(21.7)	20.2	23.9(24.8)	23.2	24.0(24.8)	23.3
$\log_{10} k_0$	14.0	14.5(15.1)	14.1	16.4(17.0)	16.0	16.5(17.0)	16.0

* Spectra simulated according to Eq. (5) for the k-values of the first column were analyzed by comparison with the complete line shape (CLS) or by line shape parameters (LSP). The resulting k-values are given in the other columns. See text for details.

^b As an indication for the agreement between the calculated and the experimental line shapes we used the sum of square deviations. Alternatively, the sum of χ^2 -values was tried (values in brackets). 250 points were used for the adaption.

cedures. The line shape $f(\nu)$ according to Gutowsky and Holm (16) takes into account the relaxation time $T_2(T_2 = 1/\pi b_{\rm R})$, but neglects line broadening by field inhomogeneities⁴. The experimental line shape function $f_{\rm exp}(\nu)$ is in agreement

⁴ In order to simplify the calculations, we assume the absence of long-range couplings, i.e. $b_C = 0$. Otherwise, one has to superpose the lines according to the known coupling pattern.

with the calculated one only if the Gutowsky-Holm line shape $f(\nu)$ is convolved (6, 20) with the experimentally determined inhomogeneity broadening $g(\nu)$ according to Eq. (5):

$$f_{\exp}(\nu) = \int_{0}^{\infty} g(\nu') f(\nu - \nu') \, d\nu'$$
(5)

Therefore, k_A can be calculated from the experimental spectra by line shape parameters (section (g)) or by numerical adaption (section (h)) according to three methods: Method 1: As k_A is determined from $f(\nu)$, this function must be calculated from $f_{\exp}(\nu)$ and $g(\nu)$ by solving Eq. (5) for $f(\nu)$ as shown in the Appendix. This method has not yet been used, although the problem can be solved elegantly by the convolution theorem (21). The inhomogeneity broadening $g(\nu)$ which is necessary for this solution may be obtained from the shape of the CH₃CHO or CHCl₃ signals. Method 2: The line shape $f_{\exp}(\nu)$ is calculated according to Eq. (5) for different rate constants k_A , taking into account the experimental function $g(\nu)$. The k_A -values are obtained by comparing these calculated shapes with the experimental ones. Method 3: However, most evaluations, including ours, use another, approximate line shape $f_{ap}(\nu)$, resulting from the Gutowsky-Holm equations by substituting $b_{\rm R} + b_{\rm I}$, the relaxation and inhomogeneity contributions, for $b_{\rm R}$. In this case, k_A is obtained by comparison of $f_{\exp}(\nu)$ and the calculated approximate function $f_{ap}(\nu)$.

In order to test the latter determination of k_A -values via approximate line shapes (Method 3), we simulated by a computer and a plotter the spectra of a system with $\Delta \nu = 20$ cps, K = 1, $b_{\rm R} = 0.05$ cps, $b_{\rm I} = 1.00$ cps, and five k-values $(k = k_A = k_B)$ (Table IV). Field distribution functions $g(\nu)$ of line width $b_{\rm I}$ with a Lorentzian, Gaussian, or triangle shape were used to calculate line shapes according to Eq. (5). These simulated "experimental" shapes $f_{\rm exp}(\nu)$ were plotted and analyzed for k by Method 3. The k-values show considerable errors when based upon a field distribution of Gaussian or triangle shape (Table IV). The corresponding $E_{\rm a}$ - and $\log_{10} k_0$ -values are 15% higher than the supposed parameters of $E_{\rm a} = 20.0$ kcal mole⁻¹ and $\log_{10} k_0 = 14.0$.

A similar investigation was carried out experimentally by Fryer, Conti, and Franconi (2). Measurements based upon best field homogeneity were compared with those based upon worse Y-gradient control. The latter also resulted in E_{a} - and k_{0} -values which were too high.

The analysis by Method 3 gives acceptable activation parameters only for a Lorentzian field distribution⁵ (Table IV); these k_A -values show only small errors (<10%) around T_c . Therefore, it is unnecessary to carry out the exact, yet

⁵ Insofar as the field distribution $g(\nu)$ as well as the Gutowsky-Holm line shape $f(\nu)$ are of the Lorentzian type, $f_{ap}(\nu)$ and $f_{ex}(\nu)$ result in the same line shape, since the convolution of two Lorentzian curves again produces a Lorentzian curve, the line width of which is the sum of the starting widths (22). At coalescence the Gutowsky-Holm line shape $f(\nu)$ deviates most from the Lorentzian type.

complicated convolutions of Methods 1 and 2, if the inhomogeneity broadening $g(\nu)$ is Lorentzian. Appropriate adjustments could always be found for our Varian HA-100 spectrometer, as was proved by experiments with the CHCl₃ signal.

The k_A -values obtained by parameters are now compared with those determined by complete line shapes. The latter procedure does *not* yield more accurate rate constants than do parameters (Table IV) provided the convolution is omitted by using Method 3 (as is done by almost all authors). This was confirmed by many other kinetic investigations (23). Therefore, in this paper the parameter procedure was preferred to the complete line shape analysis which was only used to test some k_A -values for IIA/IIB in Table III.

TABLE V
Comparison of Results Obtained for the Process IA \rightarrow IB of
NEOPENTYLBENZYLNITROSAMINE BY LINE SHAPES AND
Equilibrations ^a ; Solvent: Hexachlorobutadiene

MADTD V

	E_{a} (kcal mole ⁻¹)	$\log_{10} k_0$	ΔG^{\neq} (kcal mole ⁻¹) 100°C	ΔS [≠] (e.u.) 100°C
Line shape method	$25.3 \pm 2.2^{\text{h}}$	14.8 ± 1.2	22.0 ± 0.3	$+6.7 \pm 5.4$
Equilibration method	$24.2~\pm~0.3$	$14.1~\pm~0.2$	$22.1~\pm~0.1$	$+3.5 \pm 0.9$
Both methods	$24.7~\pm~0.1$	$14.5~\pm~0.1$	$22.0~\pm~0.1$	$+5.2 \pm 0.2$

^a E_a : activation energy; k_0 : frequency factor; $\Delta G \neq :$ free enthalpy of activation; $\Delta S \neq :$ activation entropy.

^t Deviations given for the line shape results include statistical and extrapolation errors. Other errors are merely statistical.

TABLE VI

Сомракія оf <i>N</i> ,2 1-С	ON OF RESULTS O 2,4,6-TETRAMETH SHAPES AND EC CHLORONAPHTHAL	BTAINED FOR TH YL-N-BENZYLBI QUILIBRATIONS [®] ENE/BENZOTRIC	HE PROCESS IIA \rightarrow ENZAMIDE BY LIN : SOLVENT: CHLORIDE (1:1)	IIB TE
	$E_{\rm a}$ (kcal mole ⁻¹)	$\log_{10}k_0$	$\Delta G \neq (\text{kcal mole}^{-1})$ 100°C	ΔS [≠] (e.u.) 100°C
Line shape method	$24.7 \pm 1.6^{ m b}$	13.7 ± 0.8	23.4 ± 0.3	$+1.7 \pm 3.7$
Equilibration method	$23.5~\pm~1.1$	$13.1~\pm~0.8$	$23.1~\pm~0.1$	-0.8 ± 3.6
Both methods	23.1 ± 0.2	12.8 ± 0.1	23.2 ± 0.1	-2.2 ± 0.4

^a E_a : activation energy; k_0 : frequency factor; $\Delta G \neq$: free enthalpy of activation; $\Delta S \neq$: activation entropy.

^b Deviations given for the line shape results include statistical and extrapolation errors. Other errors are merely statistical.



FIG. 6. Arrhenius plot for the process $IA \to IB$ of neopentylbenzylnitrosamine in hexachlorobutadiene, measured by line shapes. (\bullet) Obtained by averaging the k_A -values from methyl and methylene signals. (\bullet) k_A -value obtained from the coalescence of methyl signals according to Fig. 5. (\Box) Rectangles obtained by ΔT and the error of extrapolation and interpolation (see section on estimation of errors). These rectangles were drawn around the points of the adapted straight line.

(k) Results. In Tables V and VI the results obtained by line shape parameters are given for nitrosamines IA/IB and benzamides IIA/IIB.

(1) Estimation of errors. The following errors contribute to the deviations given in Tables V and VI: a statistical error, a systematic error of temperature, and an error of extrapolation and interpolation (EEI).

The *statistical* error was calculated from the measured points in the Arrhenius diagram (e.g. Fig. 6) as the standard deviation from the least-squares fit.

The systematic error of the temperature calibration ΔT is $\pm 0.5^{\circ}$ as mentioned in the experimental section.

The *EEI* results from the extrapolation and interpolation carried out to obtain $\Delta \nu$, $b_{\rm E}$, and K (Figs. 2, 3 and 4). We found $\Delta (\Delta \nu) = 0.2$ cps, $\Delta b_{\rm E} = 0.1$ cps, and $\Delta K = 0.02$ for IA/IB and IIA/IIB. The influence of those deviations resembles that of systematic errors. The EEI of each k_A -value was calculated from $\Delta (\Delta \nu)$, $\Delta b_{\rm E}$, and ΔK by means of Eq. (3) and Eq. (4) using error propagation.

26

<i>T</i> (°C)	K	$t_{0.5}$ (min)	$kA \cdot 10^4 (sec^{-1})$
44.7	1.31	2.3	27.8
40.3	1.29	3.7	17.5
36.3	1.30	6.3	10.3
31.9	1.30	10.6	6.15
28.9	1.28	18.3	3.56
23.1	1.28	32.7	1.92
15.5	1.26	111	0.635
5.7	1.25	474	0.135
5.7	1.25	482	0.133

TABLE VII

EXPERIMENTAL VALUES FOR NEOPENTYLBENZYLNITROSAMINES IA AND IB, OBTAINED BY FOULT DEATIONS: SOLVENT'HEXACHLOPONITADIENE

^a K = [B]/[A]: equilibrium constant; $l_{0.5}$: half-life; k_A : rate constant for process IA \rightarrow IB.

 $\Delta b_{\rm E}$ contributes most to the EEI, especially when $\Delta \nu$ is small. In these cases $\Delta(\Delta \nu)$ and ΔK were neglected.

The influence of the EEI is not detectable in Arrhenius diagrams, since it does not increase the scattering of points, but shifts and tilts the whole straight line. Therefore, although the EEI is overlooked very often, it is important for all methods using extrapolated or interpolated $\Delta \nu$ -, $b_{\rm E}$ -, or K-values. It would be eliminated if one could measure these values over the whole range of temperatures used for the determination of k_A . Below T_c this is sometimes possible for $\Delta \nu$ and K by adaption of the complete line shape. Some authors substitute $b_{\rm E}$ for the line width of internal tetramethylsilane; this procedure takes into account $b_{\rm I}$ but neglects $b_{\rm R}$ and $b_{\rm C}$.

The EEI of the k_A -values and ΔT define rectangles around the points of the adapted straight line in the Arrhenius diagram (e.g. Fig. 6). From two straight lines with maximum and minimum slopes passing through each rectangle we obtained the full systematic error of the activation parameters to which the statistical error (see above) was added.

RESULTS OBTAINED BY THE EQUILIBRATION METHOD

The equilibration of the benzamides IIA and IIB has already been described (7). The same procedure was applied to nitrosamines IA and IB (cf. Reference 10). Conformer IB, obtained by crystallization (see Experimental), was dissolved in hexachlorobutadiene. The gradual appearance of the signals due to IA (Fig. 1) was measured at 9 temperatures below 45° C by integration of the CH₂C₆H₅ absorptions. We suppose that this change and the coalescence of signals at higher temperatures as reported in the preceding sections are caused by the same intramolecular motion, the reorientation of the nitroso group (cf. Refs. 9 and 10).

The expressions previously (7) derived were used to obtain the half-lives, the rate constants, and the equilibrium constants for different temperatures given in Table VII. Activation parameters for IA/IB are reported in Table V (cf. Fig. 7); those from the equilibration of IIA/IIB in Table VI are based on the rate constants determined earlier (7). The errors given in Tables V and VI for the



FIG. 7. Arrhenius plot for the process $IA \rightarrow IB$ of neopentylbenzylnitrosamine in hexachlorobutadiene. k_A -values were obtained by line shapes (O) and by equilibrations (\bullet).

28

equilibration parameters and for the data combined from both methods were calculated as standard deviations from the least squares fit.

COMPARISON OF KINETIC RESULTS OBTAINED BY THE TWO METHODS

Our first attempt (7) at comparison had suffered (7,8) from using N, N, 2, 4, 6pentamethylbenzamide for the NMR line shape measurements and N, 2, 4, 6tetramethyl-N-benzylbenzamide IIA for the equilibrations, i.e. from using two similar but nonetheless different compounds. Accordingly, Gutowsky, Jonas, and Siddall (8) investigated the *same* compound, N-methyl-N-benzylformamide, by the two methods. They equilibrated liquids in which one rotamer was concentrated via a uranyl nitrate adduct, according to the technique reported by Siddall (13). However, it was pointed out that the half-lives obtained by this technique are probably minimum values, as impurities would tend to increase the observed rates (13). The difficulties encountered in these two papers (7, 8) are absent in the case of a doubly bridged biphenyl, the ring inversion of which was investigated by Oki and Iwamura (24) who used approximations for the kinetic analysis. Their results agree with the rates of racemization (25) of the optically active compound at 10.1°C and 23.3°C. However, the racemization has not yet been measured at more temperatures.

In the present paper the equilibration parameters for neopentylbenzylnitrosamines IA and IB in Table V are more accurate than those for N, 2, 4, 6tetramethyl-N-benzylbenzamides IIA and IIB in Table VI which were determined from 5 measurements in a temperature range of only 26° (7), compared with 9 equilibrations of IA/IB in a range of 39° (Table VII). The reverse is true for our line shape results, those for IIA/IIB being somewhat more accurate than those for IA/IB. Comparison of the activation parameters in Table V and in Table VI shows all values measured by the two techniques to agree well within error limits.

We believe this agreement, obtained with the *same*, *pure* sample for both methods, to be a meaningful confirmation of the accuracy of rate determinations by the line shape method.

For both compounds the activation parameters measured by line shapes tend to be somewhat greater (though within error limits) than the equilibration data, e.g. $E_a = 25.3 \pm 2.2$ and 24.2 ± 0.3 kcal mole⁻¹ for IA \rightarrow IB in Table V. In the case of IA/IB, but not for IIA/IIB, we suggested initially crystallization of one conformer, during the equilibrations at lower temperatures (e.g. 5.7°C). This might have simulated higher rates at these temperatures, i.e. lower E_{a^-} and k_0 -values. This explanation was disproved by the finding that no crystals of IA or IB could be detected after equilibrated solutions stood for 2 weeks at 5.7°C; it was stated independently that the solubility of IB, the less soluble conformer, at $\pm 1^{\circ}$ C in hexachlorobutadiene exceeds 0.6 mole liter⁻¹, the concentration of the solutions used for our measurements. The slight deviations of our results obtained

by the two methods may be caused by the systematic error discussed in section (i) or by the nonvalidity of the Arrhenius equation (cf. Refs. 7, 26) which might be detectable owing to the exceptionally large range of k_A -values accessible in the present study. For nitrosamines IA and IB this range amounts to more than 10^7 sec^{-1} , as can be seen in Fig. 7.

We have tried to adapt our k_A -values in Table III to the function

$$k_A = CT^n e^{-B/RT} \tag{6}$$

in order to look for a temperature dependence of the frequency factor. However, the sum of square deviations shows only a very flat minimum (located at n = +2 for IA/IB and at n = +9 for IIA/IIB). A real temperature dependence of the frequency factor (or of the activation energy or both) might be detected by measuring additional rate constants around 0.1 sec⁻¹ by double resonance (6).

Another interesting investigation would be the corresponding comparison of spin-echo and equilibration techniques.

Note added in proof: Our recent results obtained by double resonance agree with the data in Tables V and VI: $E_a = 23.5$ kcal mole⁻¹ and $\log_{10} k_0 = 13.7$ for IA \rightarrow IB; $E_a = 24.4$ kcal mole⁻¹ and $\log_{10} k_0 = 13.6$ for IIA \rightarrow IIB. As the statistical errors of these figures are still large, we did not detect a real temperature dependence of the frequency factor.

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APPENDIX

Eq. (5) is to be solved for the unknown function $f(\nu)$. Functions $f_{\exp}(\nu)$ and $g(\nu)$ are known by measurement. One calculates the Fourier transformes $F_{\exp}(u)$ and G(u), corresponding to $f_{\exp}(\nu)$ and $g(\nu)$:

$$F_{\exp}(u) = \int_0^\infty f_{\exp}(v) e^{-iuv} dv; \qquad G(u) = \int_0^\infty g(v) e^{-iuv} dv$$

The Convolution Theorem (21) connects the Fourier transformes according to Eq. (5) by $F_{\exp}(u) = G(u) \cdot F(u)$ or: $F(u) = F_{\exp}(u)/G(u)$. f(v) is now obtained by a Fourier synthesis (21b): $f(v) = G \int_{-\infty}^{\infty} F(u) e^{ivu} du$.

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REFERENCES

- 1. H. G. SCHMID, H. FRIEBOLIN, S. KABUSS, AND R. MECKE, Spectrochim. Acta 22, 623 (1966).
- C. W. FRYER, F. CONTI, AND C. FRANCONI, Ricerca Sci. 35, II A, 788 (1965); C. A. 64. 9111 h (1966).

- A. ALLERHAND, H. S. GUTOWSKY, J. JONAS, AND R. A. MEINZER, J. Am. Chem. Soc. 88, 3185 (1966) and References cited therein.
- A. ALLERHAND AND H. S. GUTOWSKY, J. Am. Chem. Soc. 87, 4092 (1965) and References cited therein; K. H. ABRAMSON, P. T. INGLEFIELD, E. KRAKOWER, AND L. W. REEVES, Can. J. Chem. 44, 1685 (1966).
- 5. S. FORSÉN AND R. A. HOFFMAN, J. Chem. Phys. 39, 2892 (1963).
- 6. F. A. L. ANET AND A. J. R. BOURN, J. Am. Chem. Soc. 89, 760 (1967).
- 7. A. MANNSCHRECK, A. MATTHEUS, AND G. RISSMANN, J. Mol. Spectry. 23, 15 (1967).
- 8. H. S. GUTOWSKY, J. JONAS, AND T. H. SIDDALL, III, J. Am. Chem. Soc. 89, 4300 (1967).
- 9. A. MANNSCHRECK, H. MUENSCH, AND A. MATTHEUS, Angew. Chem. 78, 751 (1966); Angew. Chem. Intern. Ed. Engl. 5, 728 (1966).
- A. MANNSCHRECK AND H. MUENSCH, Angew. Chem. 79, 1004 (1967); Angew. Chem. Intern. Ed. Engl. 6, 984 (1967).
- 11. A. MANNSCHRECK AND H. MUENSCH, Tetrahedron Letters p. 3227 (1968).
- 12. A. MANNSCHRECK, Tetrahedron Letters p. 1341 (1965) and unpublished results.
- 13. T. H. SIDDALL, III, Inorg. Nucl. Chem. Letters 1, 155 (1965).
- 14. T. H. SIDDALL, III, W. E. STEWART, AND A. L. MARSTON (personal communication).
- H. W. BROWN AND D. P. HOLLIS, J. Mol. Spectry. 13, 305 (1964); G. J. KARABATSOS AND R. A. TALLER, J. Am. Chem. Soc. 86, 4373 (1964).
- 16. H. S. GUTOWSKY AND C. H. HOLM, J. Chem. Phys. 25, 1228 (1956).
- 17. J. A. POPLE, W. G. SCHNEIDER, AND H. J. BERNSTEIN, "High-Resolution Nuclear Magnetic Resonance," p. 221, McGraw-Hill, New York 1959.
- R. C. NEUMANN, JR., D. N. ROARK, AND V. JONAS, J. Am. Chem. Soc. 89, 3412 (1967);
 A. ALLERHAND AND H. S. GUTOWSKY, J. Chem. Phys. 41, 2115 (1964); F. A. BOVEY,
 F. P. HOOD, III, E. W. ANDERSON, AND R. L. KORNEGAY, J. Chem. Phys. 41, 2041 (1964).
- 19. R. ZURMUEH, "Praktische Mathematik," p. 289, Springer-Verlag, Berlin 1957.
- 20. M. SAUNDERS AND E. L. HAGEN, J. Am. Chem. Soc. 90, 2436 (1968). C. S. JOHNSON, JR., in "Advances in Magnetic Resonance" (J. S. WAUGH, ed.) Vol. 1, p. 33, Academic Press, New York 1965.
- (a) A. PAPOULIS, "The Fourier Integral And Its Applications," p. 26, McGraw-Hill, New York 1962.
 - (b) R. R. ERNST in "Advances in Magnetic Resonance," (J. S. WAUGH, ed.) Vol. 2, p. 15, p. 118, Academic Press, New York 1966.
- A. UNSOELD, "Physik der Sternatmosphären," 2. ed., p. 258, Springer Verlag, Berlin 1955.
- 23. H. FRIEBOLIN, H. G. SCHMID, AND A. JAESCHKE (unpublished results).
- 24. M. OKI AND H. IWAMURA, Tetrahedron 24, 2377 (1968).
- 25. K. MISLOW, M. A. W. GLASS, H. B. HOPPS, E. SIMON, AND G. H. WAHL, JR., J. Am. Chem. Soc. 86, 1710 (1964).
- 26. L. J. BRUBACHER, L. TREINDL, AND R. E. ROBERTSON, J. Am. Chem. Soc. 90, 4611 (1968).