cyanoethylene was 10^6 times more reactive than acrylonitrile and had a LUMO energy that was lower by 2.06 eV.

The greater preference observed for the endo stereoisomer with Lewis acid catalysis can be explained from the changes in the frontier orbitals (Table II). The endo selectivity is controlled by the interaction between the carbonyl carbon (C3') of the dienophile and the inner carbons (C2, C3) of the diene. Upon complexation with the Lewis acid, the LUMO coefficient at the carbonyl carbon is increased in size (Figure 2), and thus greater stabilization can be realized from its interaction with the secondary HOMO coefficient of the diene. Additional stabilization for this interaction is obtained from the smaller energy difference between the LUMO of the dienophile and the HOMO of the diene.

In earlier studies a rationale was reported for the effect of catalysis on the regioselectivity which included both the primary and secondary orbital interactions of the FMO's.[6b] For simplicity, other investigatiors[4,5] have used just the primary orbital interactions which can only predict an increase in regioselectivity with catalysis while it is known that in many cases the regioselectivity is in fact decreased or reversed.[2d,3a] The ab initio FMO's in this study provide a strong theoretical justification for the inclusion of the secondary orbital interactions into the FMO approach. The difference between the primary orbital coefficients of LUMO is increased by 0.12 with both STO-3G and STP-6G basis sets, while the secondary orbital coefficient is increased by 0.14 with STO-3G and 0.13 with STP-6G. The overlap between the secondary orbitals is at a minimum 40–50% of the overlap between the primary orbitals in the transition state[14] and may be higher if nonplanarity is smaller than estimated.[15] Thus, the secondary orbital interactions are expected to have a significant effect on regioselectivity in cases where the difference between the primary orbital coefficients of the diene are small and the difference between the secondary orbital coefficients of the diene are large. Several examples of the above cases have been discussed in detail in earlier publications.[6]

It may be concluded that the ab initio calculations in this study provide further support to the important role that secondary orbital interactions play in the Lewis acid catalysis of the Diels–Alder reactions.

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Registry No. Acrolein, 107-02-8; acrolein–BF_3 complex, 105456-06-2.

(14) Alston, P. V.; Ottenbrite, R. M.; Cohen, T. *J. Org. Chem.* **1978**, *43*, 1864.
(15) Brown, F. K.; Houk, K. N. *Tetrahedron Lett.* **1984**, *25*, 4609.
(16) While this manuscript was in press, studies of Lewis acid complexes were reported by Branchadell et al. (Branchadell, V.; Oliva, A.; Bertran, J. *J. Mol. Struct. (Theochem.)* **1986**, *138*, 117), who evaluated the Lewis acid catalytic effect on the Diels–Alder reactivity–selectivity relationship by means of changes in the type of energy profile from MINDO/3 calculations, and by Nelson (Nelson, D. J. *J. Org. Chem.* **1986**, *51*, 3185), who carried out a MNDO investigation to evaluate Lewis acid complexes of carbonyl compounds.

Sterically Hindered Azobenzenes: Isolation of Cis Isomers and Kinetics of Thermal Cis → Trans Isomerization

Nigel J. Bunce,* George Ferguson, Christine L. Forber, and Greg J. Stachnyk

Guelph-Waterloo Centre for Graduate Work in Chemistry (Guelph Campus), University of Guelph, Guelph, Ontario, Canada N1G 2W1

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A series of highly hindered ortho-alkylated azobenzenes has been isolated in the cis configuration for the first time. The crystal structure of one of these compounds, *cis*-2,2',6,6'-tetraisopropylazobenzene, shows that the molecule accommodates the bulky substituents by adopting a skewed conformation and by opening up the angles of the N=N bridge (C—N=N 126.4 (2)°). This result confirms predictions that were made about the geometries of these compounds based on spectroscopic evidence and quantum calculations. The activation parameters for thermal cis → trans isomerization in this series show that there is a remarkably sharp demarcation between the existence and nonexistence of cis isomers. Provided that the cis isomer is isolable at all, it isomerizes with an activation energy of ca. 90 kJ mol^{-1}. No cases were found where the cis isomer is of only marginal stability.

We have recently reported spectroscopic and quantum mechanical studies on a series of azobenzenes substituted by alkyl groups in some or all of the ortho positions.[1] Of relevance to the present study were the cis isomers **1** to **7**. These cis compounds had electronic absorption spectra that appeared to be surprisingly insensitive to the bulk of the ortho alkyl groups. Calculations indicated that the spectra could best be explained by postulating a geometry in which the N–N–C angles of the azo bridge were opened up to ca. 125° and the phenyl rings skewed to within 30–40° of a quasi-parallel conformation. In this paper, we extend our studies of the *cis*-azobenzenes in three directions: defining the limits of steric hindrance for which a cis isomer is isolable; describing the crystal structure of the highly hindered *cis*-2,2',6,6'-tetraisopropylazobenzene; and determining the activation parameters for the cis → trans thermal isomerization of a series of sterically hindered azobenzenes. The activation parameters were obtained in order to study the effect of ortho substitution

(1) Forber, C. L.; Kelusky, E. C.; Bunce, N. J.; Zerner, M. C. *J. Am. Chem. Soc.* **1985**, *107*, 5884.

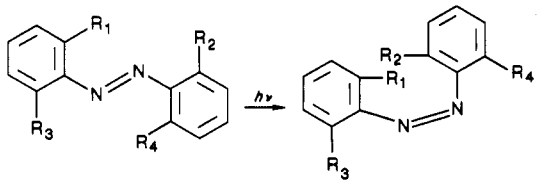
0022-3263/87/1952-0394$01.50/0

Table I. Melting Points and Activation Parameters for *cis*-Azobenzenes

no.	mp, °C	method[a] (total data points)	E_a, kJ mol^{-1}	log A	E_a (lit.)
1	69–70[b]	m (117)	91.8 ± 3.0[c]	10.47[d]	91–99[e]
2	62–63	c (51)	86.6 ± 4.3	9.94	
3	22–24	m (136)	87.1 ± 1.1	10.23	
4	106–108 dec	c (54)	93.1 ± 3.4	11.18	
5	71–72	c (62)	94.1 ± 3.0	10.77	103.8[f]
6	67–68	v (50)	96.5 ± 4.6	11.52	
7	115–117 dec	m (115)	111.2 ± 2.6	13.57	
8		c (48)	79.6 ± 1.1	11.02	
9		c (36)	91.1 ± 1.8	11.33	
10		c (93)	87.3 ± 1.1	10.77	
11		c (62)	89.7 ± 1.5	10.16	

[a] c = constant-temperature kinetic runs, v = variable-temperature kinetic runs, m = combination of constant- and variable-temperature kinetic runs. [b] Lit.[3] mp 71.4 °C. [c] ± are 95% confidence intervals. [d] Based on A in units of s^{-1}. [e] In alkane or benzene solvents, see ref 3–9. [f] See ref 9.

on the depth of the potential energy well in which the cis compounds reside.



1, $R_1 = R_2 = R_3 = R_4 = H$
2, $R_1 = R_2 = H$, $R_3 = R_4 = Me$
3, $R_1 = R_2 = H$, $R_3 = R_4 = Et$
4, $R_1 = R_2 = H$, $R_3 = R_4 = i\text{-Pr}$
5, $R_1 = R_2 = R_3 = R_4 = Me$
6, $R_1 = R_2 = R_3 = R_4 = Et$
7, $R_1 = R_2 = R_3 = R_4 = i\text{-Pr}$
8, $R_1 = R_2 = Me$, $R_3 = R_4 = t\text{-Bu}$
9, 2,4,6-tri-*tert*-butylazobenzene
10, 2,2',5,5'-tetraisopropylazobenzene
11, 2,2',5,5'-tetra-*tert*-butylazobenzene
12, 2,2',4,4',6,6'-hexa-*tert*-butylazobenzene

Results

The cis compounds were obtained by photolysis of their trans isomers in alkane solvents, followed by chromatography of the resulting mixtures over silica gel. Compounds **1–7** were all prepared successfully in this way; they were isolable (see Table I) and could be purified by conventional means, usually crystallization from hexanes. In the cases of **10** and **11**, only a few milligrams of the trans compounds were available, and there was insufficient material to isolate the cis isomers. In these cases, the evidence for the cis isomer depended upon spectral changes following irradiation, but because these changes were completely reversible thermally, it was nonetheless possible to carry out kinetic studies.

A combination of steady-state irradiation and flash photolysis was used to reach a decision on whether cis isomers of the azo compounds **8**, **9**, and **12** could be formed. Azobenzene (**1**) and the tetraisopropyl homologue **7** were taken as reference compounds. Continuous irradiation caused rapid trans → cis isomerization of **1** and much slower isomerization of **7** as shown by UV absorbance changes. With **8** and **9**, the absorbance changes were small.[2] Prolonged continuous irradiation of **8** and **9** followed by chromatography over alumina afforded solutions rich in the cis isomer. With **12**, no changes were observed upon irradiation.

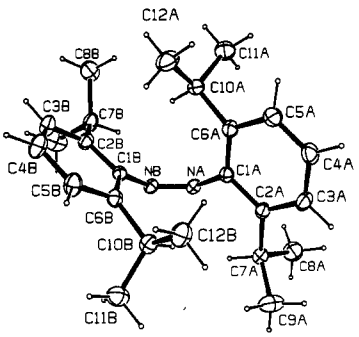


Figure 1. ORTEP diagram of *cis*-2,2',6,6'-tetraisopropylazobenzene. The isopropyl groups centered on C7A and C7B are "peripheral", and those on C10A and C10B are "interior". Principal mean dimensions are the following: N=N 1.248 (4), N–C_{sp^2} 1.450 (4), aromatic C_{sp^2}–C_{sp^2} 1.389 (4), C_{sp^2}–C_{sp^3} 1.521 (4), C_{sp^3}–C_{sp^3} 1.535 (4) Å.

Flash photolysis on compounds **1**, **7**, **8**, **9**, and **12** was carried out with absorbances monitored at convenient wavelengths in the 300–320-nm range. All compounds exhibited transient bleaching, with the bleached intermediate having a lifetime in the 50–100-μs range. The following observations all relate to the stable absorbance reached after 200 μs: azobenzene, strong reduction in absorbance; **7** and **8**, small reductions in absorbance; **9** and **12**, no change from the initial absorbance. From these experiments it was concluded that only **12** did not form a cis isomer upon photolysis; the cis isomers of **8** and **9** can be formed, but the photostationary states are predominantly trans.

The crystals of the cis isomer of compound **7** contain well-resolved molecules separated by normal van der Waals distances. Figure 1 shows a view of the molecule and our numbering scheme. Although no crystallographic symmetry is required by the space group, the molecule has close to twofold symmetry, with the twofold axis passing through the mid-point of the N=N bond.

The bond lengths (mean aromatic C_{sp^2}–C_{sp^2} 1.389, C_{sp^2}–C_{sp^3} 1.521, C_{sp^3}–C_{sp^3} 1.535, C_{sp^2}–N 1.450 (4), and N=N 1.248 (4) Å) serve to establish the structure. Intramolecular overcrowding effects are relieved mainly by angle bending, by out-of-plane displacements, and by rotation about bonds. Thus, the C—N=N angles (mean 126.4 (2)°) are significantly greater than 120° (*cis*-azobenzene has C—N=N angles 121.9°[10]), and the substituents on the phenyl rings are all displaced out of the plane (0.10–0.16 Å) in a direction away from the adjacent ring system. The phenyl rings are each rotated about the exocyclic C–N bonds so that the mean interplanar angle between a phenyl ring and the relevant C—N=N plane is 56° (a skew angle of 34° where the skew angle indicates the angle away from a "face-to-face" orientation). We had previously predicted[1] that in the cis isomer of compound **5**, the phenyl rings would be skewed by 24°, and this is entirely in accord with the corresponding skew angle reported here for the more crowded isopropyl compound.

(2) Bisle and Rau saw similar small changes in the UV spectrum of 2,2'-dimethyl-4,4',6,6'-tetra-*tert*-butylazobenzene: Bisle, H.; Rau, H. *Chem. Phys. Lett.* **1975**, *31*, 264.

(3) Hartley, G. S. *J. Chem. Soc.* **1938**, 633.
(4) Schulte-Frohlinde, D. *Justus Liebigs Ann. Chem.* **1958**, *612*, 138.
(5) Halpern, J.; Brady, G. W.; Winkler, C. A. *Can. J. Res., Sect. B* **1950**, *28*, 140.
(6) Le Fevre, R. J. W.; Northcott, J. *J. Chem. Soc.* **1953**, 867.
(7) Brown, E. V.; Granneman, G. R. *J. Am. Chem. Soc.* **1975**, *97*, 621.
(8) Andersson, J.-Å.; Petterson, R.; Tegnér, L. *J. Photochem.* **1982**, *20*, 17.
(9) Otruba, J. P., III; Weiss, R. G. *J. Org. Chem.* **1983**, *48*, 3448.
(10) Mostad, A.; Romming, C. *Acta Chem. Scand.* **1971**, *25*, 3561.

All of the isopropyl groups are oriented in a similar fashion, with the C–H groups (at C7A, C10A, C7B, and C10B) arranged syn to the exocyclic C–N bond (Figure 1). These rotations serve to position one proton on each of the isopropyl carbons C12A and C12B above and essentially equidistant from the carbon atoms of the adjacent phenyl ring (C1B to C6B and C1A to C6A, respectively), with H···C contacts in the range 2.9–3.1 Å, and in accord with the sum of the van der Waals radii of benzene and hydrogen (3.05 Å).

The activation parameters for the thermal cis → trans isomerization were obtained in isooctane solvent for all the cis compounds that could be formed. The kinetic studies were carried out by various methods, both of a conventional, constant-temperature kind and also using a variable-temperature procedure. A one-step computational method was used to calculate the activation parameters from the raw kinetic data. An outline of the latter is given in the Experimental Section, but full details will be published elsewhere. With the exceptions of the tetraisopropyl compound **7**, which has the highest activation energy in the series,[11] and the di-*tert*-butyldimethyl compound **9**, which has the lowest, the activation parameters (see Table I) are all similar (E_a = 87–97 kJ mol^{-1} and log A = 10–11) and show no strong trend with increasing steric hindrance.

Discussion

The notable feature of our results is that *cis*-azobenzenes seem to show a completely sharp demarcation between those compounds that can exist and those that apparently cannot. It appears that all ortho-alkyl-substituted azobenzenes wherein the alkyl groups are no larger than isopropyl can form stable cis isomers. It also appears that those azobenzenes with two ortho *tert*-butyl groups also can form cis isomers whether the two *tert*-butyl groups are on the same ring or different rings. Our work does not indicate whether cis isomers can be formed from compounds with three of the four ortho positions substituted with *tert*-butyl groups, but compounds with all four ortho positions substituted by *tert*-butyl groups do not form cis isomers.

It is interesting to examine the crystal structure of the tetraisopropyl compound **7**. This molecule minimizes steric hindrance by adopting a conformation in which the C—N=N—C bridge angles open up, while the phenyl rings are in a rather skewed arrangement. (This structure confirms completely the predictions[1] for these *cis*-2,2′,6,6′-tetraalkylated azobenzenes that were made by quantum mechanical calculations.) The effect of this is to put one isopropyl group on each ring in a "peripheral" position away from the distant aromatic ring, while the other is in a more "interior" position. The characteristic of the interior isopropyl groups is that they can avoid unfavorably close contact with the distant aromatic ring only in the conformation wherein the CH(CH$_3$)$_2$ hydrogen of each isopropyl group (those on C10A and C10B) points toward the N=N bridge, and the methyl substituents are bent back from the distant ring.

The 2,2′-di-*tert*-butyl compounds **8** and **11** can achieve cis configurations if each ortho *tert*-butyl group adopts a peripheral position. This is not possible for the 2,6-substituted compounds **9** and **12**, in which one (or two) *tert*-butyl groups must necessarily take up interior positions where there is serious interference with the N=N bridge. In the absence of a crystal structure for compound **9**, we assume that the absence of ortho alkyl groups on the unsubstituted benzene ring allows distortion of the molecule to accommodate the interior *tert*-butyl group. The symmetry of compound **12** does not allow for such accommodation, and thus this compound does not form a cis isomer.

The di-*tert*-butyldimethyl compound **8** must lie very close to the cutoff between the existence and nonexistence of the cis isomers. In a comparison of models of **8** and **11**, the additional methyl groups in the 6,6′ positions (on C7A and C7B in the numbering scheme of Figure 1) cause a closer approach between these new methyl groups and the methyl substituents on C10A and C10B. One would be able to rationalize either the existence (the actual case) or the nonexistence of this cis compound equally easily.

Perhaps the most striking discovery from this study is the lack of a strong trend in the cis → trans activation energies of Table I. All but two (as noted before) of the compounds that formed cis isomers had an E_a in the range 87–97 kJ mol^{-1}. In the language of transition-state theory, the enthalpies of activation are very similar to E_a, while the entropies of activation, which are in the range 33–64 J mol^{-1} K^{-1}, indicate modestly increased disorder at the transition state.[12] This is consistent with the inversion mechanism of thermal isomerization: the change of hybridization makes the process enthalpically disfavored, while the positive $\Delta S^{\ddagger}$ reflects the greater freedom as the molecule reorganizes from the highly restricted cis configuration. There appears to be no trend toward decreasing cis stability with increasing steric hindrance. If anything, there is a slight trend toward higher E_a and log A with increasing alkyl size, but since E_a and log A are closely correlated, it is hard to tell whether these small trends are real or artifacts. Consistent with this apparent trend, however, Otruba and Weiss[9] have found that the cis → trans activation energies of 2,6-dimethylated azobenzenes are ca. 10 kJ mol^{-1} higher than those of comparable azobenzenes lacking the 2 and 6 substituents. It does seem that the potential energy well that is responsible for the existence of the cis isomer is of comparable depth whether the alkyl groups are large or small, until the point is reached where steric hindrance does not permit the cis isomer to exist at all. We presume that for the nonisolable *cis*-**12**, the energy well resulting from bonding the *cis*-azobenzene is cancelled out by steric repulsions of the types discussed already. (There are, of course, two other explanations, either (i) that for some reason the photochemical trans → cis conversion proceeds with an excessively large activation energy in these instances or (ii) that the excited cis isomer lies on a one-way energy surface,[13] which leads it inexorably back to the trans.)

The lack of a strong trend in the cis → trans thermal activation energies has a bearing on the question of the mechanism of this isomerization, which has been the subject of much discussion.[9,14-20] Our results support the

(11) When the three variable-temperature runs (51 data points) were omitted, the activation parameters changed slightly: E_a = 108.0 ± 1.3 kJ mol^{-1}, log A = 13.12.

(12) Only compound **7** lies outside this range ($\Delta S^{\ddagger}$ = −11 kJ mol^{-1}), but in view of the high correlation that always exists between E_a and log A, we do not wish to advocate a change of mechanism on this evidence alone.

(13) Hamaguchi, H.; Tasumi, M.; Karatsu, T.; Arai, T.; Tokumaru, K. *J. Am. Chem. Soc.* **1986**, *108*, 1698.
(14) Wildes, P. D.; Pacifici, J. G.; Irick, G., Jr.; Whitten, D. G. *J. Am. Chem. Soc.* **1971**, *93*, 2004 and references therein.
(15) Rau, H.; Lüddecke, E. *J. Am. Chem. Soc.* **1984**, *104*, 1616 and references therein.
(16) Rau, H. *J. Photochem.* **1984**, *26*, 221.
(17) Nishimura, N.; Kosako, S.; Sueishi, Y. *Bull. Chem. Soc. Jpn.* **1984**, *57*, 1617 and references therein.
(18) Nishimura, N.; Tanaka, T.; Sueishi, Y. *J. Chem. Soc., Chem. Commun.* **1985**, 903.
(19) Afanas'ev, S. V.; Moiseeva, L. V.; Zalukaev, L. P. *Russ. J. Phys. Chem. (Engl. Transl.)* **1978**, *52*, 1445.
(20) Monti, S.; Orlandi, G.; Palmieri, P. *Chem. Phys.* **1982**, *71*, 87.

nitrogen inversion mechanism, which has generally been favored recently, over the N–N rotation mechanism.[21] It is easy to rationalize how inversion would be insensitive to steric hindrance at the ortho positions, because the route to the transition state straightens out the molecule, and the interfering substituents merely move progressively further apart. By contrast, N–N rotation is difficult to achieve without swinging the bulky groups directly past one another.

A final comment concerning both the sharp demarcation between the existence and nonexistence of cis isomers and the lack of a strong trend in activation parameters is that the *cis*-ortho-alkylazobenzenes seem to represent a unique example among trends in steric hindrance. In classical examples of increasing steric hindrance, the observed phenomenon shows a progressive and regular change as the degree of steric hindrance is increased. Such examples include the variation in the ortho:para ratios upon nitration of monoalkylbenzenes,[22] the variation in the equilibrium constants of 1-alkyl-2,2′-dimesitylethanol/1-alkyl-2,2′-dimesitylethanone systems in hexane,[23] the shifts in the electronic spectra of ortho-substituted biphenyls[24] and of α-substituted styrenes,[25] and those examples given in the review by Tidwell.[26] The *cis*-azobenzenes are unique in that with respect to both spectroscopy and kinetics of isomerization, all the isolable members of the series have essentially the same properties, i.e., no trend is apparent.

Experimental Section

Alkylated azobenzenes **2–7** were available from our previous study. The di-*tert*-butyldimethylazobenzene **8** was prepared by oxidation of 2-*tert*-butyl-6-methylaniline using AgO:[27] mp 113–114 °C; ^{1}H NMR ($CDCl_3$, 60 MHz) δ 1.3 (s, 18 H), 2.2 (s, 6 H), 7.0–7.4 (m, 6 H). Anal. Calcd for $C_{22}H_{30}N_2$: C, 81.94; H, 9.38; N, 8.69. Found: C, 81.67, 81.72; H, 9.75, 9.57; N, 8.43, 8.09. UV/vis λ_{max} (ε): 481 (1050), 301 (13 800), 244 nm (8460).

Cooxidation of aniline and 2,4,6-tri-*tert*-butylaniline by the method of Barclay et al.[28] afforded 2,4,6-tri-*tert*-butylazobenzene (**9**), mp 143.2–144 °C (lit.[28] mp 156–158 °C). Because of the disparity in the melting points, the compound was fully characterized. Anal. Calcd for $C_{24}H_{34}N_2$: C, 82.23; H, 9.78; N, 7.99. Found: C, 82.37, 82.30; H, 10.27, 9.56; N, 7.46, 7.63. MS, *m/e* (intensity) 351 (6.7), 350 (24), 259 (50), 77 (32), 57 (100). UV/vis λ_{max} (ε): trans, 460 (360), 320 (shoulder, 3600), 266 nm (15 200); cis, 465, 266, 250 nm (shoulder).

Compounds **10** and **11** were gifts kindly supplied by Dr. H. Rau; compound **12** was kindly donated by Dr. L. R. C. Barclay.

The cis compounds were isolated by dissolving the purified trans compound, 1–2 g, in ca. 250 mL of petroleum ether (the fraction of bp 30–60 °C) and irradiating with a 450-W medium-pressure mercury lamp in a water-cooled immersion well for 4–6 h. Most of the solvent was then removed by using a rotary evaporator and a cool water bath in a dark room. The concentrated solution was chromatographed over acid alumina in the dark with petroleum ether as eluting solvent until the fractions were colorless, to remove the trans compound. The solvent was then changed to diethyl ether to elute the cis compound. The second set of fractions was combined, the solvent removed, and the residue recrystallized from cold petroleum ether in a darkened room.

Flash photolyses were performed with use of a PRA Model FP1000 microsecond flash photolysis apparatus. This equipment uses the unfiltered radiation of two Nobelight Model 4419 xenon lamps with flash energy of ca. 60 J and a flash duration of 10 μs. Transient absorbances were displayed on a Techronix Model T912 storage oscilloscope. Samples were studied at ambient temperature in aerated solution with use of a 1 cm × 10 cm cylindrical quartz cuvette. The monochromator for the monitoring beam was set at a convenient wavelength in the range 300–320 nm, and care was taken to shut off the monitoring beam before the flash so as to avoid inadvertent photolysis.

Crystal data for *cis*-2,2′,6,6′-tetraisopropylazobenzene: $C_{24}H_{34}N_2$, M_r = 350.6, orthorhombic, a = 10.681 (1), b = 11.491 (2), c = 17.890 (2) Å^3, Z = 4, D_{calcd} = 1.06 g cm^{-3}, $F(000)$ = 768, Mo radiation λ = 0.71069 Å, μ(Mo Kα) = 0.6 cm^{-1}; space group $P2_12_12_1$ determined uniquely from the systematic absences ($h00$, $0k0$, $00l$ all halved).

A unique octant of data with $2° < \theta < 27°$ was measured with a small (0.25 × 0.35 × 0.35 mm) crystal with use of an Enraf-Nonius CAD4 diffractometer and graphite monochromatized Mo Kα radiation. Data collection was carried out in the dark as the sample is light sensitive; from measurements every 2 h of three reflections chosen as controls, there was no evidence of crystal decay. Accurate cell parameters and crystal orientation matrix were determined from the setting angles of 25 reflections with θ in the range 8–12°. The data were corrected for Lorentz and polarization effects. Of the 2844 reflections surveyed, 2719 were unique and not systematically absent, and of these, the 1825 with $I > 3\sigma(I)$ were labeled observed and used in the structure solution and refinement.

The structure was solved with the aid of MULTAN-82[29] and refined[30] by full-matrix least-squares calculation, initially with isotropic and finally with anisotropic thermal parameters. Difference maps computed at various stages in the refinement showed all hydrogen atoms clearly as the main features. The hydrogen atoms were included, in geometrically idealized locations (C–H 0.95 Å), but not refined in the final rounds of refinement. At convergence (with the parameter shift/error ratio < 0.01), R = 0.051 and $R_w = (\sum w\Delta^2/\sum wF_o^2)^{1/2}$ = 0.080. The final difference map was featureless (with peaks and valleys less than 0.13 e Å^{-3}). In the refinement cycles, weights were derived from counting statistics and scattering factor data were taken from ref 31.

Kinetic Procedures. Three procedures were used in the determination of the activation energy parameters.

Constant Temperature. A. A stock solution of the purified *trans*-azobenzene was prepared in isooctane (Fisher). Aliquots (4 mL) were transferred to ampules made from 8-mm-o.d. Pyrex tubing. The tubes were sealed without evacuation and then mounted uniformly around the inside of a large beaker and held in place with a cork ring. The beaker was filled with crushed ice and rotated to ensure uniform irradiation. The light source was a Rayonet RUL photoreactor equipped with eight RUL 3500 lamps having peak output at 350 nm. The samples were irradiated for 2–4 h to form the cis–trans mixture, after which each ampule was individually wrapped in aluminum foil and kept cool, being stored if necessary in a refrigerator.

The heat source used was a Haake D3-G refrigerated bath and circulator with a working temperature range of −10 to 150 °C. When the bath was stabilized at the appropriate temperature, the ampules (still wrapped in foil) were placed in the reservoir and the time was noted. At various times, one ampule from each set was removed from the bath, immediately plunged into an ice bath, and shaken well. After being left in the ice water for at least 2 min, the tubes were removed and allowed to warm to room

(21) Another aspect of the lack of a trend in the E_a values is that they seem to suggest that the ground-state energies of these azobenzenes do not change much with increasing steric hindrance. The alternative possibility, that the ground-state-energy changes are exactly canceled out by transition-state changes, seems to us to require too much of a coincidence.

(22) Norman, R. O. C.; Taylor, R. *Electrophilic Substitution in Benzenoid Compounds*; Elsevier: Amsterdam, 1965; pp 78–79.

(23) Nugiel, D. A.; Rappoport, Z. *J. Am. Chem. Soc.* **1985**, *107*, 3669.

(24) Suzuki, H. *Electronic Absorption Spectra and Geometry of Organic Molecules*; Academic: New York, 1967; pp 279–283.

(25) Suzuki, H. *Electronic Absorption Spectra and Geometry of Organic Molecules*; Academic: New York, 1967; pp 293–300.

(26) Tidwell, T. T. *Tetrahedron* **1978**, *34*, 1855.

(27) Ortiz, B.; Villanueva, P.; Walls, F. *J. Org. Chem.* **1972**, *37*, 2748.

(28) Barclay, L. R. C.; Dust, J. M.; Brownstein, S.; Gabe, E. J. *Org. Magn. Reson.* **1981**, *17*, 175.

(29) Main, P.; Fiske, S. J.; Hull, S. E.; Lessinger, L.; Germain, G.; Declercq, J. P.; Woofson, M. M. MULTAN-82, Universities of York and Louvain, 1982.

(30) Frenz, B. A. In *Computing in Crystallography*; Schenk, H., Olthof-Hazelkamp, R., van Konigsveld, H., Bassi, G. C., Eds.; Delft University: Delft, Holland, 1978; pp 64–71.

(31) Cromer, D. T.; Weber, J. T. *International Tables for X-Ray Crystallography*; Kynoch: Birmingham, England, 1974; Vol. 4, Table 2.2B.

temperature. After removal of the foil, the room lights being off, the ampule was broken open and the absorbance recorded. Absorbances were read to three decimal places with use of a Perkin-Elmer Lambda 3 spectrophotometer. The infinity readings were obtained by placing a foil-wrapped ampule of each set in a steam bath for at least 1 h before recording the absorbance.

B. For compounds obtained in small amounts, a variation on the above procedure was used. A solution with the appropriate concentration of the *trans*-azobenzene in isooctane was prepared, and about 3 mL was sealed in a 1-cm^2 quartz ampule. This ampule was irradiated in the RUL photoreactor in a water-cooled immersion well for at least 3 h. The constant-temperature bath described above was used to heat the cuvette holder of the spectrophotometer. The ampule was partially preheated in the reservoir of the constant-temperature bath before being placed into the heated cuvette holder. It was then left for 30–60 s to establish temperature equilibrium, and a zero time and absorbance were recorded. Between readings, a black-felt-covered card was placed in the light beams to prevent any photochemical isomerization. The infinity reading was obtained by placing the ampule in a steam bath in the dark for at least 1 h, putting it back in the spectrophotometer, waiting for temperature equilibration with the card in place, and finally recording the absorbance. The temperature was determined by using a similar unsealed ampule placed in the heated cuvette holder after the kinetic run was completed (usually while waiting for the infinity reading). This ampule was filled with isooctane to the same height as the sealed ampules. An electronic (thermistor) thermometer with a flexible cable was used to read the temperature.

Variable Temperature. C. Solutions and ampules were prepared as in method A and irradiated. The thermal isomerization was carried out by using a thermostated oil bath whose heater was controlled with a variable autotransformer. The temperature was measured with an electronic (thermistor) thermometer, the probe of which was placed in an ampule of isooctane similar to the test ampules. At suitable temperature intervals, one or more tubes were removed from the thermostat and cooled quickly in an ice bath. The corresponding temperature and time were recorded, and the absorbance was measured after the ampule was allowed to return to room temperature. The infinity readings were obtained by leaving one or more ampules in a steam bath for at least 1 h before recording their absorbances.

Data Analysis. Activation energies were calculated from the raw kinetic observations of absorbance, temperature, and time by a one-step procedure, full details of which will be published elsewhere. Briefly, the computational method consists of substituting the Arrhenius equation directly into the first-order rate expression (Abs, Abs_0, and Abs_{inf} are absorbances at time t, time 0, and the infinity reading).

Thus,

$$\int_0^t \frac{d(Abs - Abs_{inf})}{Abs - Abs_{inf}} = -\int_0^t k\, dt = -\int_0^t Ae^{-E_a/RT}\, dt \quad (1)$$

For a constant-temperature kinetic run, integration affords eq 2, while when the temperature varies, eq 1 must be integrated

$$Abs - Abs_{inf} = (Abs_0 - Abs_{inf}) \exp(-At \exp(-E_a/RT)) \quad (2)$$

numerically. In either case, an iterative procedure allows trial values of A and E_a to be fitted to the known values of Abs, Abs_0, time (t), and temperature (T).

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Supplementary Material Available: Final atomic coordinates, details of molecular geometry, and thermal parameters (9 pages). Order information is given on any current masthead page. A structure factor listing is available from G.F. (28 pages). Tables of all raw kinetic data are available from N.J.B. (18 pages).

Retinoids. 6.[1] Preparation of Alkyl- and Trimethylsilyl-Substituted Retinoids via Conjugate Addition of Cuprates to Acetylenic Esters[†]

Ludger Ernst,[‡] Henning Hopf,*[§] and Norbert Krause[§]

Gesellschaft für Biotechnologische Forschung (GBF), Mascheroder Weg 1, D-3300 Braunschweig, FRG, and the Institut für Organische Chemie der Technischen Universität, Hagenring 30, D-3300 Braunschweig, FRG

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Five retinoids bearing the ethyl, *tert*-butyl, and trimethylsilyl groups in the 9-position of retinal and the ethyl and *tert*-butyl groups in the 13-position have been synthesized. The key step of the syntheses involves the conjugate addition of lithium diethylcuprate, lithium di-*tert*-butylcuprate, and lithium bis(trimethylsilyl)cuprate, respectively, to the acetylenic esters **4** and **13**. The stereoselectivity of this reaction was examined in detail; it proceeds stereoselectively cis in THF at −78 °C. Various isomers of the newly prepared retinoids were isolated by preparative HPLC and characterized by the usual spectroscopic methods. The dependence of the configuration and conformation of the polyene chain on the introduced group was studied by means of NMR and UV spectroscopy.

Introduction

Retinal (**1**) plays a pivotal role in two light energy converting processes, (i) the process of vision in vertebrates[2] and (ii) the proton pumping process in *Halobacterium halobium*;[3] the proteins responsible for these processes, rhodopsin and bacteriorhodopsin, respectively, both contain retinal as the prosthetic group[2,4] (Figure 1).

[†] Dedicated to Professor Dr. S. Hünig on the occasion of his 65th birthday.

[‡] Gesellschaft für Biotechnologische Forschung.

[§] Institut für Organische Chemie der Technischen Universität.

(1) Part 5: Hopf, H.; Krause, N. *Tetrahedron Lett.* **1985**, *26*, 3323–3326.

(2) Balogh-Nair, V.; Nakanishi, K. In Stereochemistry; Tamm, Ch., Ed.; Elsevier: Amsterdam, 1982; pp 283–334.

(3) (a) Oesterhelt, D. *Angew. Chem.* **1976**, *88*, 16–24; *Angew. Chem., Int. Ed. Engl.* **1976**, *15*, 17. (b) Henderson, R. *Annu. Rev. Biophys. Bioeng.* **1977**, *6*, 87–109.

(4) Oesterhelt, D.; Stoeckenius, W. *Nature (London), New. Biol.* **1971**, *233*, 149–152.

0022-3263/87/1952-0398$01.50/0