A plot of gas-phase vs solution-phase acidities for these radical cations is reasonably linear with a slope near unity (Figure 1), indicating that solvation for these highly delocalized radical cations remains nearly constant. Similar plots have been obtained for gas-phase vs aqueous-phase basicities of hydrocarbon bases giving highly delocalized carbocations,[26] and for gas-phase vs $Me_2SO$-phase acidities of hydrocarbons giving delocalized carbanions.[22]

It is also possible that the radical cations and radical solvation terms, $\Delta G_s^\circ(HA^{\bullet+})$ and $\Delta G_s^\circ(A^\bullet)$, in the cycle (Scheme I) are proportional to one another. This would also lead to a linear relationship. The cycle allows one to estimate the solvation energy for the radical cation when the solvation energy of the radical is known. For example, adding $T\Delta S$ in $Me_2SO$ (−0.97 kcal/mol) and the gas phase (−8.4 kcal/mol) to the free energy terms for the aniline radical-cation acidity in solution and the gas phase given in Tables I and II gives enthalpy values of −8 and −213 kcal/mol, respectively.[27] The enthalpy of solvation of the proton by $Me_2SO$ is reported to be −276 kcal/mol,[28] and that of the aniline radical can be assumed to be the same as that of aniline, −13.5 kcal/mol.[29] The heat of solvation of the aniline radical cation, $\Delta H_s(HA^{\bullet+})$, calculated by eq 6, where $\Delta H_i^\circ(g)$ and $\Delta H_i^\circ(s)$

$$\Delta H_s^\circ(HA^{\bullet+}) = \Delta H_i^\circ(g) + \Delta H_s^\circ(A^\bullet) + \Delta H_s^\circ(H^+) - \Delta H_i^\circ(s) \quad (6)$$

are enthalpies of ionization of $HA^{\bullet+}$ in the gas phase and in solution, is then found to be −84.5 kcal/mol. This value is in good agreement with the value of −76.6 kcal/mol found for the anilinium cation in water,[32] when the difference in solvents is taken into account.[33]

### Summary and Conclusions

The nearly linear plot of acidities of radical cations in the gas phase with those in $Me_2SO$ solution (Figure 1) shows that solvation for these delocalized species remains relatively constant. The order of acidities of the parent uncharged acids HA is similar in the two media except for $CpH_2$ and $PhNH_2$, where solvation effects cause minor differences. The intrinsic radical-cation acidity order for radical cations $HA^{\bullet+}$ is quite different from that for the corresponding acids HA. Removal of an electron from the hydrocarbon acids enhances their gas-phase acidities to the point where they are stronger acids by about 10–40 kcal/mol than are the corresponding SH, OH, and NH radical-cation acids. The effects of structural changes on the acidities are rationalized in terms of their effects on the radical cations (stabilization is acid weakening) and on the radicals formed on deprotonation (stabilization is acid strengthening). One of the largest effects of this kind was observed for the $PhNH_2^{\bullet+}$ radical cation, where a highly favorable overlap between the odd electron in the benzene ring weakens the acidity by ~20 kcal/mol, relative to the $PhOH^{\bullet+}$ radical cation. The enthalpy of solvation of the aniline radical cation in $Me_2SO$ is estimated to be −84.5 kcal/mol.

**Acknowledgment.** This work was supported by a grant from the National Science Foundation. We thank T. A. Cripe for suggesting the comparison of gas-phase and solution-phase radical-cation acidities, and F.G.B. thanks the Department of Chemistry of the University of California, Irvine, where this paper was written, for their hospitality.

(26) Figure 18 in: Taft, R. W. *Prog. Phys. Org. Chem.* **1983**, *19*, 248–346.
(27) Aue, D. H.; Bowers, M. T. In *Gas Phase Ion Chemistry*; Bowers, M. T., Ed., Academic Press, New York 1979; Vol. 2 Chapter 9 pp 2–52.
(28) Domain, R.; Rinfret, M.; Benoit, R. L. *Can. J. Chem.* **1976**, *54*, 2101–2109.
(29) Calculated from the heat of solution of liquid aniline in $Me_2SO$ (−2.2 kcal/mol)[30] and the heat of vaporization of aniline (11.3 kcal/mol).[31]
(30) Benoit, R. L.; MacKinnon, M. J.; Bergeron, L. *Can. J. Chem.* **1981**, *59*, 1501–1504.
(31) *CRC Handbook of Chemistry and Physics*, 67th ed.; Weast, R. C., Ed.; CRC Press: Boca Raton, Fl, 1986–1987.
(32) Arnett, E. M. *J. Chem. Educ.* **1985**, *60*, 385–391.
(33) If the enthalpy of transferring 1 mol of anilinium cation from $H_2O$ to $Me_2SO$ is assumed to be similar to that of a proton (−6.1 kcal/mol),[30] it follows that the heat of solvation of $PhNH_3^+$ in $Me_2SO$ should be about −83 kcal/mol. Solvation of $PhNH_3^+$ should be a good model for that of $PhNH_3^{\bullet+}$.

# Stereoselective Azine Formation in the Decomposition of Phenyldiazomethanes

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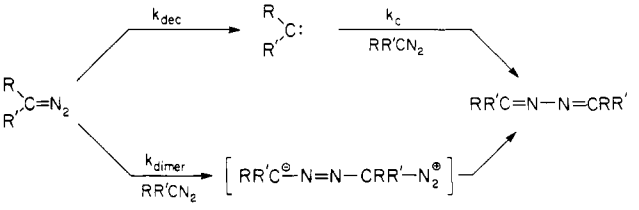
**Abstract:** The bimolecular dimerization of phenyldiazomethane (**1**) and 1-diazo-1-phenylethane (**2**) to form the corresponding azines (**3** and **4**) is stereoselective for the *E,Z* isomer (>95:5 *E,Z*:*E,E*). The *E,Z* isomer can be isolated from the reaction of **2**, and it can be observed but not isolated from the reaction of **1**. Both (*E,Z*)-**3** and -**4** revert thermally to the more stable *E,E* isomer. The kinetic parameters of this process were determined for (*E,Z*)-**4**: $E_a$ = 22.3 kcal/mol, log $A$ = 11.2. The stereoselectivity is accounted for within the context of the accepted mechanism for azine formation via diazo compound dimerization.

Azines often are the major thermal decomposition products of diazo compounds.[1] They can result from the reaction of a carbene with a diazo compound and from the bimolecular reaction of two diazo compounds. In dilute solution the carbene reaction pathway usually dominates, whereas in concentrated solution or the neat state, the bimolecular reaction is important. With phenyldiazomethane (**1**) in $CH_3CN$ at 85 °C the two processes occur with equal rates when [**1**] = 0.024 M.[2] The bimolecular reaction of 1-diazo-1-phenylethane (**2**) totally dominates the decomposition pathways when [**2**] ≃ 1.0 M (70 °C, hexane/benzene).[3] The mechanism for the reaction (Scheme I) is thought to involve nucleophilic attack of the carbon of the first diazo compound upon

**Scheme I**



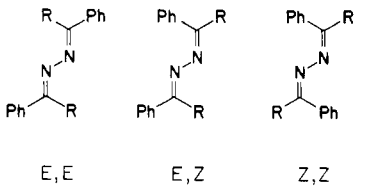

R = Ph, R' = H: 1 R = Ph, R' = H: 3
R = Ph, R' = $CH_3$: 2 R = Ph, R' = $CH_3$: 4

(1) Regitz, M; Mass, G. *Diazo Compounds: Properties and Synthesis*; Academic Press: New York, 1986; pp 66–72.
(2) Bethell, D.; Whittaker, D. *J. Chem. Soc. B* **1966**, 778–782.

0002-7863/89/1511-1795$01.50/0 

the terminal nitrogen of the second. The resulting intermediate containing a carbanionic carbon and a diazonium group loses nitrogen to form the azine.

Decomposition of unsymmetrical diazo compounds can give rise to three geometrical azine isomers in the *s-trans* conformation: *Z,Z*, *Z,E*, and *E,E*. The *E,E* isomer is usually the lowest energy isomer when there is a significant size difference between the groups attached to the carbon. For example, the phenyl group prefers the *trans* orientation with respect to the N–N bond in benzaldehyde azine (**3**) and acetophenone azine (**4**). In some cases small amounts of the other azine isomers can be observed by NMR in concentrated samples,[4] but not for **3** and **4**. A photochemical equilibrium composed of substantial amounts of the other isomers often can be achieved through direct or sensitized photolysis of the *E,E* isomer.[5-7] McBride and co-workers report that sensitization of (*E,E*)-**4** with benzil leads to a 68% conversion to (*E,Z*)-**4**.[8] No one has reported similar results with benzaldehyde azine; indeed, calculations suggest that conversion through direct irradiation may not be possible.[9]




This paper examines the reaction of phenyldiazomethane and 1-diazo-1-phenylethane to form azines and the subsequent azine isomerism. The discovery of the stereoselectivity was made initially in studying the complexes of β-cyclodextrin with diazo compounds.[10] We noticed that the included azine side products differed from the azines produced through independent syntheses. Although β-CD is known to exert control on many reactions, it was not the source of the effect in this case. The β-CD complexation results relevant to this work are also reported.

## Experimental Section

NMR spectra were recorded on a QE-300 spectrometer. Gas chromatography was performed on a Hewlett-Packard 5790A instrument using a 30-m capillary column of OV-1 and an FID detector. UV and IR spectra were obtained with a Beckman DU-70 and a Perkin-Elmer 1320 spectrophotometer, respectively. Melting points were determined with a Thomas-Hoover capillary melting point apparatus and are not corrected. Combustion analysis was performed by Desert Analytics, Tuscon, AZ. Azines of benzaldehyde and acetophenone were prepared by reaction with hydrazine hydrate.[11] Tosylhydrazones of benzaldehyde and acetophenone were prepared through condensation of the carbonyl compound with tosylhydrazine.[12] The diazo compounds were generated by vacuum pyrolysis of the tosylhydrazone sodium salts and were condensed in an ice/EtOH-cooled flask.[12,13] After the mass of the diazo compound was determined, it was diluted to a specific volume with an inert, volatile solvent ($Et_2O$ and pentane). Solutions of various concentrations were made by taking a known volume of the solution, removing the solvent under aspirator pressure at 0 °C, and then diluting with the appropriate amount of solvent. Purity of the samples was determined by NMR spectroscopy. Diazo compounds taken directly from the preparation were >90% pure, whereas after further manipulation, the purity dropped to >80% (cf. the sample compositions at 0 min in Figure 1). The impurities were composed of the isomeric azines. In particular, the corresponding carbonyl compounds comprised <2% of the sample.

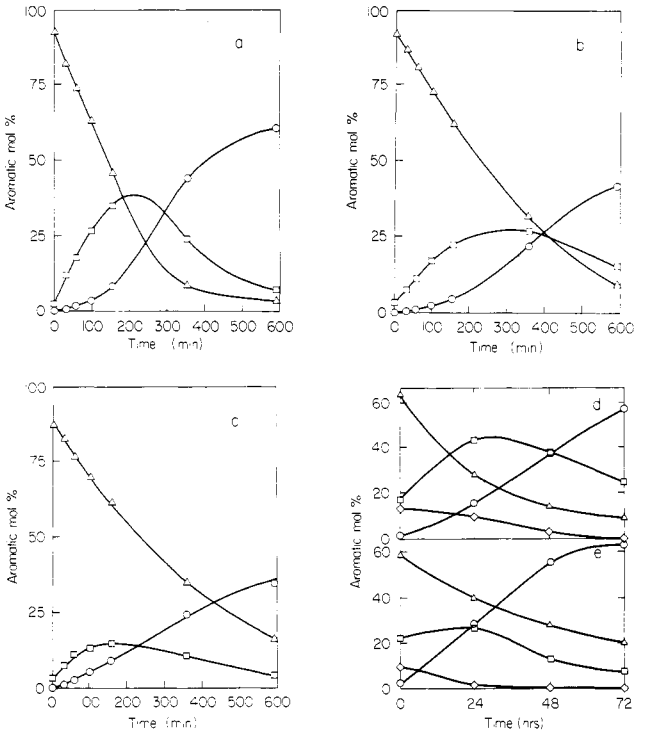



**Figure 1.** Composition plots for the reactions of **1** and **2**: (a) **1**, 50 °C, 2 M in $CD_3CN$; (b) **1**, 50 °C, 1 M in $CD_3CN$; (c) **1**, 50 °C, 2 M in toluene-$d_8$; (d) **2**, room temperature, 0.5 M in $CD_3CN$; (e) **2**, room temperature, 0.5 M in toluene-$d_8$. (△) Diazo compound; (○) *E,E* azine; (□) *E,Z* azine; (◇) *Z,Z* azine.

**Inclusion Complex with β-Cyclodextrin.** A solution of phenyldiazomethane (850 mg, 7.2 mmol) in $Et_2O$ (30 mL) was placed above a solution of β-cyclodextrin (12.0 g, 10.6 mmol) in $H_2O$ (200 mL) that had been cooled to 10 °C. The solutions were stirred together rapidly with ice-bath cooling, and a stream of $N_2$ was directed over the $Et_2O$ layer. After 6 h the $Et_2O$ layer had disappeared, and the pink solid was isolated by filtration and washed with water. The paste was dried for 1 day in vacuo, affording 5.1 g of complex. NMR spectra indicated a ratio of 0.9 guests/β-CD. The guest distribution (relative percent yield based on integration of aromatic region) was as follows: phenyldiazomethane (68), *E,Z* azine (21), *E,E* azine (1), *E,Z*:*E,E* ratio = 21. A portion of the complex (2.34 g) was digested in boiling HOAc (25 mL) for 10 min. This mixture was diluted with $H_2O$ (250 mL) and extracted with 3 × 50 mL of $Et_2O$. The organic layers were combined, washed with saturated aqueous $NaHCO_3$, and dried over $Na_2SO_4$. Analysis of the solution by capillary gas chromatography gave the following distribution (relative percent yield): benzyl acetate (62), azine (20).

A solution of 1-diazo-1-phenylethane (560 mg) in $Et_2O$ (50 mL) was placed above a solution of β-CD (7.9 g, 7.0 mmol) in $H_2O$ (150 mL). The layers were stirred together rapidly with ice-bath cooling, and a stream of $N_2$ was directed over the $Et_2O$ layer. After 4 h the $Et_2O$ layer had disappeared, and the solid was isolated by filtration. It was washed with $H_2O$ and dried in vacuo overnight, affording 3.2 g of a creamy purple solid. Analysis of the solid by NMR showed a ratio of guests/β-CD of 1.3:1. The guest distribution (relative percent yield based on integration of aromatic region) was as follows: phenyldiazoethane (62), *E,E* azine (3), *E,Z* azine (24), *Z,Z* azine (11), (*E,Z* + *Z,Z*):*E,E* ratio = 7.3. A portion of the complex (1.7 g) was digested in boiling HOAc for 10 min. Workup as above and analysis by GC gave the following distribution (relative percent yield): α-methylbenzyl acetate (67), azine (7).

**Decomposition of Phenyldiazomethanes. Neat Reaction.** Small amounts of the diazo compounds that had been caught in the condenser tube used in their preparation were allowed to react under reduced light over 1–2 days. Only the *E,E* azine was detected by NMR from phenyldiazomethane: $^1H$ NMR (DMSO-$d_6$) δ 8.72 (s, 2 H), 7.88 (m, 4 H),

(3) Overberger, C. G.; Anselme, J.-P. *J. Org. Chem.* **1964**, *29*, 1188–1190.
(4) Elguero, J.; Jacquier, R.; Marzin, C. *Bull. Soc. Chim. Fr.* **1969**, 1374–1378.
(5) Appenroth, K.; Reichenbacher, M.; Paetzold, R. *Tetrahedron* **1981**, *37*, 569–573.
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(8) Malament, D. S.; McBride, J. M. *J. Am. Chem. Soc.* **1970**, *92*, 4586–4593.
(9) Gustav, K.; Vettermann, S. *J. Mol. Struct.* **1983**, *105*, 239–248.
(10) Abelt, C. J.; Millis, M. B.; Pleier, J. M. *Abstracts of Papers*; 195th National Meeting of the American Chemical Society, Toronto, Canada; American Chemical Society: Washington, DC; ORGN 220.
(11) Elguero, J.; Jacquier, R.; Marzin, C. *Bull. Soc. Chim. Fr.* **1968**, 713–732.
(12) Creary, X. *Org. Synth.* **1985**, *64*, 207–216.
(13) Diazo compounds are toxic and potentially explosive. Appropriate safeguards should be employed with these materials.

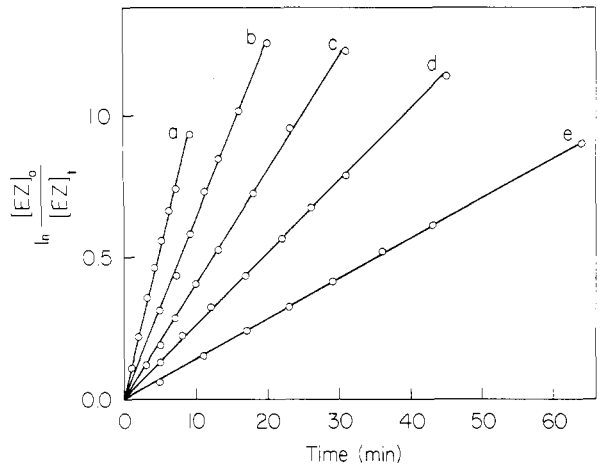



**Figure 2.** Kinetic plots for the thermal isomerization of (*E,Z*)-**4** at various temperatures: (a) 75 °C; (b) 70 °C; (c) 65 °C; (d) 60 °C; (e) 55 °C.

7.51 (m, 6 H); $^{13}$C NMR (DMSO-$d_6$) $\delta$ 161.6, 133.9, 131.5, 129.0, 128.5. A mixture of *E,Z* to *E,E* (62:38) was found after 2 days with 1-diazo-1-phenylethane. *E,E*: $^1$H NMR (DMSO-$d_6$) $\delta$ 7.91 (m, 4 H), 7.45 (m, 6 H), 2.22 (s, 6 H); $^{13}$C NMR (DMSO-$d_6$) $\delta$ 157.6, 138.4, 129.6, 128.3, 126.6, 15.0.

**Decomposition over Water.** A solution of phenyldiazomethane (0.20 M, 3.6 mL) in $Et_2O$ was placed over 250 mL of $H_2O$ cooled to 5 °C, and the solvent was removed over 30 min with a stream of $N_2$. The solution was stirred rapidly for 2 h. The mixture was extracted twice with $Et_2O$, the combined organic layers was dried over $Na_2SO_4$, and the solvent was removed in vacuo. NMR showed mainly *E,E* azine and no *E,Z* azine.

A solution of 1-diazo-1-phenylethane (0.22 M, 9.0 mL) in $Et_2O$ was placed over 100 mL of $H_2O$, and the $Et_2O$ was removed in vacuo. The solution was stirred overnight, and the solid product was isolated by filtration (120 mg, 53%). Analysis of the solid by NMR showed mainly the *E,Z* azine (*E,Z*:*E,E*:*Z,Z* = 92:5:3): mp 76–79 °C; $^1$H NMR (DMSO-$d_6$) $\delta$ 7.69 (m, 2 H), 7.46–7.33 (m, 8 H), 2.41 (s, 3 H), 2.28 (s, 3 H); $^{13}$C NMR (DMSO-$d_6$) $\delta$ 156.9, 156.8, 137.7, 136.3, 129.7, 128.3, 128.2, 128.0, 127.7, 126.2, 24.2, 14.6; IR (KBr) 1585, 1565, 1420, 1360, 1290, 1250, 750, 680 cm$^{-1}$; UV (hexane) 266 nm (1500 M$^{-1}$cm$^{-1}$). Anal. Calcd for $C_{16}H_{16}N_2$: C, 81.32; H, 6.82. Found: C, 81.25; H, 6.70. (*Z,Z*)-**4**: $^1$H NMR (DMSO-$d_6$) $\delta$ 7.47 (m, 10 H), 2.25 (s, 6 H); $^{13}$C NMR (DMSO-$d_6$) $\delta$ 156.6, 136.3, 128.8, 127.9, 127.8, 23.9.

**Reaction in Concentrated Solution.** A solution of phenyldiazomethane (380 mg, 3.22 mmol, 25 mL) in pentane was divided into three portions (10, 10, and 5 mL), and each was concentrated under aspirator pressure at 0 °C. They were diluted with deuterated solvent (0.64 mL each with toluene-$d_8$, $CD_3CN$, $CD_3CN$, respectively), placed under Ar, and heated to 50 °C. The reactions were monitored by NMR (Figure 1). The NMR spectra of the *E,Z* isomer could be determined from samples where its formation was greatest: $^1$H NMR (DMSO-$d_6$) $\delta$ 8.35 (s, 1 H), 7.97 (s, 1 H), 7.94–7.83 (m, 4 H), 7.54–7.44 (m, 6 H); $^{13}$C (DMSO-$d_6$) $\delta$ 155.9, 152.6, 134.1, 132.1, 131.8, 131.1, 130.6, 129.1, 128.7, 128.2.

A solution of 1-diazo-1-phenylethane (620 mg, 4.70 mmol, 25 mL) in $Et_2O$ was divided into two portions (1.3 mL each), and each was concentrated in vacuo at 0 °C. They were diluted with deuterated solvent (0.5 mL each with toluene-$d_8$ and $CD_3CN$), purged with Ar, and left to decompose at room temperature under Ar and reduced lighting. The reaction progress was monitored by NMR (Figure 1).

**Isomerization of (*E,Z*)-Acetophenone Azine.** A solution of the azine (0.097 M) in DMSO-$d_6$ was placed in an NMR tube and inserted in the NMR probe, which had been heated to a given temperature (55, 60, 65, 70, or 75 °C). The conversion of the *E,Z* isomer to the *E,E* isomer was determined by integration of the aromatic resonances at 7.91 (*E,E*, 4 H) and 7.67 ppm (*E,Z*, 2 H). The conversion as a function of time is presented in Figure 2.

## Results

Stirring a supersaturated solution of $\beta$-cyclodextrin with an ether solution of **1** or **2** results in precipitation of a complex after the ether is removed with an $N_2$ stream. The solids are probably inclusion complexes as opposed to coprecipitates based on analogy with our results with diazirines.[14] This assignment is not important with respect to the present study. About one-third of the included aromatic guest molecules are azines. The azine mixture is composed largely of the *E,Z* isomer, ca 95:5 for **1** and 63:28:9 (*E,Z*:*Z,Z*:*E,E*) for **2**. These isomers are identical with the major products of the diazo compound reactions in the absence of $\beta$-CD. Their assignment as *E,Z* isomers follows from both chemical and spectral evidence (vide infra).

Decomposition of the diazo compounds in concentrated solution or the neat state also produces mainly the *E,Z* azine. With **1** the reaction in the neat state and neat over $H_2O$ provided only the *all-trans* azine, presumably through facile isomerization of (*E,Z*)-**3**. In order to demonstrate the intermediacy of this isomer, concentrated solutions of **1** were heated at 50 °C, and the reaction was monitored by NMR. The compositions of the reaction mixtures as a function of time are shown in Figure 1. No evidence for formation of the *Z,Z* isomer was obtained. The stereoselectivity of the reaction can be estimated by the ratio of initial slopes of the plots for formation of (*E,Z*)-**3** and (*E,E*)-**3**. In these experiments the selectivities for the latter was great: 2 M $CD_3CN$, 97:3; 1 M $CD_3CN$, 94:6; 2 M toluene-$d_8$, 82:18. In all reactions the evolution of the components showed similar patterns. The diazo compound is consumed at a rate that decreases. The *E,Z* isomer initially is produced at a rate nearly matching the rate of diazo compound disappearance. It reaches a maximum concentration and then decreases at a rate that also decreases. Finally, the *E,E* isomer grows in at an increasing rate and then a decreasing rate.

Unlike the decomposition of **1**, the unsymmetrical azine could be isolated from the reactions of **2** in the neat state and over water. In the neat state complete decomposition was slow and required at least 2 days, whereas over water the decomposition was complete in less than a day. Isomerization to (*E,E*)-**4** was not a problem over water, but it was significant in the reaction in the neat state. The product isolated from the reaction over water was nearly all *E,Z* azine; the *E,Z*:(*E,E* + *Z,Z*) ratio was 92:8. The decomposition of **2** in concentrated solution at room temperature also was monitored, and the results (Figure 1) were similar to those obtained with **1**.

The thermal isomerization of (*E,Z*)-**4** to (*E,E*)-**4** was monitored at various temperatures by NMR. The conversion was determined by integration, and the rates of the unimolecular reactions were determined from the slopes of the plots of ln $[E,Z]_0/[E,Z)_t$ vs time (Figure 2). The activation energy ($E_a$) was determined between each pair of data points using the formula $E_a = \ln (k_2/k_1)[T_2T_1R/(T_2 - T_1)]$; a value of 22.3 ± 1.0 kcal/mol was obtained. The preexponential factor was determined for each rate constant using the calculated $E_a$; $A = (1.75 \pm 0.05) \times 10^{11}$ s$^{-1}$. This activation energy compares favorably with the barriers found for other azines (ca. 24 kcal/mol).[5,15]

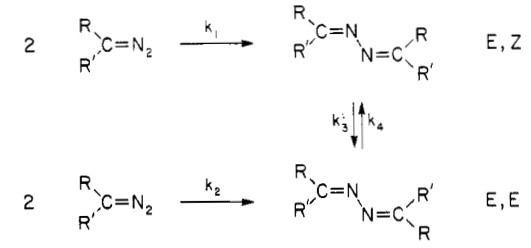
## Discussion

The assignment of the *E,Z* structure to the decomposition products of **1** and **2** is straightforward. The product from **2** cleanly reverts thermally to (*E,E*)-**4**. The NMR spectra indicate an unsymmetrical structure, since two methyl resonances are observed in the proton spectrum, and the carbon spectrum reveals 12 different carbons. Both the *E,E* and *Z,Z* isomers are symmetrical even in the *s-cis* conformation; therefore, the product must have the *E,Z* structure. The *Z,Z* isomer was observed as a minor component. Its assignment is based on the fact that solutions containing it and (*E,Z*)-**4** produce only the *E,E* isomer. The $^{13}$C spectra provided the best evidence for this structure. Only six resonances could be ascribed to this material, and the methyl carbon resonance at 23.9 ppm is very similar to the chemical shift for the methyl carbon *trans* to the N–N bond (24.2 ppm) in (*E,Z*)-**4**. The assignment of the structure for the first-formed azine

(14) Abelt, C. J.; Pleier, J. M. *J. Org. Chem.* **1988**, *53*, 2159–2162.

(15) The possibility of acid catalysis was not explicitly addressed. We did find that (*E,Z*)-**4** is quite sensitive to trace acid. In $CDCl_3$, which always contains a trace of acid, the azine suffers rapid isomerization ($\tau_{1/2} \sim 30$ min), whereas in DMSO, the half-life is on the order of days. These results suggest that acid-catalyzed isomerization is not important in the kinetic runs in DMSO.

**Scheme II**



from **1** is also straightforward, in spite of the fact that it could not be isolated. The reaction composition plots (Figure 1) indicate that it also reverts to the *all-trans* isomer. The NMR spectra of mixtures in which it was the major constituent indicate an unsymmetrical structure. Two imine H's appear upfield from the corresponding resonance in the *all-trans* isomer (0.39 and 0.76 ppm, respectively). In acetaldehyde azine, where the *E,E* and *E,Z* forms exist as an equilibrium mixture, the corresponding upfield shifts are 0.22 and 0.68 ppm.[4] All ten different carbon nuclei are revealed in the $^{13}C$ NMR spectrum. These results are the first report of this compound; neither photochemical nor thermal equilibrium entries have been successful in generating any observable amount of (*E,Z*)-**3**.

The results suggest that the diazo dimerization reaction occurs with high stereoselectivity. With **2** the *E,Z* isomer can be isolated nearly isomerically pure in preparative reactions. The stereoselectivity with **1** is evident from monitoring the reaction in concentrated solutions and from the β-cyclodextrin inclusion results. High concentrations and warm temperatures (50 °C) were used in monitoring the reaction of **1** in order to maximize the formation of (*E,Z*)-**3** on a short time scale. The stereoselectivities represent lower limits, since the thermal reversion to the *E,E* isomer certainly occurs even during the initial time interval. The β-cyclodextrin procedure provides a solid containing largely the *E,Z* azine as the second greatest constituent next to the desired diazo compound. This procedure is a kinetic one in the sense that when a complex is created between β-CD and an aromatic guest, it precipitates immediately since the solubility of the complex is greatly reduced relative to β-CD. Once precipitated, the complex is effectively static. Thus the procedure can be thought of as providing a "snapshot" for the reaction composition after a short time.

Ignoring the formation of (*Z,Z*)-**4** from 1-diazo-1-phenylethane, one can analyze the reaction progress plots in terms of the following simplified mechanistic scheme (Scheme II). The diazo compound can dimerize to give either the *E,Z* or *E,E* azine, and the azines exist in equilibrium with each other. Two of these reactions are insignificant. The rate of *E,E* to *E,Z* isomerism is small compared to that of the reverse reaction. The equilibrium of the azine isomers lies decidedly with the *E,E* isomer since no *E,Z* isomer was detected in concentrated samples of either *E,E* azine.[4] The dominance of the *trans* orientation of the phenyl group in seen in other hydrazone derivatives; for example, in acetophenone phenylhydrazone >99% of the compound exists in this form.[16] In the kinetic isomerization plots, the equilibrium would manifest itself in a negative deviation from the line at longer times, but no significant effect was observed. The formation of *E,E* isomer from diazo compound also must not be significant. The observed initial rate of formation of this structure is small. Since isomerization of the *E,Z* isomer must contribute to this rate, the rate of formation from diazo dimerization must be even smaller than the observed rate.

The mechanism can be simplified further to involve just the dimerization of the diazo compound to form the *E,Z* azine followed by isomerization of the azine to the *E,E* isomer. This scheme is in accord with the shapes of the reaction plots. Diazo compound disappearance is concave upward, indicating a positive second derivative expected for a dimerization reaction. The *E,Z* isomer plot shows a maximum where the rate of formation from the diazo compound equals the rate of conversion to the *E,E* isomer. The *E,E* graph is initially concave upward but shows an inflection point where the *E,Z* graph has a maximum. Some idea of the relative rates of diazo dimerization vs azine isomerization can be estimated by the position of the maxima where $k_1/k_3 = [E,Z]/[\text{diazo}]^2$. For **1** in acetonitrile (50 °C) these rate constants are nearly equal ($k_1/k_3 = 1.6$). In toluene, the rate of isomerization is nearly 5 times faster ($k_1/k_3 = 0.23$). For **2** (25 °C), on the other hand, the rate of dimerization is 16 times the isomerization rate ($k_1/k_3 = 16$) in acetonitrile. This factor can explain why the kinetically unstable *E,Z* isomer could be isolated from **2** but not **1**. Although the plots are in accord with the simple mechanistic scheme, extraction of rate constants reveals that the scheme is no longer valid after a short time. For example, the calculated rate constant for diazo compound disappearance increases with time. This phenomenon might be explained by the carbene reaction, which becomes increasingly important as the diazo compound concentration decreases. Also, other products not considered in the mechanism such as *cis*- and *trans*-stilbenes are formed in the reaction. Finally, diazo compounds are known to catalyze the decomposition of azines at high temperatures.[17,18] As the reaction mixture becomes complex, it is not surprising to have other processes become increasingly important.

The formation of (*Z,Z*)-**4** from **2** is not considered in Scheme II. A more complete analysis would include its rate of formation from diazo dimerization and its isomerization to (*E,Z*)-**4**. Since direct isomerization to the *E,E* isomer has been shown not to occur in other azines, this process should not be important here.[5] The concentration of the *Z,Z* isomer only decreases during the reaction, so its rate of isomerization must be faster than that of the *E,Z* isomer. The possibility that only the *Z,Z* isomer is formed initially can be excluded on the basis that the *E,Z* isomer is still growing in while the *Z,Z* isomer is decreasing. Since none of the *Z,Z* isomer was detected in the reactions of **1**, it is reasonable to conclude that its formation in the reactions of **2** is minor compared to the formation of the *E,Z* isomer.

In considering the mechanism for dimerization of the diazo compound, we note that there may be one detail that may be the determining factor for the observed stereoselectivity. The diazo group can be considered as an zwitterionic moiety. One plane contains an allylic anion, whereas the perpendicular plane contains a diazonium cation. Since the attack of the anion of one diazo group occurs with the diazonium portion of the other, the two planar diazo molecules approach in perpendicular planes. Steric arguments place the phenyl (larger) group of the electrophilic diazo compound away from the incoming nucleophilic molecule. Creating the C–N bond also generates an azo group, and thermodynamic considerations suggest that the azo group will be *trans*. In azoisopropane, the difference in energy between the *cis* and *trans* structures is around 8 kcal/mol.[19,20] This difference, if translated partially into transition-state energy, could account for the observed stereoselectivity. At this point one phenyl group is situated *cis* with respect to the N–N bond. The loss of $N_2$ will occur most rapidly when the C–$N_2$ bond is aligned parallel to the incipient diene π-system. In particular, loss of nitrogen must be fast with respect to rotation of the carbanionic carbon about the C–N bond since rotation would lead to the *E,E* azine. Because the C–N bond is a part of an allyl system, rotation is not expected to compete with $N_2$ loss. Formation of the *Z,Z* isomer occurs from a geometry where the phenyl group is gauche to the N–N bond, whereas the *E,Z* isomer results when H (in **1**) or $CH_3$ (in **2**) is gauche to the N–N bond. The steric difference between phenyl and methyl is smaller than the difference between phenyl and hydrogen, and this factor may explain the small amounts of the *Z,Z* isomer observed from **2** but not **1**. Besides the high

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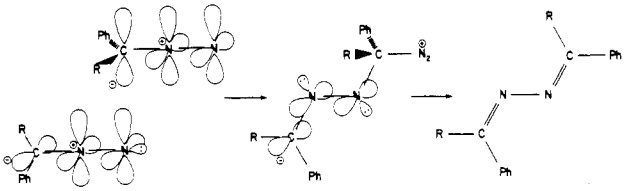
stereoselectivity, the solvent effects also support the initial step of the mechanism. The nucleophilic attack forms a charge-separated zwitterion. This process is expected to be facilitated by polar solvents that can stabilize charge separation. As expected, in acetonitrile the rate of loss of diazo compound is greater than in toluene. The lower stereoselectivity in toluene can be explained in part by the slower rate of reaction, so that the isomerization mechanism competes more effectively. This mechanism also predicts that **2** would suffer dimerization faster than would **1**. The methyl group increases the nucleophilicity of the carbon center, but it does not greatly affect the electrophilicity of the diazonium moiety.



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# Ozonolysis of 1-Substituted 2,3-Diphenylindenes and *o*-(1-Substituted-2-phenyl-3-methoxy-2-propenyl)benzophenones. Remarkable Effects of the Method of Generation of the Carbonyl Oxide Intermediates on the Stereochemistries of Both the Ozonide and the Methanol-Derived Isochroman Products

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**Abstract:** Ozonolyses of 1-substituted 2,3-diphenylindenes **1a,b** and *o*-(1-substituted-2-phenyl-3-methoxy-2-propenyl)benzophenones **8a,b** in methanol–methylene chloride at −70 °C, which should proceed through common carbonyl oxide intermediates **11a,b**, afforded stereoisomeric methoxy hydroperoxides, **6a,b** and **9a,b**, respectively. The ozonide stereochemistry was also affected by the method of generation of the carbonyl oxide intermediate **11a**: ozonolyses of 1,2,3-triphenylindene (**1a**) in $CCl_4$, $CH_3CN$, $CH_3CO_2H$–$CH_2Cl_2$, and $CF_3CH_2OH$–$CH_2Cl_2$ gave predominantly the *exo*-ozonide **2a**, whereas the endo isomer **3a** was obtained exclusively from the ozonolysis of keto olefin **8a** in $CH_3CO_2H$–$CH_2Cl_2$ and $CF_3CH_2OH$–$CH_2Cl_2$. Moreover, in the ozonolysis of the keto olefin **8a**, protic solvents assisted ozonide formation; *endo*-ozonide **3a** was certainly obtained in the ozonolysis in the protic solvents (around 25% yield). No ozonides were isolated, however, from ozonolysis reactions carried out in aprotic solvents, $CCl_4$ and $CH_3CN$.

The chemistry of carbonyl oxides, key intermediates in ozonolysis, has attracted much attention.[2] To obtain further insight into the mechanism of ozonolysis of indene derivatives,[3] we have undertaken ozonolyses of 1-substituted 2,3-diphenylindene **1a,b** and *o*-(1-substituted-2-phenyl-3-methoxy-2-propenyl)benzophenone **8a,b**, each of which should give rise to a corresponding common ozonolysis intermediate **11a,b** (Scheme I).[4,5] Our results to date suggest that (a) the substrate, from which the carbonyl oxide **11a,b** is derived, exerts an unexpected influence on the stereochemistries of both the ozonide and the methanol-derived isochroman product and that (b) in the case of the carbonyl oxide intermediates **11a,b** generated from the keto olefins **8a,b**, protic solvents do not retard but instead accelerate the ozonide formation; such an assistance is not observed in the analogous indene-ozonolysis reactions.

## Results

**Ozonolysis of 1,2-Disubstituted 3-Phenylindenes.** The ozonolysis of 1,2,3-triphenylindene (**1a**) in $CCl_4$, $CH_3CN$, $CF_3CH_2OH$–$CH_2Cl_2$, and $CH_3CO_2H$–$CH_2Cl_2$ gave, in each case, a mixture of *exo*-ozonide **2a** and the endo isomer **3a** in excellent yield, the

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