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Kinetic and Computational Studies of a Novel Pseudopericyclic Electrocyclization. The First Evidence for Torquoselectivity in a 6-π System

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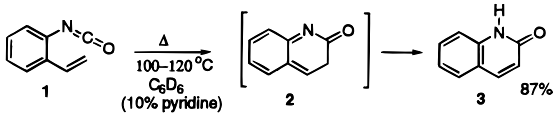
Our research program has long maintained an interest in structure−reactivity relationships with respect to electrocyclic reactions. In earlier work, substituent effects in the 4-π electrocyclic interconversion of cyclobutene and butadiene were examined,[1] with this work and that of others culminating in the invention of the concept of torquoselectivity by Houk in 1984.[2]

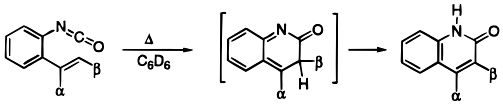
More recently we have been interested in designing experiments which could provide similar insight to 6-π electrocyclizations. Houk has predicted similar, albeit diminished, torquoelectronic effects for such processes.[3] Unfortunately, steric effects play a dominant role in determining the dynamics of the classic 1,3,5-hexatriene to 1,3-cyclohexadiene electrocyclization process, to such an extent that the impact of torquoselectivity cannot be assessed via studies of this system.[4]

In pursuit of an electrocyclization system which would allow unambiguous evaluation of 6-π electron torquoselectivity, we initiated an investigation of substituent effects on the rates of cyclization of *o*-vinylphenyl isocyanates.[5−7] Lacking cis (or trans) substituents at the isocyanate terminus of its 6-π system, this rearrangement system should be free of the usual steric effects which have impeded past efforts to examine 6-π electron torquoselectivity.[4]



Log A = 10.4±0.2; E_a = 25.2±0.2 kcal/mol; $\Delta S^{\ddagger}$ = -13±1 cal/deg

Table 1. Experimental Rate Constants and Calculated Activation Energies and Heats of Reaction for the Thermal Electrocyclizations of α- and/or β-Substituted *o*-Vinylphenyl Isocyanates in C_6D_6



substituent				$\Delta G^{\ddagger}$ (kcal/mol)	calcd[a]		
α	β	T, °C	k (s^{-1})		E_a (1→2)	E_{rxn} (1→2)	E_{rxn} (1→3)
H	H	109.4	$9.8(0.5) \times 10^{-5}$	29.8	29.8	19.2	−23.1
H	CH_3	112.6	$7.3(0.5) \times 10^{-5}$	30.1	29.1	20.8	−25.3
H	F	178.9	$2.0(0.3) \times 10^{-6}$	38.6	32.7	25.5	−21.1
H	CF_3	182.3	$9.0(0.5) \times 10^{-5}$	35.5	32.8	22.2	−24.4
CH_3	H	35	2.4×10^{-4} [b]	23.2	26.1	16.9	−24.3
CF_3	H	149.3	$6.9(0.2) \times 10^{-5}$	33.0	31.9	22.8	−21.3
CH_3	F	101.6	$3.80(0.01) \times 10^{-4}$	28.0	29.0	23.0	−22.0
H	CN				34.7	27.2	−20.8
H	CHO				32.3	23.5	−23.1
OCH_3	H				21.9	16.3	−23.5

[a] MP2/6-31G*//RHF/6-31G* + ZPE. [b] See footnote 15.

Parent system **1** underwent thermal rearrangement smoothly to 2-quinolinone product **3**,[8,9] with the reaction exhibiting good first-order behavior. Activation parameters were obtained which were consistent with a concerted, pericyclic pathway for the reaction.[10] In view of the novelty of the system and its potential for polar effects, we believed that it was essential to carry out a computational study concurrent with the experimental one. Utilizing ab initio [MP2/6-31G*//RHF/6-31G*] methodology,[11−13] the structures and energies of the ground states, transition structures, and products of the cyclization/rearrangement sequence (**1** → **2** → **3**) for **1** and a number of its α- and β-substituted derivatives were computed.[14]

Table 1 provides the kinetic and computational data which were obtained in our investigation of the reactivity of such α- and β-substituted vinylphenyl isocyanates. From this data, it can be seen that substitution, particularly by polar substituents, gives rise to strong kinetic effects which can largely be attributed to polar influences on the thermodynamics of the endothermic, rate-determining step of these processes.[17,18]

Interestingly, these transition structures (i.e., Figure 1) proved *not* to be of a classic, disrotatory, 6-π electrocyclic nature. Instead, the isocyanato function remained essentially coplanar with the benzene ring (−3.7° out of plane) in the transition state,

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(1) Dolbier, W. R., Jr.; Koroniak, H.; Burton, D. J.; Bailey, A. R.; Shaw, G. S.; Hansen, S. W. *J. Am. Chem. Soc.* **1984**, *106,* 1871−1872. Dolbier, W. R., Jr. *J. Am. Chem. Soc.* **1987**, *109,* 219−225.

(2) Kirmse, W.; Rondan, N. G.; Houk, K. N. *J. Am. Chem. Soc.* **1984**, *106,* 7989−7991. Rondan, N. G.; Houk, K. N. *J. Am. Chem. Soc.* **1985**, *107,* 2099−2111. Dolbier, W. R., Jr.; Koroniak, K.; Houk, K. N.; Sheu, C. *Acc. Chem. Res.* **1996**, *29,* 471−477.

(3) Evanseck, J. D.; Thomas, B. E., IV; Spellmeyer, D. C.; Houk, K. N. *J. Org. Chem.* **1995**, *60,* 7134−7141.

(4) Dolbier, W. R., Jr.; Palmer, K.; Koroniak, H.; Zhang, H. W.; Goedken, V. *J. Am. Chem. Soc.* **1991**, *113,* 1059−1060. Dolbier, W. R., Jr.; Palmer, K. W. *J. Am. Chem. Soc.* **1993**, *115,* 9349−9350. Dolbier, W. R., Jr.; Palmer, K. W. *Tetrahedron Lett.* **1993**, *34,* 6201−6204.

(5) There is literature precedent for 6-π electrocyclizations involving the isocyanato group,[6] although not specifically of an *o*-vinylphenyl isocyanate type.

(6) Overman, L. E.; Tsuboi, S. *J. Am. Chem. Soc.* **1977**, *99,* 2813−2815. Eloy, F; Deryckere, A. *Helv. Chim. Acta* **1969**, *52,* 1755−1762. Eloy, F.; Deryckere, A. *J. Heterocycl. Chem.* **1970**, *7,* 1191−1193. MacMillan, J. H.; Washburne, S. S. *J. Org. Chem.* **1973**, *38,* 2982−2984.

(7) All isocyanate substrates (**1**) were prepared in situ via thermal Curtius rearrangements of the respective acyl azides at room temperature in C_6D_6.

(8) Rates of rearrangement of the isocyanates to the respective 2-quinolinones (**3**) were determined by measuring the decrease of an appropriate NMR (^{1}H or ^{19}F) signal with respect to an internal standard. Quinolinone products were isolated in >85% yield and fully characterized.

(9) 2-Quinolinones are often erroneously referred to as their less stable tautomers, 2-hydroxyquinolines.

(10) The rates of electrocyclization were similar with and without the added pyridine (±10%), but the Arrhenius behavior was somewhat better in the presence of pyridine.

(11) All calculations were performed with the GAMESS[12] and *Gaussian 94*[13] program systems, on Silicon Graphics Power Challenge XL and IBM RS/6000 SP compute servers, respectively. Stationary points were optimized at the restricted Hartree−Fock (RHF) level and characterized as minima or transition structures by harmonic frequency analysis. RHF vibrational frequencies and zero-point energy corrections are scaled by 0.8929. MP2 energy calculations on the RHF geometries utilized the frozen-core approach.

(12) General Atomic and Molecular Electronic Structure System, 22 November 1995 and 18 March 1997 versions: Schmidt, M. W.; Baldridge, K. K.; Boatz, J. A.; Elbert, S. T.; Gordon, M. S.; Jensen, J. H.; Koseki, S.; Matsunaga, N.; Nguyen, K. A.; Su, S.; Windus, T. L.; Dupuis, M.; Montgomery, J. A., Jr. *J. Comput. Chem.* **1993**, *14,* 1347−1363.

(13) *Gaussian 94* (Revision C.3): Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Gill, P. M. W.; Johnson, B. G.; Robb, M. A.; Cheeseman, J. R.; Keith, T. A.; Petersson, G. A.; Montgomery, J. A.; Raghavachari, K.; Al-Laham, M. A.; Zakrzewski, V. G.; Ortiz, J. V.; Foresman, J. B.; Peng, C. Y.; Ayala, P. A.; Wong, M. W.; Andres, J. L.; Replogle, E. S.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Binkley, J. S.; Defrees, D. J.; Baker, J.; Stewart, J. P.; Head-Gordon, M.; Gonzalez, C.; Pople, J. A. Gaussian, Inc., Pittsburgh, PA, 1995.

(14) B3LYP and BLYP investigations of this system yield very similar transition structures, as do calculations of the transition structure of the non-benzo analogue.

(15) The α-methyl derivative rearranged at a rate competitive with that of the Curtius rearrangement, and thus its rate could only be estimated using the standard procedure for such two-step consecutive, irreversible processes.[16]

(16) Moore, J. W.; Pearson, R. G. *Kinetics and Mechanism,* John Wiley & Sons: New York, 1981; p 290.

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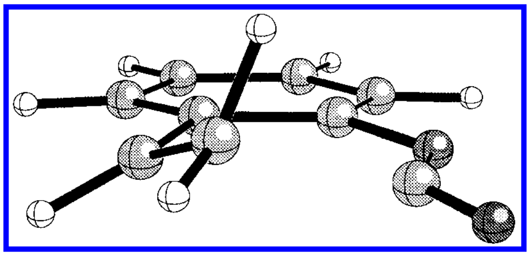

Figure 1. Transition structure for the electrocyclization of *o*-vinylphenyl isocyanate.

Table 2. Comparison of the Rate Constants for Electrocyclization of the *E*- and *Z*-Isomers of Some β-Substituted *o*-Vinyl Phenyl Isocyanates[26,27]

substituent					calcd[a,b]	
α	β	T, °C	k_E/k_Z	$\Delta\Delta G^\ddagger$	$\Delta\Delta E_a$	$\Delta\Delta E_{rxn}$ (1→2)
H	CH_3	112.6	11.7	−1.9	−2.0	+2.0
H	CF_3	182.3	3.2	−1.0	−0.9	+2.9
CH_3	F	101.6	82.1	−3.3	−7.4	+0.6
H	CHO				+2.2	+3.2

[a] kcal/mol. [b] MP2/6-31G*//RHF/6-31G* + ZPE.

with the vinyl group twisted (28.2° out of plane),[20] thus orienting its terminal *p*-orbital for favorable overlap with the carbon *p*-orbital of the *carbonyl* π-bond, rather than with that of the C=N π-bond, which would have been the case for the classic, disrotatory process. The short bond length (1.883 Å) of the forming bond in the isocyanate cyclization is indicative of the lateness of this transition state, whereas the length of the forming bond (2.118 Å) in the pericyclic cyclization of *o*-divinylbenzene is typical of such pericyclic reactions.[21,22]

Such a transition structure permits the maintenance of conjugation within the phenyl isocyanate system, where one of the carbonyl nonbonded pairs becomes a bonding pair as the new σ-bond is formed. This description is consistent with Lemal's definition of a *pseudopericyclic* process as one in which "nonbonding and bonding atomic orbitals interchange roles".[23] The above-described process of σ-bond formation gives rise to a "disconnection" in the cyclic array of overlapping orbitals because the atomic orbitals which are switching functions are mutually orthogonal.

The potential importance of pseudopericyclic reactions, while being acknowledged occasionally since Lemal's invention,[24] has recently been given new emphasis through a series of papers by Birney,[25] who has concluded that, as in the electrocyclization of **1**, "when a pericyclic reaction has even one possible orbital disconnection, this may result in a pseudopericyclic transition structure."

Although the 6-π electrocyclizations of our *o*-vinylphenyl isocyanates would thus not appear to be classic, disrotatory pericyclic processes, they should still have the potential to exhibit torquoselectivity in their *monorotatory* processes. Indeed, the results given in Table 2, which provide a measure of the torquoelectronic influence of *E* versus *Z* β-substituents on the electrocyclization of **1**, are such that there can be little doubt that their source must be torquoelectronic in nature.

The k_E/k_Z ratios are clearly not *steric* in origin, since the smallest substituent (F) gives rise to the largest, whereas the largest (CF_3) gives rise to the smallest observed kinetic effect! Second, the results are consistent with both Houk's general expectations for a smaller degree of torquoselectivity in 6-π electrocyclizations[3,28] and our own calculations for these specific systems (Table 2).[11−14,29] Another factor which probably serves to diminish the influence of torquoelectronics in this specific system is the significant endothermicity of the reaction,[30] which to a significant extent is derived from the loss of amide-like stabilization of the isocyanate group.[32]

In conclusion, computational and experimental evidence has been presented for a novel pseudopericyclic mechanism being involved in the electrocyclizations of *o*-vinylphenyl isocyanates, such reactions also providing the platform for obtaining the first evidence of torquoselectivity in a 6-π electrocyclization process.

Acknowledgment. Support of this research in part by the National Science Foundation is acknowledged with thanks. We are also grateful to Academic Computing and Network Services at Florida State University. Insightful discussions with Professor Birney regarding pseudopericyclic reactions and early communication of his results in this area are greatly appreciated.

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(17) The rate-determining (and thus irreversible) nature of the electrocyclization step (**1** → **2**) was demonstrated by (a) the lack of significant kinetic effect of added base, pyridine and (b) a study of the cyclization of *cis*- and *trans*-β-deuterio **1**, which gave no indication of reversibility. We believe the proton-transfer step which converts **2** → **3** to be a bimolecular process because, according to our calculations, the concerted [1.5]-H migration transition structure is *much* too high in energy ($E_{a(2\rightarrow3)}$ = 31 kcal/mol) to be responsible for this process.

(18) The recognized inductive influences of substituents such as F and CF_3 on carbonyl stability[19] are sufficient to understand the impact of these substituents on the stability of cyclization products (**2**).

(19) Chambers, R. D. *Fluorine in Organic Chemistry*; John Wiley & Sons: New York, 1973.

(20) This can be compared with our comparable computed dihedral angles of 33.0° for both vinyl groups in the "normal" pericyclic transition structure for rearrangement of *o*-divinylbenzene.

(21) Houk, K. N.; Evanseck, J. D. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 682−708.

(22) Further calculations have indicated that similar transition structures should be involved for the ketene and, perhaps surprisingly, even for the allene analogues. In the allene transition structure the terminal CH_2 of the allene has twisted 60.5° from its beginning orthogonal position to provide the overlap required for *exo*-methylene double-bond formation!

(23) Ross, J. A.; Seiders, R. P.; Lemal, D. M. *J. Am. Chem. Soc.* **1976**, *98*, 4325−4327. Bushweller, C. H.; Ross, J. A.; Lemal, D. M. *J. Am. Chem. Soc.* **1977**, *99*, 629−631.

(24) Okamura, W. H.; Peter, R.; Reischl, W. *J. Am. Chem. Soc.* **1985**, *107*, 1034−1041. Elnagar, H. Y.; Okamura, W. H. *J. Org. Chem.* **1988**, *53*, 3060−3066. Henriksen, U.; Snyder, J. P.; Halgren, T. A. *J. Org. Chem.* **1981**, *46*, 3767−3768. Burke, L. A.; Elguero, J.; Leroy, G.; Sana, M. *J. Am. Chem. Soc.* **1976**, *98*, 1685−1690.

(25) Birney, D. M.; Ham, S.; Unruh, G. R. *J. Am. Chem. Soc.* **1997**, *119*, 4509−4517. Birney, D. M. *J. Org. Chem.* **1996**, *61*, 243−251.

(26) The rate constants for rearrangement of the respective *E*- and *Z*-isomers were obtained as described earlier[8] using a ~50:50 mixture of isomers.

(27) Although selectivity was certainly observed for the *E*- vs *Z*-cyclization of the simple β-fluoro system, the system did not exhibit good Arrhenius behavior at the high temperatures required for their rearrangement, and we therefore do not feel comfortable presenting such data at this time. The α-methyl-β-fluoro system, rearranging at a much lower temperature, had much more reliable kinetic behavior.

(28) Our k_E/k_Z ratio of 11 for the β-methyl substituent can be compared with the torquoselective factor of 120 which was observed for outward versus inward rotation of a 3-methyl substituent in the 4-π electrocyclic ring opening of cyclobutene.[2]

(29) Whereas the experimental and calculated values for k_E/k_Z correlate well for β-methyl and β-trifluoromethyl substituents, for reasons we do not yet understand, this ratio seems to be overestimated in calculations for the β-fluoro substituent.

(30) The more endothermic a process, the later its transition state and the more likely that the kinetics of the process will be determined by the thermodynamics of the reaction, rather than by orbital interactions, which generally exert their greatest influence in exothermic reactions which have early transition states.[31]

(31) Houk, K. N. *Acc. Chem. Res.* **1975**, *8*, 361−391.

(32) Apropos, the computed $\Delta E_{rxn(1\rightarrow2)}$'s for the ketene and allene analogues are *exothermic* (−3.7 and −11.1 kcal/mol, respectively).