Diels–Alder Reactions of Phenyl-Substituted 2-Pyrones: Direction of Addition with Phenylacetylene

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ABSTRACT: The Diels–Alder reactions of unsymmetrically substituted acetylenes with 2-pyrones containing unsymmetrically substituted diene fragments proceed with varying degrees of regioselectivity, depending on the positions and types of substituents. Extended Hückel MO calculations of the net charge distribution on the reactants can be used to predict the direction of addition except in cases where secondary overlap of frontier molecular orbitals occurs.

Diels–Alder reactions of 2-pyrones with acetylenes produce benzene derivatives by the loss of carbon dioxide from the intermediate adduct.[1] Prior work[2–4] indicated that in the case of the addition reaction of an unsymmetrical acetylene with a 2-pyrone having an unsymmetrically substituted diene fragment, the major isomer was the one predicted by net atomic charge considerations. The addition of the reactants occurs in the manner that aligns the most electronegative (terminal) carbon in phenylacetylene with the most electropositive carbon in the pyrone (C-6). This method for predicting the isomeric product was found to have limited utility; 5-phenyl-2-pyrone (**4**) reacts with phenylacetylene to afford *p*- and *m*-diphenyl as predicted (**3**/**2** = 9:1)[3] while 4,5,6-triphenyl-2-pyrone (**7**) reacts with phenylacetylene in a manner opposite that predicted to yield 1,2,3,4- and 1,2,3,5-tetraphenylbenzene (**8**/**9** = 5:1).[2] Clearly some other factor is influencing the reaction in the latter case.

Recent work with monophenylated 2-pyrones indicates that prediction of the correct isomer depends not only on net atomic charge consideration but also upon the presence or lack of secondary overlap of the frontier molecular orbitals in the transition state. The presence of favorable secondary overlap explains the apparently anomalous preferences in almost all the observed cases.

The reactions of phenylenebispyrones with diethynylbenzenes afford polyphenylenes of varying degrees of meta and para catenation, depending on the particular monomer employed.[3] Because the amount of ortho, meta, and para catenation in the product is dependent in part on the direction of addition in the 4 + 2 cycloaddition, it was necessary to determine the isomer distribution with model compounds and to attempt a prediction of the direction.

Results and Discussion

In order to screen methods of correctly predicting the product isomer, the Diels–Alder reaction of a series of monosubstituted 2-pyrones was investigated (Table I). The net atomic charges were calculated with an iterative extended Hückel molecular orbital (MO) computer program. Coulomb integrals H_{ii} were obtained from the Mulliken populations (M) and were adjusted for charge with Cusachs' equation $H_{ii} = A{\cdot}M - B + C{\cdot}q_i = H_{ii} - C{\cdot}q_{ii}$ where H_{ii} is the adjusted Coulomb integral, q_i is the charge, and A, B, and C are the parameters for each particular orbital of each element.[5] The resonance integrals were calculated according to Cusachs' formula[6] $H_{ij} = (2.0 - |S_{ij}'|)S_{ij}(H_{ij} + H_{jj})/2.0$ where S_{ij} is the overlap and $|S_{ij}'|$ is the overlap in the diatomic framework. Orbital exponents were evaluated on each repetition and were expressed as functions of the charge by means of Slater's formula[7] $\zeta = (1/n)(z - 0.85\alpha) - 0.35(\beta - 1.0 - q_i)$ where n is the principal quantum number, z is the atomic charge, α is the number of core electrons, β is the number of valence electrons, and q_i is the charge. The Hamiltonian matrix elements were iterated using a damping technique to a set of self-consistent charges. Through the equation $q_i^{n} = q_i^{n-1} - \lambda(q_i^{n-1} - q_i^{n'})$ where $\lambda = 0.1$, the newly calculated charges $q_i^{n'}$ are damped and q_i^{n} was used to calculate the new H_{ii}. This was repeated until the root mean square variation in charges was less than 0.02 on iteration. Convergence is assisted by a level shift operator technique.[8] Where the bond distances and angles for the compounds had not been experimentally determined, they were obtained from the angles and distances listed for similar compounds and/or functional groups.[9]

Since the calculation of the net atomic charges in a large molecule is subject to approximation, the carbon-13 nuclear magnetic spectra were obtained when possible. The carbons having the greatest chemical shift downfield from tetramethylsilane are those expected to have the larger positive net atomic charges. The assignments of chemical shifts (Table II) are in agreement with those found for related compounds.[10] Although there is no consistent correlation between the two, both chemical shift information and net atomic charge calculations confirm that, regardless of the substitution of the pyrone ring, the 6-carbon is the more positive of the two pyrone carbon atoms involved in the Diels–Alder cycloaddition in the pyrones studied.

The reaction of 4-phenyl-2-pyrone[11,12] (**1**) with phenylacetylene at 210 °C in 1,2,4-trichlorobenzene gave both *m*- and *p*-terphenyl in a 2:1 ratio as determined by GLC in comparison with authentic samples. The major meta isomer is the one predicted by extended Hückel MO calculations of the net atomic charges of the reactants (Table II). The fourth pyrone in the series of phenylated pyrones, 6-phenyl-2-pyrone (**5**), was synthesized by modification of literature procedures.[3,13–16] The products of the reaction of **5** with phenylacetylene at 300 °C in toluene were both *o*- and *m*-terphenyl (**6**/**2** = 5.4:1). In this case the minor meta isomer is the one predicted by consideration of the net atomic charges of the reactants (Table II).

Consideration of net atomic charges alone is therefore not sufficient to predict the preferred isomer in the cycloaddition reaction of 2-pyrones. Investigation of the geometry of the transition state of the cycloaddition reaction indicates secondary overlap of frontier molecular orbitals can occur for the pyrones substituted only at the 3 and 6 positions. Scheme I shows that the secondary overlap found in the reaction of **5** and phenylacetylene is indeed favorable and can account for the formation of the isomer opposite to that predicted by consideration of net atomic charges alone. Transition states similar to that observed for **5** which have favorable secondary overlap can be drawn for a number of 2-pyrones with conjugated substituents at positions 3 and 6. Inspection of Table I shows that consideration of this secondary overlap results in the correct prediction of the preferred isomer.

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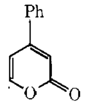
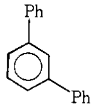
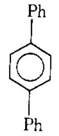
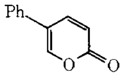
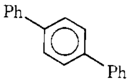
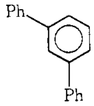
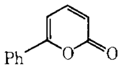
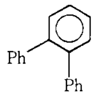
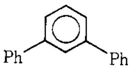
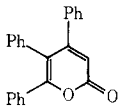
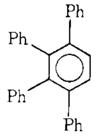
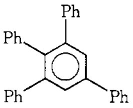
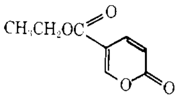
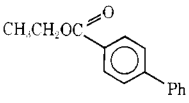
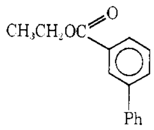
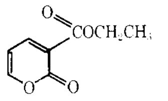
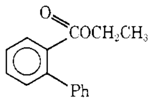
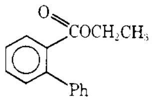
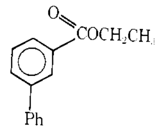
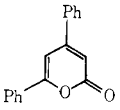
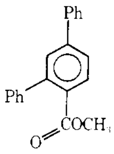
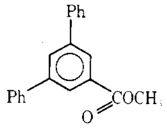
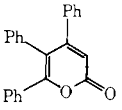
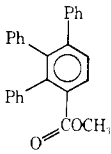
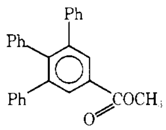
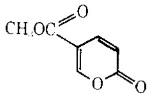
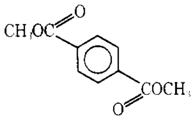
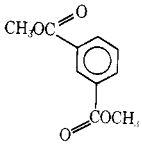
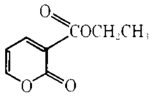
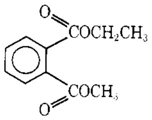
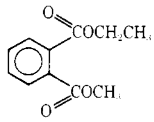
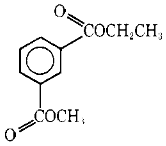
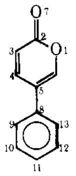
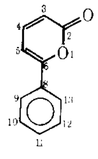
Table I
Reactions of 2-Pyrones

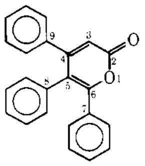
Pyrone	Total yield of products, %	Observed products (% total)		
		Secondary overlap prediction	Net atomic charge prediction	Other
		With Phenylacetylene		
 1	69	*a*	 (67) 2	 (33) 3
 4	100^b	*a*	 (90)	 (10)
 5	34	 (83) 6	 (16)	
 7	40^c	 (83) 8	 (17) 9	
 10	60^c		 (100)	 (0)
 11	60^c		 (67)	 (33)
		With Methyl Propiolate		
 12	70^c	 (70)	 (30)	
	55^c	 (55)	 (45)	
	40^c	*a*	 (60)	 (40)
	50^c		 (20)	 (80)

[a] No secondary overlap. [b] Reported value.[3] [c] Reported value.[2]

The persistent appearance of the atomic charge predicted isomer in all cases and the low overall reaction yields observed in many cases indicate that both charges and secondary overlap influences are in competition. Indeed, the major product of the reaction of pyrone 11 and methyl propiolate can be explained by neither influence. The extended Hückel method neglects steric factors, so this contribution cannot be evaluated easily and may be of major importance in this last case. Other methods of predicting orientation in the observed Diels–Alder reactions, such as bond formation between the "softest" atoms,[17] do not seem to account for the experimental observations.

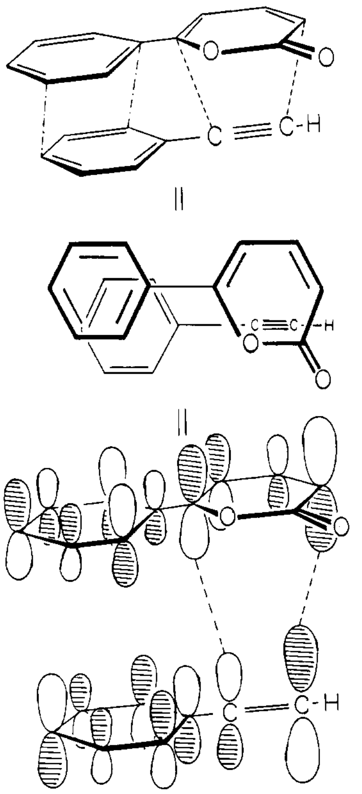
Table II
Properties of 2-Pyrones

Pyrone	Atom	Atomic charge	Chemical shift[a]	Pyrone	Atom	Atomic charge	Chemical shift[a]
	1	−0.158			1	−0.226	
	2	0.196	161.14		2	0.227	161.96
	3	0.179	116.44		3	0.092	113.98
	4	0.234	143.92		4	0.116	143.84
	5	0.101	120.60		5	0.094	101.06
	6	0.266	148.34		6	0.180	161.04
	7	−0.451			7	−0.475	
	8	0.141	133.46		8	0.067	131.29
	9	0.098	125.92		9	0.057	125.58
	10	0.081	129.24		10	0.041	128.95
	11	0.025	128.36		11	0.047	130.86
	12	0.085	129.24		12	0.050	128.95
	13	0.150	125.92		13	0.053	125.58

Pyrone	Atom[b]	Chemical shift[a]
	1	
	2	161.79
	3	113.45
	4	158.35
	5	118.45
	6	159.13
	7	132.68
	8	136.97
	9	134.37

[a] δ, downfield from tetramethylsilane in $CDCl_3$ solution. [b] Charges not calculated because of the large number of atoms.

Scheme I



Experimental Section

^{1}H-NMR spectra were obtained on a Varian EM 360 NMR spectrometer and ^{13}C-NMR spectra measured on a Bruker HX-90E fourier transform spectrometer equipped with an SPX high-power amplifier, a broad band decoupler, and a Model B-NC 12 computer.

6-Phenyl-2-pyrone (5). This reaction was carried out using a modification of the reported procedure.[16] A solution of 122 g (0.64 mol) of 1,1,3-trichloro-3-ethoxypropene[13,14] in 93 mL of glacial acetic acid at 0 °C was mixed with a solution of 103 g (0.56 mol) of acetophenone and 16 mL (0.89 mol) of water also in 93 mL of glacial acetic acid at 0 °C. The reaction mixture was kept at 6 °C for 5 days. The crystals of 5,5-dichloro-2,4-pentadienophenone (**13**) were filtered and recrystallized from 95% ethanol to yield 100 g (0.44 mol, 80%) of yellow needles: mp 76–79 °C (lit.[16] 76–77 °C); IR (KBr) 1655 cm^{-1} (C=O, conj), 1610, 1600, 1585 cm^{-1} (C=C); NMR ($CDCl_3$) δ 6.62 (d, 1 H, J = 11 Hz, =CHCO), 6.97 (d, 1 H, J = 24 Hz, $CH{=}CCl_2$), 7.18–7.60 (m, 4 H, $=CHCH{=}CCl_2$, *m*-, *p*-C_6H_5), 7.70–8.00 (m, 2 H, *p*-C_6H_5); mass spectrum (70 eV) *m/e* 227, 190, 149, 105, 77, 59, 51, 28. Anal. Calcd for $C_{11}H_8Cl_2O$: C, 58.18; H, 3.55. Found: C, 58.00; H, 3.62.

Compound **13** was converted to 6-phenyl-2-pyrone by the reported method[15] to give a 40% yield: mp 69 °C (pentane/benzene = 9:1) (lit.[15] 68 °C); IR (KBr) 1720 (C=O), 1640, 1550 cm^{-1} (C=C); NMR ($CDCl_3$) δ 6.22 (d, 1 H, J = 9 Hz, 3-CH), 6.62 (d, 1 H, J = 7 Hz, 5-CH), 7.38 (dd, 1 H, $J_{3,4}$ = 9 Hz, $J_{4,5}$ = 7 Hz, 4-CH), 7.24–7.55 (m, 3 H, *m*-, *p*-C_6H_5), 7.60–7.90 (m, 2 H, *o*-C_6H_5); ^{13}C NMR, see Table II; mass spectrum (70 eV) *m/e* 174, 172 (P), 147, 144, 105, 77, 51, 28. Anal. Calcd for $C_{11}H_8O_2$: C, 76.73; H, 4.68. Found: C, 76.78; H, 7.65.

4-Phenyl-2-pyrone (1). 4-Phenyl-2-pyrone (1) was prepared by the reported method[11,12] to give an 18% yield of crude product which was recrystallized from heptane–benzene (9:1): mp 78–79 °C (lit.[12] 75–76 °C); IR (KBr) 1710, 1630, 1530 cm^{-1}; NMR (CD_3COCD_3) δ 6.48 (dd, 1 H, $J_{3,5}$ = 2 Hz, $J_{3,6}$ = 1 Hz, 3-CH), 6.68 (dd, 1 H, $J_{3,5}$ = 2 Hz, $J_{5,6}$ = 5.5 Hz, 5-CH), 7.42–7.82 (m, 6 H, 6-CH, C_6H_5). Anal. Calcd for $C_{11}H_8O_2$: C, 76.73; H, 4.68. Found: C, 76.65; H, 4.84.

5-Phenyl-2-pyrone (4). 5-Phenyl-2-pyrone (4) was prepared as described,[3] giving white needles, mp 71 °C (lit.[3] 68–69 °C).

4,5,6-Phenyl-2-pyrone (7). 4,5,6-Phenyl-2-pyrone (7) was synthesized as described,[18] mp 251–254 °C (lit.[18] 245–246 °C).

The Reaction of 6-Phenyl-2-pyrone with Phenylacetylene. A solution of 116 mg (0.67 mmol) of 6-phenyl-2-pyrone and 249 mg (2.4 mmol) of freshly distilled phenyl acetylene in 10 mL of dry toluene was placed in a 50-mL Carius tube. The solution was degassed by two successive freeze (liquid nitrogen)–evacuate–thaw cycles. The ampule was sealed and placed in a 500-mL Paar bomb containing 90 mL of toluene. The bomb was heated to 300 °C for 24 h. The bomb was cooled and the ampule was opened. The ampule contents were removed and the ampule was rinsed four times with 1 mL of Skelly B. The ampule contents and washings were placed in a 25-mL volumetric flask and diluted to volume with Skelly B. A 5.00-mL aliquot of this solution was removed. The internal standard, 2-phenylnapthalene (27.4 mg, 0.13 mmol), was dissolved in the aliquot and the solution was analyzed by gas chromatography (255 °C, 10 ft × 0.375 in., 15% SE-30 on Chromasorb P) by comparison with authentic standard solutions. The reaction yielded 28.5% *o*- and 5.3% *m*-terphenyls (o/m = 5.4:1) for an overall yield of 33.9% terphenyl.

The Reaction of 4-Phenyl-2-pyrone with Phenylacetylene. A solution of 7.2 mg (0.42 mmol) of 4-phenyl-2-pyrone and 92 mg (0.90

mmol) of freshly distilled phenylacetylene in 2.1 mL of 1,2,4-trichlorobenzene was placed in a 10-mL glass ampule. The solution was degassed by two successive freeze (liquid nitrogen)–evacuate–thaw cycles. The ampule was sealed and placed in a 500-mL Paar bomb containing 75 mL of 1,2,4-trichlorobenzene in order to partially equalize the pressure inside and outside the ampule. The bomb was heated to 210 °C for 69 h. The bomb was cooled and the ampule was opened. Gas chromatography of the solution (240 °C, 5 ft × 0.375 in., 15% SE-30 on Chromosorb P) gave overlapping peaks of *m*- and *p*-terphenyls. Comparison of the peak shape with standard solutions of authentic samples indicated the ratio of meta to para was 2:1. The yield as determined by comparison with standard solutions by gas chromatography was 68.5%. The infrared spectrum of the sample collected by preparative gas chromatography indicated the presence of both *m*- and *p*-terphenyls.

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References and Notes

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Polyphenylenes via Bis(2-pyrones) and Diethynylbenzenes. The Effect of *m*- and *p*-Phenylene Units in the Chain

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ABSTRACT: Polyphenylenes with varying degrees of meta and para catenation have been synthesized utilizing the Diels–Alder 4 + 2 cycloaddition reaction of bis(2-pyrone) monomers with diethynylbenzenes. The polyphenylenes are yellow to brown, insoluble, highly crystalline, and thermally stable. Increasing amounts of meta catenation lower the T_m and improve solubility.

The 4 + 2 cycloaddition reaction of diacetylenes with bis(diene) monomers such as bis(cyclopentadienes) or bis(pyrones) has been demonstrated to afford high molecular weight polyphenylenes.[1-10] In the step-growth Diels–Alder polymerization, the elimination of either carbon monoxide or carbon dioxide, depending on the bis(diene) system used, simultaneously generates a benzene ring in the polymer backbone and prevents reversibility of the initial adduct. The properties of these polyphenylenes are different, in some respects, from those of unsubstituted polyphenylenes prepared by other means. Polyphenylenes prepared either from benzene by a Friedel–Crafts reaction under oxidative conditions or the 1,4-polymerization of 1,3-cyclohexadiene followed by hydrogenation are brown to black, crystalline, and insoluble in any solvents.[8]

By contrast, the high molecular weight phenylated polyphenylenes obtained from Diels–Alder reactions of bis(cyclopentadienes) with diacetylenes are light yellow, amorphous, completely soluble in common organic solvents, and have good thermal stability. They are, however, subject to thermal degradation due to the loss of the pendant phenyl groups.[2,11] Unphenylated poly(*p*-phenylene) prepared by a Diels–Alder reaction of 5,5′-*p*-phenylenebis(2-pyrone) (1) with *p*-diethynylbenzene is yellow, insoluble in all solvents, highly crystalline, and thermally stable.[12] The unusually high solubility of the phenylated polyphenylenes can be attributed to either pendant phenyl substitution or to the presence of meta catenation (ca. 50%)[9] in the newly formed benzene ring.

Because of the differences in the physical properties of the various polyphenylenes, the synthesis of unphenylated polyphenylenes with varying amounts of meta catenation was of particular interest.

Monosubstituted bis(cyclopentadienone)[13] and bis(sulfone)[14] monomers are not suitable choices for the preparation of unphenylated polyphenylenes because of monomer unbalancing side reactions. Monosubstituted 2-pyrones, however, are stable monomers and react with acetylenes to afford benzene derivatives.[15] Furthermore, the catenation of the products of the reactions of acetylenes and monosubstituted 2-pyrones can be predicted by consideration of the net atomic charge distribution of the reactants and any secondary overlap of frontier molecular orbitals.[16,17]

Results and Discussion

There are two ways to introduce meta catenation into the backbone of the Diels–Alder polyphenylene. Either the monomers used must contain meta substitution prior to the Diels–Alder reaction or the reaction itself must produce a new meta catenated ring. The synthesis of a poly(*m*-phenylene) requires both meta-substituted monomers and the formation of a meta-catenated benzene ring during the cycloaddition reaction. Since the only variable is the position of attachment to the 2-pyrone ring, 4,4′- and/or 6,6′-bis(2-pyrone) monomers are required to prepare an all meta-catenated polymer. Unfortunately, 4-phenyl-2-pyrones react with phenylacetylenes

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