90-04-0; 4-NH_2PhOCH_3, 104-94-9; 3-NH_2PhCH_3, 108-44-1; 4-NH_2PhCH_3, 106-49-0; 3-NH_2PhNO_2, 99-09-2; 4-NH_2PhNO_2, 100-01-6; H_2NCH_2Ph, 100-46-9; 4-NH_2PhBr, 106-40-1; Ph_3P, 603-35-0; $(PhO)_3P$, 101-02-0; $(EtO)_3P$, 122-52-1; 2-aminopyridine, 504-29-0; 2-chloro-3-aminopyridine, 6298-19-7; 4-aminoisoquinoline, 23687-25-4; imidazole, 51741-29-8; 1-aminoindole, 56480-48-9; norbornene, 498-66-8; indole, 120-72-9; 1-methylindole, 603-76-9.

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Reaction of Azomethine *N*-Oxides. 6. Spectroscopic Study of Lewis Acid Catalyzed Reactions of Nitrones with *N*-Phenylmaleimide

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The effect of the Lewis acid $AlCl_3$ on the reactivity and stereoselectivity of the 1,3-dipolar cycloaddition reactions of some azomethine *N*-oxides with *N*-phenylmaleimide in benzene at room temperature has been spectroscopically investigated. Decrease of the reactivity and increase of the stereoselectivity of the cycloaddition reactions are observed.

The effect of Lewis acids on the reactivity, regioselectivity, and stereoselectivity of Diels-Alder reactions have been thoroughly investigated. (*1-9*) In general, large rate accelerations (*1-3*) and greatly increased regioselectivity (*4*, *7*) and stereoselectivity (*8*, *9*) are observed.

Frontier orbital theory also predicts that Lewis acids like BF_3 and $AlCl_3$ will affect rates and selectivities in 1,3-dipolar cycloadditions. Lewis acids catalyzed 1,3-dipolar cycloaddtions of both diphenylnitrilimine (*10*) and benzonitrile oxide (*11*) have been studied. The two examples undergo rapid 1,3-dipolar cycloadditions in the presence of the Lewis acids $AlCl_3$ and BF_3, respectively. In conjunction with our interest in the reactions of azomethine *N*-oxides with electron-deficient compounds, (*12-17*) we now wish to report the spectroscopic study of the effect of the Lewis acid $AlCl_3$ on the reactivity and stereoselectivity of the 1,3-dipolar cycloaddition reactions of the azomethine *N*-oxides (nitrones) (**1a-e**) with the symmetrical electron-poor dipolarophile **2** in benzene as a solvent. The aldonitrones (**1a-e**) react with the *N*-phenylmaleimide (**2**) in dry benzene at room temperature to give two stereoisomers, the *cis*-isoxazolidines (**3a-e**) and the *trans*-isoxazolidines (**4a-e**) (Figure 1). The major adducts formed were the thermodynamically more stable trans adducts (**4a-e**) (51-69%). The configuration of the isoxazolidines were determined on the basis of the magnitude of the coupling constant between H_3 and H_4 of the isoxazolidine ring (Figure 1); the larger values (J = 7-9 Hz) were assigned to the cis coupling constants H_3 and H_4 of **3a-e**, and the smaller values (J = 1-2 Hz) to the trans coupling constants between the corresponding protons of **4a-e** (*18*, *19*) (Table I). On the other hand, heating of the cis isomers **3a-e** in *p*-xylene gave the thermodynamically more stable trans isomers **4a-e** in very good yield (100%).

However, in the presence of an $^1/_{10}$ M ratio of $AlCl_3$, the reactions of the nitrones **1a-e** with **2**, under the same conditions, slow down and the cis stereoisomer ratio was increased (3-17%). The ratio of the cis and trans products were determined from the integration of the resonance of the H_3 proton nuclear magnetic resonance spectra of the reaction mixtures.

The decrease of the reactivity of the reactions has been attributed to the complexation between the Lewis acid $AlCl_3$ and the nitrones **1a-e**. This assumption has been confirmed by observation of the UV spectra of the mixtures of each of the nitrones **1a**, **1d**, as well as **1e** and $AlCl_3$ in benzene (Table II). A new broad band in the UV spectrum, 317-365 nm, is observed immediately on mixing equimolar solutions of the Lewis acid $AlCl_3$ with each of the nitrones **1a**, **1d**, and **1e** in benzene (Table II). These absorptions were ascribed to the complex formation. However, the reaction of the nitrone **1c** with **2**, in the presence of $^1/_{10}$ M ratio of $AlCl_3$, in benzene led to formation of more trans isomer. This behavior may be ascribed to the difficulty of the complexation of the nitrone **1c** with the Lewis acid $AlCl_3$.

Attempts to study the effect of an equimolar ratio of $AlCl_3$ to both reactants **1a-e** and **2** on the reactions failed because of the difficulty of the solubility of aluminum chloride in benzene.

Experimental Section

Melting points are uncorrected. IR spectra were taken on a Shimadzu-408 spectrophotometer as KBr disk. UV-vis spectra were recorded on a Beckman Model 26 recording spectrophotometer. ^1H NMR spectra were measured in $CDCl_3$ or CD_3SOCD_3 as solvents by using Varian XL 100 (100 MHz) and EM 390 (90 MHz) with Me_4Si as internal standard. Elemental analyses were performed by the microanalytical Unit of Cairo University. The nitrones **1a-e** (*20*) were prepared according to literature procedures.

General Procedure of the Cycloaddition of the Nitrones (1a-e) and N-Phenylmaleimide (2). A solution of 1 mmol of nitrone (**1a-e**) in 3 mL of dry benzene was added to a solution of 173 mg (1 mmol) of *N*-phenylmaleimide in 2 mL of dry benzene. The reaction mixture was stirred at room temperature until the thin-layer chromatogram (TLC) showed the disappearance of the starting compounds. The solvent was then removed at room temperature with a rotary evaporator. The NMR spectrum of the residue showed two cycloaddition adducts in different ratios (Table I). The isomers were separated by

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Table I. Physical Data of the Cycloadduct Isomers

isomer[a]	mp, °C	yield,[b] %	cryst solv	IR (OCNCO), cm^{-1}	^1H NMR[c] ($CDCl_3$), ppm
3a	190–192	37 (40)	*d*	1788, 1715	4.1 (dd, 1 H, $J_{4,3}$ = 8 Hz, $J_{4,5}$ = 9 Hz, H-4), 4.92 (d, $J_{5,4}$ = 9 Hz, H-5), 5.4 (d, 1 H, $J_{3,4}$ = 8 Hz, H-3), 6.0 (s, 2 H, CH_2), 6.8–7.6 (m, 13 H, C_6H_5)
3b	185–186	41 (46)	*d*	1785, 1721	3.7 (s, 3 H, OCH_3), 4.0 (dd, 1 H, $J_{4,3}$ = 8 Hz, $J_{4,5}$ = 9 Hz, H-4), 4.9 (d, $J_{5,4}$ = 9 Hz, H-5), 6.1 (d, 1 H, $J_{3,4}$ = 8 Hz, H-3), 6.7–7.7 (m, 14 H, C_6H_5)
3c	203–204	49 (46)	*e*	1782, 1718	3.85 (s, 3 H, OCH_3), 3.95 (s, 3 H, OCH_3), 4.1 (d, 1 H, $J_{4,5}$ = 7 Hz, H-4), 5.35 (d, 1 H, $J_{5,4}$ = 7 Hz, H-5), 5.85 (s, 1 H, H-3)8 6.5–7.5 (m, 13 H, C_6H_5)
3d	204–206	32 (49)	*f*	1790, 1725	2.5 (s, 3 H, CH_3), 4.18 (dd, 1 H, $J_{4,3}$ = 9 Hz, $J_{4,5}$ = 8 Hz, H-4), 5.08 (d, 1 H, $J_{3,4}$ = 9 Hz, H-3), 5.24 (d, 1 H, $J_{5,4}$ = 8 Hz, H-5), 6.81–7.6 (m, 14 H, C_6H_5)
3e	176–178	31 (47)	*f*	1788, 1720	2.35 (s, 3 H, CH_3), 4.0 (dd, 1 H, $J_{4,5}$ = 9 Hz, $J_{4,3}$ = 7 Hz, H-4), 4.91 (d, 1 H, $J_{5,4}$ = 9 Hz, H-5), 5.29 (d, 1 H, $J_{3,4}$ = 7 Hz, H-3), 6.8 (m, 14 H, C_6H_5)
4a	173–174	63 (60)	*d*	1790, 1721	3.95 (dd, 1 H, $J_{4,3}$ = 1 Hz, $J_{4,5}$ = 7 Hz, H-4), 5.1 (d, 1 H, $J_{5,4}$ = 7 Hz, H-5), 5.62 (d, 1 H, $J_{3,4}$ = 1 Hz, H-3), 6.0 (s, 2 H, CH_2), 6.45–7.5 (m, 3 H, C_6H_5)
4b	127–128	59 (54)	*d*	1780, 1710	3.82 (s, 3 H, OCH_3), 3.95 (dd, 1 H, $J_{4,3}$ = 1 Hz, $J_{4,5}$ = 7.5 Hz, H-4), 5.1 (d, 1 H, $J_{5,4}$ = 7.5 Hz, H-5), 5.7 (d, 1 H, $J_{3,4}$ = 1 Hz, H-3), 6.55–7.55 (m, 14 H, C_6H_5)
4c	173–175	51 (54)	*e*	1785, 1718	3.77 (s, 3 H, CH_3), 3.92 (s, 3 H, OCH_3), 4.15 (t, 1 H, J = 8 Hz, H-4), 5.2 (d, 1 H, $J_{5,4}$ = 7 Hz, H-5), 6.5 (d, 1 H, $J_{3,4}$ = 2 Hz, H-3), 7.0–7.5 (m, 13 H, C_6H_5)
4d	173–175	68 (51)	*e*	1785, 1715	2.62 (s, 3 H, CH_3), 3.85 (dd, 1 H, $J_{4,5}$ = 7 Hz, $J_{4,3}$ = 2 Hz, H-4), 5.1 (d, 1 H, $J_{5,4}$ = 7 Hz, H-5), 5.83 (d, 1 H, $J_{4,3}$ = 2 Hz, H-3), 6.5–7.82 (m, 14 H, C_6H_5)
4e	149–150	69 (53)	*g*	1789, 1725	2.4 (s, 3 H, CH_3), 4.05 (dd, 1 H, $J_{4,5}$ = 7 Hz, $J_{4,3}$ = 2 Hz, H-4), 5.12 (d, 1 H, $J_{5,4}$ = 7 Hz, H-5), 5.73 (m, 1 H, H-3), 6.5–7.5 (m, 14 H, C_6H_5)

[a] Satisfactory elemental analyses were submitted. [b] Yield in parentheses for isomer in presence of $AlCl_3$. [c] Spectra of **3a–c** were measured in Me_2SO. [d] Benzene. [e] Ethanol–CH_2Cl_2. [f] Ethanol. [g] Ethanol–hexane.

Table II. Wavelengths Maxima of the Nitrones 1b, 1d, and 1e (4 × 10^{-2} M), as well as Their Complexes with $AlCl_3$ (4 × 10^{-2} M) in Benzene at Room Temperature

compd	λ_{max}, nm	compd	λ_{max}, nm
1b	303	1d + $AlCl_3$	325
1b + $AlCl_3$	317	1e	329
1d	322	1e + $AlCl_3$	365

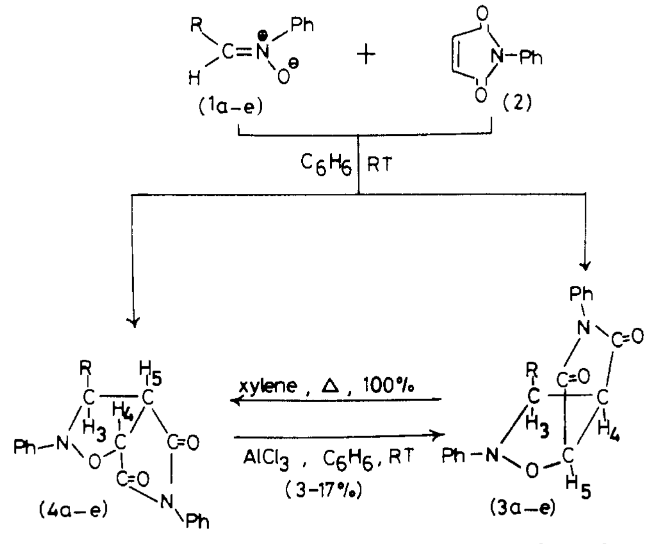

Figure 1. a: R = 3,4-methylenedioxypheyl. b: R = 4-CH_3O-C_6H_4. c: R = 2,4-dimethoxyphenyl. d: R = 2-CH_3-C_6H_4. e: R = 3-CH_3-C_6H_4.

fractional crystallization from the proper solvent (Table I) to give **3a–e** and **4a–e**.

General Procedure of the Lewis Acid Catalyzed Reaction of the Nitrones (1a–e) and N-Phenylmaleimide (2). A solution of 1 mmol of nitrone (**1a–e**) in 2 mL of dry benzene was added over a period of 10 min to a stirred suspension of 13.3 mg (0.1 mmol) of $AlCl_3$ in 5 mL of dry benzene. A solution of 173 mg (1 mmol) of *N*-phenylmaleimide in 3 mL of dry benzene was then added dropwise during a period of 20 min and the mixture was stirred at room temperature until the TLC showed the disappearance of the starting compounds. The reaction mixture was washed with dilute hydrochloric acid and then with water. The organic layer was separated and dried over anhydrous sodium sulfate. The solvent was then removed with a rotary evaporator. The NMR spectrum of the residue showed two cycloaddition adducts in different ratios. The two residue isomers were separated by fractional crystallization from the proper solvent to give **3a–e** and **4a–e**.

General Procedure of the Effect of Heat on 3a–e and 4a–e. A solution of (2 mmol) **3a–e** in 10 mL of dry *p*-xylene was refluxed for 12 h. Then the solution was evaporated under reduced pressure to give 2 mmol of the trans isomers **4a–e**. These isomerization reactions have been confirmed by comparison of the NMR spectra and the melting points of the products obtained.

Registry No. **1a**, 95794-11-9; **1b**, 3585-93-1; **1c**, 100858-29-5; **1d**, 35427-93-1; **1e**, 62500-20-3; **3a**, 100858-30-8; **3b**, 35216-22-9; **3c**, 100858-31-9; **3d**, 88743-89-9; **3e**, 88823-69-2; **4a**, 100937-73-3; **4b**, 35216-21-8; **4c**, 100937-74-4; **4d**, 88765-52-0; **4e**, 88743-90-2; $AlCl_3$, 7446-70-0; *N*-phenylmaleimide, 941-69-5.

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