

Functionalization of Phenyl Rings by Imidoylnitrenes. 2. Cycloaddition or Electrophilic Aromatic Substitution?

Hossein A. Dabbagh* and Saied Ghaelee

Department of Chemistry, Isfahan University of Technology, Isfahan, Iran

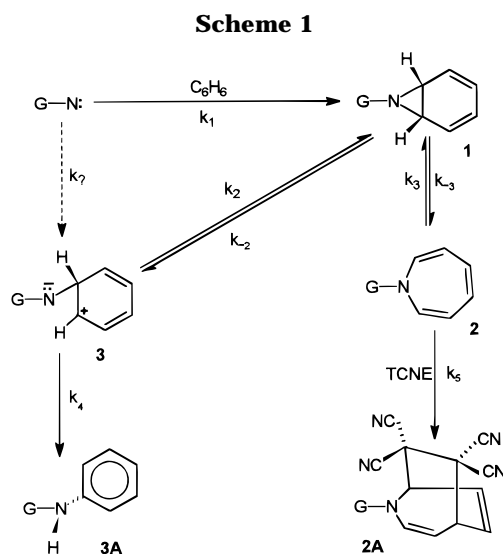
Received June 9, 1995[®]

The thermal decomposition of *N*-[(cyanoaryl)oxy]imidoyl azides with various substituted benzenes (OCH₃, NHCOCH₃, C(CH₃)₃, *p*-xylene, CH₃, H, Cl, CO₂CH₃, NO₂) has been studied in detail. With electron-rich aromatic nuclei, the addition of a nitrene yields a benzenonium ion (**3**) intermediate. Benzaziridine (**1**) and/or **3** intermediate is formed from benzene. Electron-poor aromatic nuclei generated only intermediate **1**, in which no benzenonium diradical is formed. Intermediate **3** is stabilized by extended conjugation through an extra resonance structure. For electron-rich aromatic compounds at 65–120 °C, the thermodynamically-controlled products, *N*-arylisoureas ((*Z*)-NH-Ar), were produced in very high yield. Azepenes (the kinetically-controlled products) were detected by neither ¹H-NMR nor a trapping experiment using tetracyanoethylene (TCNE). In the case of benzene 95% azepene was produced, which at 80 °C converted to isourea ($k = 7.0 \times 10^{-5} \text{ s}^{-1}$). The ortho/para ratio resembles that of electrophilic aromatic substitution reactions. The Hammett plot of $\log k_X/k_H$ or $\log f_p$ versus σ^+ -values showed excellent correlation, with ρ^+ -values of -2.80 and -3.10 , respectively (poor correlation resulted with σ -values). The Hammett ρ^+ - or ρ -values are inconsistent with a radical mechanism for these reactions.

Introduction

Reactions of nitrenes with benzene and its derivatives, as well as those of electrophilic aromatic substitution, are among the most studied of all organic processes. Both reactions involve an electron-deficient nitrogen that obtains electrons from aromatic nuclei.^{1–21}

Reactions of nitrenes have been rationalized to be a cycloaddition reaction of singlet nitrene with an electron-rich aromatic nuclei or a mixture of triplet \rightleftharpoons singlet nitrenes with electron-poor aromatic nuclei. The formation of azepene **2** at low temperatures supports the idea that **2** is a kinetically controlled product and that isourea



3A is a thermodynamically controlled product (Scheme 1, Figure 1).^{1–3,7,12,13}

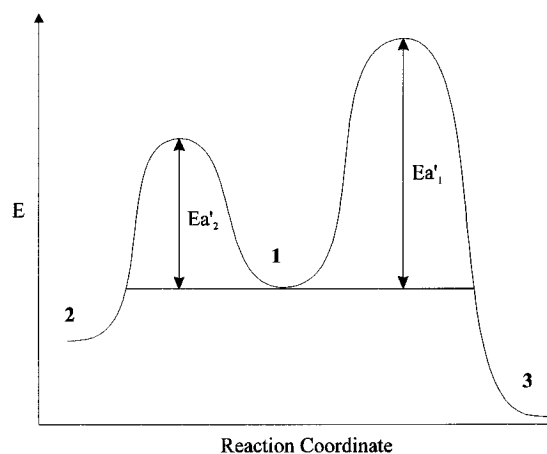


Figure 1. Hypothetical potential energy diagram for Scheme 1.

In electrophilic aromatic substitution reactions, it has been established that the result is the formation of a π -complex that subsequently converts to a σ -complex.^{4–6} STO-3G calculations⁸ and CNDO/2 calculations⁹ show the highest electron density for the benzene derivatives with electron-donating groups (**4**) to be at the ortho and para positions. The electron density at the meta position is

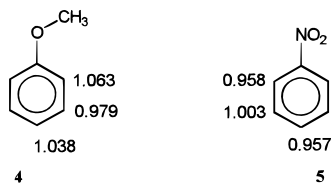
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[®] Abstract published in *Advance ACS Abstracts*, April 1, 1996.

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higher for the substituted benzenes (**5**) with electron-withdrawing groups.



The PMO description of molecular orbital and energy levels for the pentadienyl cation indicates that the LUMO is ψ^3 , with the highest coefficients located at carbons 1, 3, and 5 of the pentadienyl system. These are ortho and para to the position occupied by the electrophile. An electron-donating group at the 2 or 4 position stabilizes the system much less because of nodes at these carbons in the LUMO. Electron-withdrawing substituents destabilize the system when they occupy the 1, 3, or 5 position of the pentadienyl cation, and the destabilizing effect would be less at the 2 or 4 position.^{6,9-11} The energy of the HOMO is consistent with decreased activity for rings with electron-withdrawing substituents. Aromatic rings with acceptor substituents are relatively unreactive and less likely to have early transition states. For such compounds, the stability of the σ -complex intermediate is likely to be the most important factor in controlling product formation (predominately meta substitution).

The question is this: Could electrophiles with moderate reactivity such as imidoynitrenes (GN) first make a π -complex at an ortho or para position with the highest electron density and then open directly to a σ -complex?

The objective of this study was to detect any possible azepene formed at lower temperatures during the reactions by NMR or trapping with TCNE, as well as to measure total relative reaction rate, reaction rate factors, and the rate of conversion of azepene to isourea. To accomplish this objective, an azide that decomposes at low temperatures and that produces a nitrene with both moderate reactivity and high selectivity was sought. The mechanism of the addition of *N*-[(trifluoromethyl)sulfonyl](1,3,5-trimethylphenoxy)nitrene (**6N**) and *N*-cyano-(2,6-dimethylphenoxy)nitrene (**7N**) at 65–120 °C to the benzene with electron-rich groups (OCH₃, CH₃, NH-COCH₃, *p*-xylene, H), moderately deactivating groups (Cl, CO₂CH₃), or strongly electron-withdrawing (NO₂) groups, was investigated in detail.

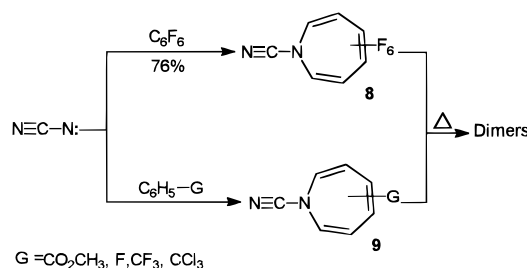


Results and Discussion

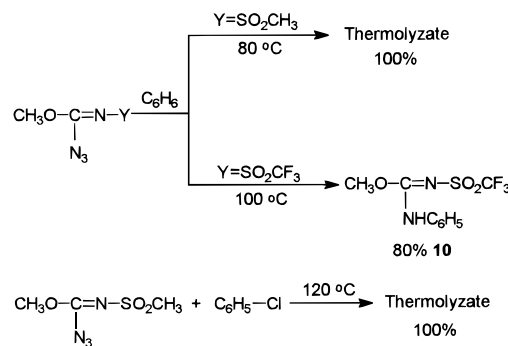
The question as to whether the aromatic substitution reaction of nitrenes is accomplished through a radical or an ionic mechanism was first considered by Heacock and Edmison.¹²

Abramovitch et al.^{3,7} speculated that the process of thermal decomposition of sulfonyl azide in aromatic solvents involves the addition of a singlet nitrene (due to the absence of biaryls) to the aromatic nucleus, resulting in benzenaziridine **1**, which undergoes ring opening to benzenonium ion **3** and/or the azepene **2**. On the basis of trapping experiments at 120 °C, they concluded that there is an equilibrium, $\mathbf{3} \rightleftharpoons \mathbf{1} \rightleftharpoons \mathbf{2}$, that lies mainly on the side of **3**. They added that the conversion of **1** to

Scheme 2



Scheme 3



Thermolyzate = Products of rearrangements, fragmentations, dimerization, and polymerization of nitrenes.

2 is a kinetically-controlled step ($k_2 > k_3$), whereas the conversion of **1** to **3** would be the product of thermodynamic control (Scheme 1, Figure 1). The researchers' attempt to generate nitrene at low temperatures (80 °C) failed, whereas at 90 °C they could detect about 0.3% azepene by thin layer chromatography (TLC). The results of the thermolysis of methanesulfonyl azide with electron-withdrawing substituted benzenes showed a pattern similar to that observed for highly electrophilic free radicals, suggesting the presence of a triplet nitrene. With a less deactivated substrate such as methyl benzoate, benzonitrile, and benzotrifluoride, the substitution pattern suggested that a mixture of singlet and triplet species had been produced.

Marsh and Simmons¹³ showed that the reaction of *N*-cyanogen azide at 44–60 °C with benzene produced *N*-cyanoazepene in high yield, stabilizing at –87 °C but spontaneously dimerizing to a white crystalline solid (mp 220–221 °C) at ambient temperature. Electron-releasing groups such as methyl produced a mixture of the three isomeric methyl *N*-cyanoazepenes, which at room temperature rearranged to ortho- and para-substituted phenylcyanamides at a 2:1 ratio. The absence of the meta isomer was assumed to be because the *N*-cyanoazepenes had isomerized to *N*-cyano-7-azanorcaradines, which had undergone highly selective azirane ring openings to the observed products. Electron-withdrawing substituents such as F, CCl₃, or CF₃ produced only the azepenes **8** and **9**. Furthermore, when heated, they showed less of a tendency to rearrange to cyanamides, but rather dimerized (Scheme 2).

Subba Rao and Lwowski¹⁴ converted [*N*-(cyanoethoxy)carbimido]nitrene in benzene photochemically to a stable mixture (1.17:1 ratio) of *N*-[*N*-(cyanoethoxy)carbimido]azepene and *N*-phenyl-*N*-cyano-*O*-ethoxyisourea.

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Table 1. Comparison of the Isomers Ratio for the Reaction of (Phenylsulfonyl)nitrene, Nitration, Imidoynitrene, and Triphenylmethyl Radical with Benzene Derivatives

benzene deriv	$(C_6H_5)_3C^{\cdot}$		$CH_3SO_2N^{\cdot a}$		$^+NO_2^b$		$ZO(-C=NY)N^{\cdot}$	
	ortho/para	% meta	ortho/para	% meta	ortho/para	% meta	ortho/para	% meta
nitrobenzene	2.2	10 ^c	1.87 NR	13 ^d NR	3	92	NR	NR ^{e,f}
methylbenzoate	1.8	20 ^g	14.3 32	54 34 ^d	6.5	70	NR	NR
chlorobenzene	1.3	39 ^g	0.89	2	0.5	1	1.22 NR	0 ^f NR ^h
methylbenzene	4.8	11 ^c	1.6	1	1.6	3	2.6 1.6	0 ^f 0 ^h
acetanilide	NA	NA	NA	NA	0.24	2	1	0 ^f
methoxybenzene	2.35	43 ^g	2.6	2	0.48	1	0.85 0.58	0 ^h 0 ^{h,j}

^a Refers to ref 12. ^b Refers to ref 19. ^c Refers to ref 20. ^d Refers to ref 7 ($CH_3SO_2N^{\cdot}$). ^e Refers to no nitrene–aromatic adducts. ^f Refers to this work ($Z = 2,6$ -dimethylphenyl; $Y = CN$). ^g Refers to ref 21. ^h Refers to ref 16 ($Z = OCH_3$; $Y = SO_2CH_3$). ⁱ Not available. ^j Refers to ref 16 ($Z = 2,6$ -dimethylphenyl; $Y = SO_2CH_3$).

Table 2. Reaction of Imidoynitrenes [$ZO(-C=NY)N^{\cdot}$] with Benzene and Its Derivatives

benzene deriv (Ar)	% therm ^b	k_X/k_H	f_p^*	f_0	$ZO(C=NY)NHAr$			rel % yield of isourea ^c	% TCNE ^a adducts
					% para	% ortho	% meta		
nitrobenzene	100				NR ^d	NR	NR	0 ^{d,f}	
methylbenzoate	100				NR	NR	NR	0 ^{e,f}	
chlorobenzene	90	0.29	0.77	0.47	45	55	<i>g</i>	100 ^{e,f}	
benzene	72	1	1	1	NA ^h	NA	NA	5 ^{l,k}	95 ^k
methylbenzene					28	72	<i>g</i>	100 ^{e,j}	
	30	6	10	13	38	62	<i>g</i>	100 ^{f,i}	0
acetanilide	10	23	69	34	50	50	<i>g</i>	100 ^{e,i}	
<i>p</i> -xylene	51				NA	NA	NA	100 ^{i,j}	0
<i>tert</i> -butylbenzene					64	36	<i>f</i>	100 ^{i,j}	
	65				75	24	<i>f</i>	100 ^{i,j}	
methoxybenzene					54	46	<i>f</i>	100 ^{f,i}	
	2	126	408	174	63	37	<i>f</i>	100 ^{i,j}	

^a Tetracyanoethylene. ^b Percent thermolyzate. ^{*} Partial reaction rate factors. ^c Yield by ¹H-NMR. ^d No nitrene–aromatic adducts. ^e At 120 °C. ^f Refers to this work ($Z = 2,6$ -dimethylphenyl; $Y = CN$). ^g Undetectable amount. ^h Not applicable. ⁱ At 65 °C. ^j Refers to ref 16 ($Z = OCH_3$; $Y = SO_2CH_3$). ^k Percent azepene. ^l Refers to ref 16 ($Z = 2,6$ -dimethylphenyl; $Y = SO_2CH_3$).

Dabbagh and Lwowski,¹⁶ in a study of the effect of electron availability in the aromatics, synthesized nitrenes reactive enough to attack only the electron-rich aromatic nuclei but not sufficiently reactive to attack benzene. This submarginal nitrene required only a slight increase of the electron-withdrawing effect of G in GN to make its reaction with benzene observable. The products of over twenty reactions of these imidoynitrenes with electron-rich substituted aromatic nuclei at 80–100 °C produced isoureas only, with no azepene detected by the NMR or TCNE trapping technique (Scheme 3). The researchers subsequently discovered evidence that the reaction of imidoynitrenes with electron-rich aromatic nuclei resembles that produced by electrophilic aromatic substitution, except that in the latter case benzene produces azepene as a major product.^{14–17}

Reaction of *N*-[(Trifluoromethyl)sulfonyl](2,4,6-trimethylphenoxy)imidocarbonyl Azide (6) with Nitrobenzene. Azide 6 decomposed completely at 120 °C in the presence of nitrobenzene for 24 h (similar results were obtained at 80 °C after 48 h) but yielded no products incorporating the nitrobenzene ring. When thermolyzed in such inert media, all the azides discussed here and quite a few others¹⁶ gave remarkably constant product mixtures called “thermolyzates”. It was observed (by the TLC, IR, ¹H-NMR) that their composition does not depend on the nature of the solvent and cosolute and are characteristic of any given azide.

Reaction of *N*-Cyano(2,6-dimethylphenoxy)imidocarbonyl Azide (7) with Nitrobenzene. Azide 7 with nitrobenzene at 120 °C for 24 h gave 100% thermolyzate.

Reaction of Azide 7 with Methyl Benzoate. Azide 7 with methyl benzoate at 90 °C for 15 h gave 100% thermolyzate.

Reaction of Azide 7 with Chlorobenzene. Azide 7, when decomposed in chlorobenzene at 105 °C for 15 h, produced N₂ in quantitative amounts (similar results were obtained at 80 °C for 48 h). Tracing the reaction progress by TLC showed complete decomposition of azide and formation of two major products: *N*-4-(chlorophenyl)-*N*-cyano-*O*-(2,6-dimethylphenyl)isourea (11), and *N*-(2-chlorophenyl)-*N*-cyano-*O*-(2,6-dimethylphenyl)isourea (12). About 90% thermolyzate with no trace of azepene 13 was detected by the ¹H-NMR (Tables 1 and 2 and Scheme 4).

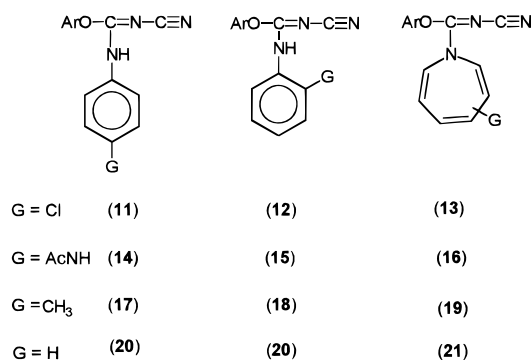
Reaction of Azide 7 with Acetanilide. Azide 7 in a 20 mol excess of dioxane at 100 °C for 24 h gave nearly 100% N₂ and equal amounts of *N*-(4-acetamino)-*N*-cyano-*O*-(2,6-dimethylphenyl)isourea (14), *N*-(2-acetamino)-*N*-cyano-*O*-(2,6-dimethylphenyl)isourea (15), and 10% thermolyzate. The higher ortho/para ratio could be attributed to stabilization of the ortho σ complex by hydrogen bonding. No trace of azepene 16 was detected.

Reaction of Azide 7 with Toluene in the Presence of Tetracyanoethylene (TCNE). Thermolysis of azide 7 in an excess of toluene (1:50) at 75 °C for 48 h produced a near statistical 1:2 ratio of *N*-(4-tolyl)-*N*-cyano-*O*-(2,6-dimethylphenyl)isourea (17), *N*-(2-tolyl)-*N*-cyano-*O*-(2,6-dimethylphenyl)isourea (18), and 30% thermolyzate. No

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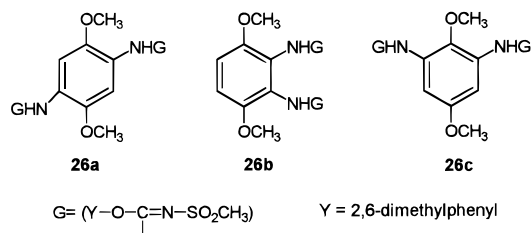
Scheme 4



Ar = 2,6-dimethylphenyl; values in (product number)

Ac = CH₃CO

Scheme 5



trace of azepene **19** or azepene-TCNE adducts was detected by ¹H-NMR or TLC.

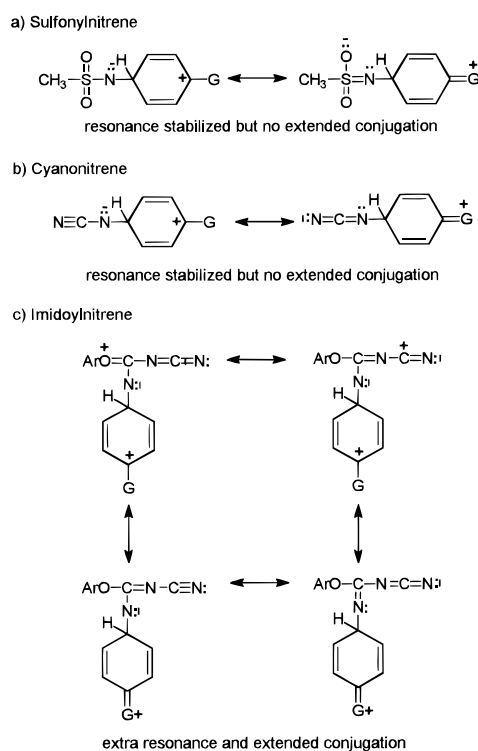
Reaction of Azide **7 with Benzene.** Thermolysis of azide **7** in an excess of benzene at 65 °C for 48 h produced 5% *N*-phenyl-*N*-cyano-(2,6-dimethylphenoxy)isoureas (**20**), 95% *N*-[*N*-cyano(2,6-dimethylphenoxy)imidocarbonyl]-azepene (**21**), and 72% thermolyzate (Table 2, Scheme 4, and Figure 3).

Thermolysis of Azepene **21 in Tetrachloromethane-Acetonitrile.** A mixture of 95% **21**, 5% **20**, tetrachloromethane, and acetonitrile-*d*₃ (95:5) in an NMR tube was placed in an oil bath (80 °C). Reaction progress was followed by ¹H-NMR for 309 h. All the azepenes converted to isourea **20** with a rate constant of $k = 7.0 \times 10^{-5} \text{ s}^{-1}$ and also to small amounts of a complex mixture (Figure 3 and Table 2). This experiment in DMSO-*d*₆ at 100 °C produced similar results in several hours.

Reaction of *N*-(Cyanoethoxy)imidocarbonyl Azide (22**) with *p*-Xylene and TCNE.**¹⁶ Reaction of azide **22** with a 10 molar excess of *p*-xylene and TCNE in acetonitrile at 80 °C for 24 h produced nearly 100% nitrogen, 61% *N*-(2,5-dimethylphenoxy)-*N*-cyano-*O*-methylisourea (**23**), 41% thermolyzate, and no TCNE adducts (Table 2).

Reaction of *N*-(Methylsulfonyl)(2,6-dimethylphenoxy)imidocarbonyl Azide (24**) with 1,4-Dimethoxybenzene.**¹⁶ Reaction of azide **24** with 1,4-dimethoxybenzene (1:1) in acetonitrile at 80 °C for 24 h produced 70% of a mixture of 50% monosubstituted *N*-(2,5-dimethoxyphenyl)-*N*-(*N*-methylsulfonyl)-*O*-(2,6-dimethylphenoxy)isourea (**25**) and 20% disubstituted products **26**. No azepene was observed. There are three possible structures for the isourea **26**, but the structures **26a** and **26b** matched those of the ¹H-NMR and ¹³C-NMR (Scheme 5). When the azide **24** was allowed to react with 1 mol of isourea **25** under similar conditions described above, the isourea **26** was produced. TLC, ¹H-NMR, ¹³C-NMR, elemental analysis, and melting point of the product all matched those of **26a** or **26b**. Formation of **26a** or **26b** over **26c** is a clear indication that the electronic effect

Scheme 6



(donation by CH₃O and GNH) produces a highly stabilized resonance structure (σ -complexes) that controls the addition of the second mole of GN. Para and ortho to the first GNH (2 or 4 position) are the most stabilized positions (each has two extra resonance intermediates). Cycloaddition reactions (formation of benzaziridine) are less sensitive to the electronic effects of the ortho- or para-directing substituents, indicating that some amount of **26c** should have been produced. Further studies are underway to identify the structure of **26a** or **26b**.

Discussion

The thermal decomposition of sulfonyl azide and other similar azides with aromatic nuclei has been speculated to involve the addition of a singlet nitrene to form a benzaziridine intermediate. Although this intermediate was never detected—even at -110 °C¹⁸—nor was it trapped with TCNE,⁷ the basis for the proposed mechanism is the formation of the trapped azepenes. The fact that the azepenes could not be isolated is assumed to be due to their instability at higher temperatures; as such, they appear to be the kinetically-controlled products that at high temperatures convert to thermodynamically-controlled products—namely, the isoureas. Subsequently,¹⁶ it was realized that in a reaction of imidoylnitrenes with electron-rich aromatic nuclei, no azepenes can be trapped with TCNE.

To account for the lack of formation of the azepenes, the reaction of **7** with aromatic nuclei at a temperature of 65 °C or higher was investigated. With nuclei bearing an electron-releasing group or a moderately deactivating

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group, only the isoureas were produced. The highly deactivating groups NO_2 and CO_2CH_3 produced thermolyzate. In a single attempt, the reactivity of nitrene **6N** was tested with nitrobenzene, resulting in 100% thermolyzate. In all the cases studied (except those in which benzene was used) the formation of azepene was not detected by ^{13}C -NMR, ^1H -NMR, or TLC; nor was it detected by a trapping method using TCNE (Tables 1 and 2). The reaction of nitrene **7N** with benzene at 65°C produced a 28% mixture of 5% isourea **20** and 95% azepene **21**. Following the conversion of the kinetically-controlled products (azepenes) to the thermodynamically-controlled products (isoureas) by ^1H -NMR, it was discovered that indeed at 80°C the azepene **21** converted to isourea **20** in 320 h with a first-order rate constant of $7.00 \times 10^{-5} \text{ s}^{-1}$ (Table 2, Figure 3) and also to a small amount of a complex mixture. All attempts to separate **20** from **21** failed. In every case, a mixture of nearly 95% **21**/5% **20** was produced on crystallization.

What is the mechanism operating for the electron-rich aromatic nuclei?

To demonstrate the effect of the substituents on the position of the transition state, the total relative reaction rates (k_X/k_H) were calculated using eq 1. The partial relative reaction rates (f_o and f_p) were calculated by using the total relative reaction rates and mole fraction of each isomer obtained from ^1H -NMR (Table 2, eq 3).

The plots of $\log k_X/k_H$ ($r = 0.94160$) or $\log f_p$ ($r = 0.88170$) vs σ showed a poor correlation. The correlation with σ^+ is much better, the ρ value of the plot of σ^+ vs $\log k_X/k_H$ being -2.80 ($r = 0.99270$) and the ρ value of $\log f_p$ being -3.10 ($r = 0.99520$), (Table 2). The plots (using the data from Table 3 of ref 12) of $\log k_X/k_H$ ($r = 0.50930$) or $\log f_p$ ($r = 0.04860$) vs σ^+ or the plots of $\log k_X/k_H$ ($r = 0.78970$) or $\log f_p$ ($r = 0.06620$) vs σ showed no correlation.

A numerically large ρ^+ value suggests a strong substituent effect; that is, a late transition state that resembles the σ -complex. The small slope would indicate very small development of the positive charge, resulting in a relatively weak interaction with the substituent. With a less reactive electrophile such as imidoynitrene the transition state develops later (highly reactive nitrene has an early transition state and shows no correlation with σ^+), the bond with electrophile forms more completely, and a substantial positive charge develops on the ring.

The data suggest that in the case of the electron-rich benzene derivatives there is no evidence for the formation of a high energy intermediate benzaziridine **27** or azepene **21** (Hammett ρ^+ , f_p , ortho/para 0% meta, and no TCNE-nitrene-arene adducts). The low energy π -complex is formed first and then converted directly to intermediate benzonium ion (**29_o** or **29_p**) and followed by a hydrogen transfer to make isoureas **32** (Tables 1 and 2, Scheme 7, and Figure 2). As shown in the hypothetical energy diagram (Figure 2) formation of the azepenes has a much higher energy level of activation than that of benzonium ion (the higher the resonance stabilized energy for the intermediates (**29_{o,p}**), the lower the activation energy level will be for the formation of isourea). The activation energy level of (**29_m**) is much higher (no trace of meta isourea was detected using TLC, column chromatography, or ^1H -NMR). The benzonium intermediates (**29_{o,p}**) was stabilized by extra resonance in the aromatic nuclei and by extended conjugation in the nitronium anion (Scheme 6). In the case of benzene, the resonance-

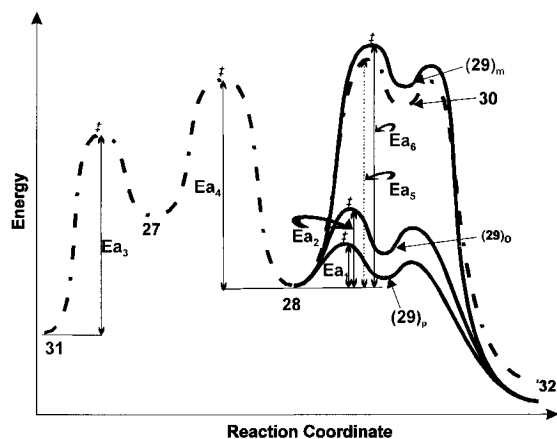
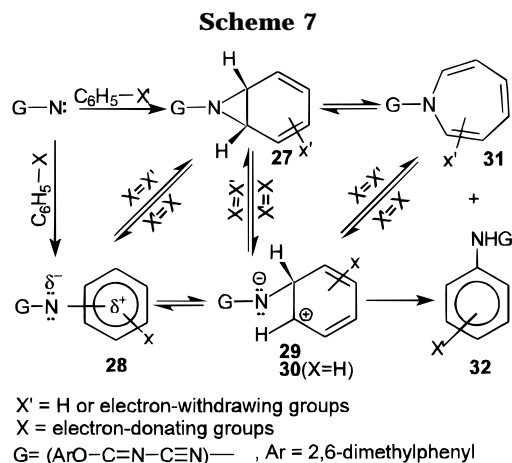


Figure 2. General hypothetical potential energy profile for electrophilic aromatic substitution versus cycloaddition reaction of nitrenes with aromatic nuclei (see Scheme 7).



stabilized energy is much lower (having a higher activation energy level with a lower total yield) for the phenyl ring. The nitronium anion, however, is stabilized by the extended conjugation in nitrene residue favoring **27** over **30** (the ratio of **27** to **30** depends on the amounts of resonance-stabilized energy). For the electron-withdrawing aromatic nuclei ($X = \text{NO}_2, \text{CO}_2\text{CH}_3$), the activation energy level is very high, which accounts for why no trace of azepenes or isoureas can exist (Tables 1 and 2). The cyanonitrene (its high reactivity, low selectivity resembling those of a radical mechanism) reacts with electron-poor aromatic nuclei to produce azepenes in high yield and at higher temperatures shows less of a tendency to convert to isoureas (very unstable σ -complexes, $E_{a3} \ll E_{a5}$, or E_{a6}).

The extra-resonance structures and extended conjugation in imidoynitrene **7N** (cyanonitrene has no extended conjugation) lowers the activity of nitrene, increases its selectivity, and stabilizes the σ -complex (Scheme 6). The ortho-para ratio, good Hammett correlation, f_o , f_p , and lack of formation of the meta isomer all indicate that the reaction of certain imidoynitrenes to electron-rich benzenes are very similar to that produced by electrophilic aromatic substitution. Radical mechanisms have partial rate factors of near unity, very poor or no Hammett correlation, a large amount of meta isomer, and a higher ortho-para ratio (Table 1).

Conclusion

Most reactive nitrenes ($\text{MeSO}_2\text{N}:$, $\text{PhSO}_2\text{N}:$, and $\text{NCN}:$) when functioning as electrophiles exhibit early transition

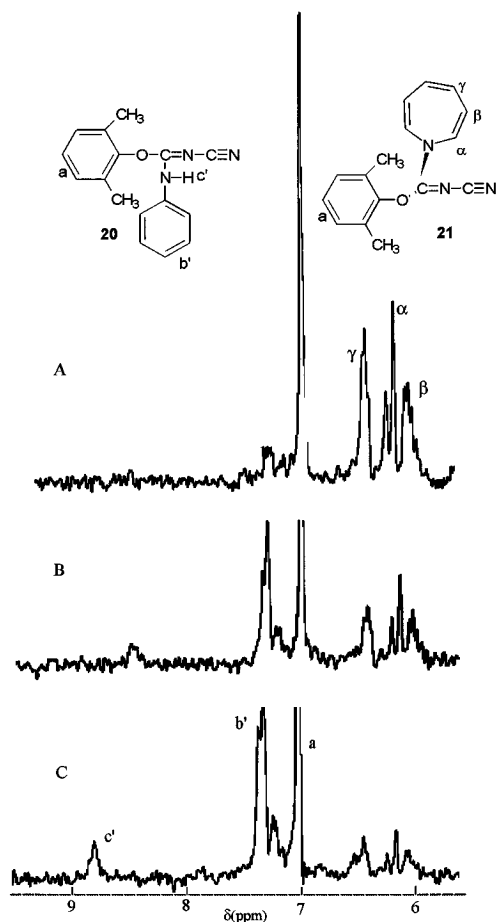


Figure 3. Portion of 90 MHz $^1\text{H-NMR}$ spectra of conversion of azepene **21** to isourea **20** at (A) 17 h, (B) 140 h, and (C) 237 h in $\text{CCl}_4\text{-CD}_3\text{CN}$ (95:5) at 80 $^\circ\text{C}$.

states with less of a positive charge developed. As indicated by partial rate factors and ρ^+ -values, electrophiles with moderate reactivity (such as imidoynitrenes) exhibit a later transition state with more of a positive-charge character (σ -complex) that is stabilized by the electron-releasing groups similar to electrophilic aromatic substitution. In the case of benzene, a mixture of σ -complex and benzaziridine intermediates is formed and can interconvert depending on the intermediates' activation energy level and the amount of resonance stabilization provided by the imidoynitrene residue.

Experimental Section

General. The $^1\text{H-NMR}$ spectra were taken on a Varian EM390 (90 MHz) and the $^{13}\text{C-NMR}$ on a Bruker FT-NMR (80 MHz). The elemental analysis was performed by Research Institute of Petroleum Industries (RIPI). The IR spectra were obtained on a Shimadzu ZU-435. Melting points were taken by the Gallenkamp melting point apparatus and are uncorrected. Yields were calculated by the $^1\text{H-NMR}$ and/or isolated products and not optimized; most experiments were done once or twice only. All reaction temperatures reported were those of the oil bath. All starting materials and solvents were purified with the proper purification technique before use.

Calculation of the Total Relative Reaction Rates ($k_{\text{H}}/k_{\text{X}}$). Due to the complexity of the reaction mixture, calculation of the total relative reaction rate using the conventional method of mixing arenes was not considered. The method of quenching an aliquot of the reaction mixture at regular time intervals would have been time consuming, and the experimental ($^1\text{H-NMR}$) error would have been similar to that resulting from the method using an internal standard. The

chosen method, therefore, was to use the relative percent of the thermolyzate of the reaction of nitrene with benzene as an internal standard and to compare it with the relative percent of thermolyzate of the reaction of nitrene with substituted benzene (eq 1).

$$k_{\text{X}}/k_{\text{H}} = \frac{(\% \text{ nitrene-arene adducts}/\% \text{ thermolyzate})_{\text{X}}}{(\% \text{ nitrene-benzene adducts}/\% \text{ thermolyzate})_{\text{H}}} \quad (1)$$

Calculation of the Relative Percent of Thermolyzate.

Completion of all reactions was followed by TLC and/or $^1\text{H-NMR}$. Excess solvents and/or aromatic substrates, when removed by vacuum distillation, produced a viscous residue. The relative area (%) of the thermolyzates was calculated using the area of aryl groups ($^1\text{H-NMR}$) of the crude residue. The total area of the phenyls of the nitrene-arene adduct (T_{n}) was measured (for percent nitrobenzene, chlorobenzene, and benzene) by using the area of NH,s relative to the area of the phenyl groups. For methyl benzoate, toluene, anisole, or acetanilide, the area of NH,s and/or CH₃,s relative to the area of phenyls groups were used (eq 2). A typical $^1\text{H-NMR}$ chemical shifts in NH, phenyls, and azepene is shown in Figure 3. For detailed experimental procedures, see ref 16.

$$\% \text{ thermolyzate} = [T_{\text{p}}/(T_{\text{p}} + T_{\text{n}})]100 \quad (2)$$

T_{p} = total area of phenyls of the crude mixture

T_{n} = total area of phenyls of the nitrene-arene adducts

Calculation of the Relative Percent of Ortho, Para, and Meta Isomers and/or Azepenes.¹⁶

Generally speaking, the relative percent of the ortho-para or meta isomer was calculated using the $^1\text{H-NMR}$ area of each isomer in a crude mixture. To assign each peak to the corresponding isomers, the crude mixture was extracted by the proper solvent (such as diethyl ether, methanol, or a mixture of ethyl acetate and *n*-hexane extracts of the ortho, para, and meta isomers and/or azepenes). The residue was checked by TLC and/or NMR for any possible trace of unextracted products (thermolyzates are insoluble in these solvents). This mixture was passed through a column filled with silica gel and the proper solvent.

Calculation of the Partial Rate Factors of the Para (f_{p}) and Ortho (f_{o}) Isomers. The partial rate factors were calculated using the total reaction rates and mole fraction of each isomer (Table 2, eq 3).

$$f = 6k_{\text{subs}}(\text{fraction } Z \text{ products})/Yk_{\text{benz}} \quad (3)$$

Y = no. of equivalent positions

Z = fraction of para or ortho isomer

Azides: *N'*-cyano(2,6-dimethylphenoxy)imidocarbonyl azide (7), *N'*-(cyanoethoxy)carbimidoyl azide (22), and *N'*-(methylsulfonyl)(2,6-dimethylphenoxy)imidocarbonyl azide (24) were prepared as described earlier.^{15,16}

***N'*-(Trifluoromethanesulfonyl)(2,4,6-trimethylphenoxy)imidocarbonyl Azide (6).** To a stirred solution of (2,4,6-trimethylphenoxy)tetrazole (**6T**) (3.00 g, 14.7 mmol)¹⁷ in 250 mL of anhydrous peroxide-free were added THF dropwise at 0 $^\circ\text{C}$ under dry nitrogen and (2.93 g, 16.2 mmol) trifluoromethanesulfonyl chloride (TFMC) in 25 mL of THF for over 30 min. Triethylamine (1.64 g, 16.2 mmol) was added after another 30 min for over 1 h. Triethylammonium hydrochloride was removed and washed with two 30 mL portions of THF. The combined solution was concentrated under reduced pressure to give a white solid that crystallized twice in ether-hexane (40:60) to give pure azide **6**: dec 87–88.5 $^\circ\text{C}$; IR (KBr) 3000–3100 (w), 2150 (s), 2060 (m), 1600 (s), 1450 (s); $^1\text{H-NMR}$ (CDCl_3) δ ppm 2.1 (s, 3H), 2.25 (s, 6H), 7.4 (s, 2H).

Thermolysis of Azides. Reaction of 6 with Nitrobenzene. A solution of **6** (2.00 g, 6.20 mmol) with 50 mL of nitrobenzene was heated in an oil bath at 120 \pm 2 $^\circ\text{C}$ for 24 h. TLC indicated no unreacted azide. Concentration of the

solution under reduced pressure left a dark brown viscous residue. The $^1\text{H-NMR}$ spectrum showed several overlapping singlets between 2 and 2.3 ppm (area 50) and at 6.8–7.2 ppm (integral 24) and a broad signal at 3.2 ppm (area 12). No signal was found corresponding to the nitrene–nitrobenzene adducts.

Reaction of *N*-Cyano(2,6-dimethylphenoxy)imidocarbonyl Azide (7) with Nitrobenzene. A solution of 7 (3.05 g, 16.3 mmol) with 50 mL of nitrobenzene was heated in an oil bath at 120 ± 2 °C for 24 h. The TLC indicated no azide. Concentration of the solution under reduced pressure left a dark brown residue. $^1\text{H-NMR}$ spectra showed a typical azide decomposition product (thermolyzate, several overlapping singlets between 2 and 2.4 ppm and at 6.9–7.3 ppm) and no nitrene–nitrobenzene adducts.

Reaction of 7 with Methyl Benzoate. A solution of 7 (3.05 g, 16.3 mmol) with 100 mL of methyl benzoate was heated in an oil bath at 93 ± 2 °C for 15 h. TLC indicated no azide. Concentration of the solution under reduced pressure left a dark brown residue. $^1\text{H-NMR}$ spectra showed a typical azide decomposition product (thermolyzate) and no nitrene–methyl benzoate adducts.

Reaction of 7 with Chlorobenzene. A solution of 7 (3 g, 13.95 mmol) with 60 mL of chlorobenzene was heated in an oil bath at 105 ± 2 °C for 15 h. TLC indicated no azide. Concentration of the solution under reduced pressure left a dark brown residue. The $^1\text{H-NMR}$ spectra showed a mixture of 55% *N*-(2-chlorophenyl)-*N*-cyano-*O*-(2,6-dimethylphenyl)isourea (12), 45% *N*-(4-chlorophenyl)-*N*-cyano-*O*-(2,6-dimethylphenyl)isourea (11), and no 13, with the total yield of 10% and 90% yield of thermolyzate. Separation of ortho and para isomers by chromatography on silica gel with chloroform (98%) and ethyl acetate (2%) gave 40 mg of para isomer 11: mp 204–205 °C; $^1\text{H-NMR}$ (acetone- d_6) δ ppm 2.15 (s, 6H), 6.95 (s, 3H), 7.2 (d, 2H, $J = 6$ Hz), 7.6 (d, 2H, $J = 6$ Hz), 7.7 (dd, 2H, $J = 3$ Hz), 9.3 (br s, 1H). Anal. Calcd for $\text{C}_{16}\text{H}_{14}\text{N}_3\text{OCl}$: C, 64.09; H, 4.71; N, 14.02. Found: C, 63.80; H, 4.90; N, 13.80 and 20 mg of ortho isomer 12: mp 175–176 °C. $^1\text{H-NMR}$ (CD_3CN) δ ppm 2.15 (s, 6H), 7.05 (s, 3H), 7.2–7.6 (m, 4H), 9.80 (br s, 1H).

Reaction of 7 with Acetanilide. A solution of 7 (2.15 g, 10 mmol) with 13.5 g of acetanilide in 50 mL of dried peroxide-free dioxane was heated in an oil bath at 95 ± 2 °C for 16 h. The TLC indicated no azide. Concentration of the solution under reduced pressure left a yellow residue. The $^1\text{H-NMR}$ spectra showed a mixture of 50% ortho isomer *N*-(2-acetamino)-*N*-cyano-*O*-(2,6-dimethylphenyl)isourea (15), 50% para isomer *N*-(4-acetamino)-*N*-cyano-*O*-(2,6-dimethylphenyl)isourea (14), and no 16, with the total yield of 90% and 10% yield of thermolyzate. Separation of ortho and para isomers was achieved by chromatography on silica gel with *n*-hexane–ethyl acetate (60%–40%) of para isomer 14: mp 206–208 °C; $^1\text{H-NMR}$ ($\text{CD}_3\text{CN}-\text{CCl}_4$) δ ppm 2.1 (s, 3H), 2.25 (s, 3H), 7.2 (s, 3H), 7.08 (d, 2H, $J = 9$ Hz), 7.65 (d, 2H, $J = 9$ Hz), 8.35 (br s, 2H); $^{13}\text{C-NMR}$ (CDCl_3 -acetone- d_6) δ ppm, 16.59, 21.76, 120.90, 122.54, 126.40, 127.26, 127.77, 130.11, 130.58, 131.01, 137.12, 144.19, 182.12. Ortho isomer 15: mp 181–182 °C; $^1\text{H-NMR}$ (CCl_4 -acetone- d_6) δ ppm 2.15 (s, 3H), 2.25 (s, 6H), 7.20 (s, 3H), 7.45–7.92 (m, 4H), 8.60 (br s, 1H), 8.70 (br s, 1H). Anal. Calcd for $\text{C}_{18}\text{H}_{18}\text{N}_4\text{O}_2$: C, 67.07; H, 5.63; N, 17.38. Found: C, 66.50; H, 5.50; N, 17.40.

Reaction of 7 with Toluene and Tetracyanoethylene (TCNE). A solution of 7 (1.00 g, 4.65 mmol) with TCNE (0.06 g, 4.68 mmol) in 50 mL of dried toluene was heated in an oil bath at 80 ± 2 °C for 15 h. The TLC indicated no azide. Concentration of the solution under reduced pressure left a brown residue. The $^1\text{H-NMR}$ spectra showed a mixture of 62% ortho isomer *N*-(2-tolyl)-*N*-cyano-*O*-(2,6-dimethylphenyl)isourea (18) [$^1\text{H-NMR}$ ($\text{CD}_3\text{CN}-\text{CDCl}_4$) δ ppm 2.2 (s, 6H), 2.45 (s, 3H), 7.45 (s, 3H), 7.3 (dd, 4H, $J = 3$ Hz), 9.1 (br s, 1H)] and 38% para isomer *N*-(4-tolyl)-*N*-cyano-*O*-(2,6-dimethylphenyl)isourea (17) [$^1\text{H-NMR}$ (CD_3CN) δ ppm 2.2 (s, 6H), 2.4 (s, 3H), 7.2 (s, 3H), 7.3 (m, 4H), 8.6 (s, 1H)] with the total yield of greater than 70% with less than 30% yield of thermolyzate. No trace of azepene 19 or azepene–TCNE adducts was observed.

Reaction of 7 with Benzene. A solution of 7 (3.0 g, 13.95 mmol) in 250 mL of dried benzene was refluxed at 65 ± 2 °C for 48 h. The TLC indicated unreacted azide. Reflux was continued until all azides were consumed. Concentration of the solution under reduced pressure left a brown residue. $^1\text{H-NMR}$ spectra showed a mixture of 5% *N*-phenyl-*N*-cyano-*O*-(2,6-dimethylphenyl)isourea (20) [$^1\text{H-NMR}$ ($\text{CD}_3\text{CN}-\text{CCl}_4$) δ ppm 2.21 (s, 6H), 7.5 (m, 5H), 7.2 (s, 3H), 9.5 (s, br, 1H)] and 95% *N*-(*N*-cyano(2,6-dimethylphenoxy)azepene (21) [$^1\text{H-NMR}$ ($\text{CD}_3\text{CN}-\text{CCl}_4$) δ ppm 2.2 (s, 6H), 6.0–6.6 (m, 5H), 7.2 (s, 3H)] with 28% total yield and 72% thermolyzate. All attempts to separate 20 from 21 produced pure crystals of a nearly 95%–5% mixture.

Thermolysis of Azepene 21 in Tetrachloromethane Acetonitrile. A pure mixture of 95% azepene 21 and 5% 20 (crystallized in ethyl ether– CCl_4) and tetrachlorocarbon–acetonitrile- d_3 (95:5) in an NMR tube was placed in an oil bath (80 °C). The reaction progress was followed by the $^1\text{H-NMR}$. The rate of isomerization of 21 to 20 was followed by integration of the aromatic region (Figure 3) in the $^1\text{H-NMR}$ spectra of mixtures of azepene 21 (δ 5.90) and isourea 20 (δ 7.10–7.40). After 309 h all the azepene 21 had converted to isourea 20 with a small amount of a complex mixture. The first order rate constant of $7.0 \times 10^{-5} \text{ s}^{-1}$ was observed.

Thermolysis of a Mixture of Isourea 20 and Azepene 21 in DMSO- d_6 . Thermolysis of the mixture of 5% 20 and 95% 21 and DMSO- d_6 was carried out in an NMR tube heated at 100 ± 2 °C for several hours. The azepene 21 converted mostly to isourea 20.

Reaction of *N*-(Cyanoethoxy)imidocarbonyl Azide (22) with *p*-xylene and Tetracyanoethylene (TCNE).¹⁶ Thermolysis of a mixture of 22, *p*-xylene, and TCNE produced *N*-(2,5-dimethylphenyl)-*N*-cyano-*O*-methylisourea (23) in high yield, but no azepene or TCNE–azepene adducts were produced.

Reaction of *N*-(Methylsulfonyl)(2,6-dimethylphenoxy)imidocarbonyl azide (24) with 1,4-dimethoxybenzene was reported earlier.¹⁶

Acknowledgment. This work was supported by the Isfahan University of Technology Research Consul Grant No. IUT-500-34575. The authors would like to thank Dr. Leslie Powell of IUT for her valuable assistance.

JO951053F