

Electrophilic Aromatic Substitution by Ethoxycarbonylnitrenium Ion. Reactions of Ethyl Azidoformate with Aromatics in the Presence of Trifluoroacetic Acid

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Electrophilic aromatic substitution by ethoxycarbonylnitrenium ion occurs in reactions of ethyl azidoformate with aromatics in the presence of trifluoroacetic acid, giving ethyl *N*-arylcarbamates.

Electrophilic aromatic substitution by nitrenium ions is of great interest in organic chemistry, but has not yet been established. We recently reported the presence of an ethoxycarbonylnitrenium ion in the decomposition of ethyl azidoformate in acetic acid,¹ but aromatic substitution by this species was not found,[†] possibly because of its competing

reaction with the neighbouring acetate anion.¹ We selected the title reaction to avoid this difficulty, and here report the first elucidation of aromatic substitution by a nitrenium ion. The adoption of trifluoroacetic acid (TFA) was based on the low nucleophilicity of the trifluoroacetate anion.

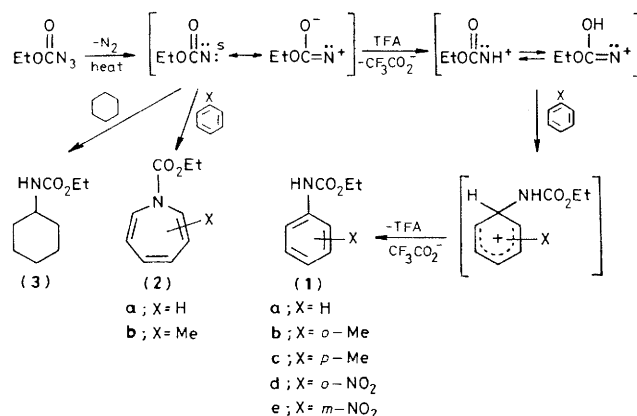
The thermal reaction of ethyl azidoformate (0.5 M) with benzene, toluene, or nitrobenzene in the presence of TFA (30% v/v) [thermolysis (i)] yielded ethyl *N*-phenylcarbamate (**1a**), ethyl *N*-(*o*- and *p*-tolyl)carbamates (**1b**) and (**1c**), or ethyl *N*-(*o*- and *m*-nitrophenyl)carbamates (**1d**) and (**1e**),

[†] The data are unpublished, but the details will be reported in the near future.

Table 1. Reactions of ethyl azidoformate (0.5 M) with aromatics in the presence of TFA (30% v/v) and those allowed to occur in the absence of TFA and then subjected to addition of TFA (30 %v/v) at 25 °C.^a

Substrate	T/°C	t/h	% of azide decomposed	Yield, ^b %					o/p ratio (1b)/(1c)
				(1a)	(1b)	(1c)	(1d)	(1e)	
Benzene	125	1	93(83)	57(25)					
Benzene	109	2	60(54)	63(28)					
Toluene	125	1	93(83)		33(22)	20(8.6)			1.7(2.6)
Toluene	109	2	60(54)		42(24)	24(9.3)			1.8(2.6)
Nitrobenzene	125	1	93(93)				17(ca. 0)	11(ca. 0)	
Nitrobenzene	110	2	70(65)				16(ca. 0)	10(ca. 0)	

^a The data in parentheses refer to thermolysis (ii) (see the text). ^b Yield based on azide decomposed.

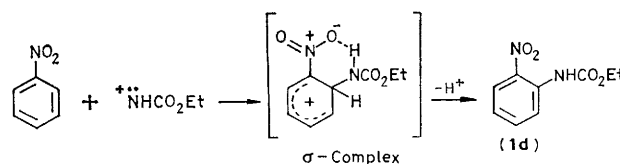
**Scheme 1**

respectively. The yields are summarized in Table 1. G.l.c. peaks for the other products were negligible, presumably because of formation of some polymers.

The products (1a)–(1c) were also formed by thermolysis in the absence of TFA with subsequent addition of TFA (30% v/v) at 25 °C [thermolysis (ii)]. The data are shown in parentheses in Table 1. In this case, azepine (2a) or (2b) is given by attack of ethoxycarbonylnitrene on benzene or toluene,² and the TFA then causes each azepine to rearrange to yield (1a), or (1b) and (1c) (see Scheme 1). The rearrangement went to completion at 25 °C in 1 h. The yields for thermolysis (i) were ca. twice as high as those in the azepine route *via* nitrene. For thermolysis (ii), carbamates (1d) and (1e) were not produced even after TFA was added at 25 °C for 10 days.† The results suggest that an electrophile, more reactive to aromatics than the nitrene, is involved in thermolysis (i). This electrophile might be the ethoxycarbonylnitrenium ion since a cation attacks at the *ortho*- and *para*-positions in toluene and at the *meta*-position³ in nitrobenzene. The attack at the *o*-position in nitrobenzene may be explained by the high stability of the resulting σ -complex (Scheme 2).

The relative reactivity of cyclohexane with respect to benzene was determined from the relative yield of ethyl *N*-cyclohexylcarbamate (3) with respect to (1a). The relative reactivity for thermolysis (ii) was ca. five times greater than that for thermolysis (i) (Table 2). This difference in relative reactivity cannot be explained in terms of change in the nitrene multiplicity because it is the singlet nitrene, not the triplet nitrene, that reacts with cyclohexane⁴ or benzene⁵ to give (3) or *N*-ethoxycarbonyl-1*H*-azepine (2a), respectively.

† The thermolysis of the azide (0.5 M) in nitrobenzene was carried out at 125 °C for 1.5 h; the mixture was then subjected to reaction with added TFA (30% v/v) at 110 °C for 2 h, and the yields of (1d) and (1e) were ca. 0%.

**Scheme 2**

Thus, the result supports the idea that thermolysis (i) involves the nitrenium ion intermediate which is more reactive to benzene than to cyclohexane. Carbamates (1a)–(1c) may be produced *via* both the nitrenium ion and nitrene in thermolysis (i) in view of the fact that the formation of (3) *via* the nitrene is not negligible.

Ortho- and *para*-attacking partial rate factors (o_f and p_f) for toluene were determined (Table 2). The partial rate factors and *ortho/para* ratios (see Table 1) were lower for thermolysis (i) than for thermolysis (ii). The low selectivities indicate that the nitrenium ion is more reactive than the nitrene.

Partial rate factors (k_f), *i.e.*, p_f for toluene, m_f for nitrobenzene, or m_f for acetophenone, were determined for the formation of ethyl *N*-arylcarbamates in TFA (80% v/v)–nitrobenzene (20% v/v) containing <3% v/v toluene, benzene, or acetophenone, respectively. The mixed solution permits us to assume an exclusive transformation of the nitrene into the nitrenium ion since the nitrene is not active enough to react with nitrobenzene (Table 1). The correlation⁶ between $\log k_f$ and σ^+ gives a linear plot with $\rho = -1.7$. The ρ value is more negative than that (-1.32) obtained from the correlation with σ_p for the disappearance of substituted benzenes in reactions of the nitrene with aromatics.⁷ A less negative ρ value, *i.e.*, low substrate selectivity, for the reaction with the nitrenium ion, may be rationalized by an early transition state, which resembles a π -complex,^{8,9} because the nitrenium ion is highly reactive. The nitrenium ion is characterized by the apparently unreconcilable low substrate and high positional selectivities (to the latter selectivity refer selective attack on the *ortho*- and *para*-positions in toluene and on the *ortho*- and *meta*-positions in nitrobenzene). However, this observation is in good agreement with the suggestion⁹ that the transition state of highest energy (which determines substrate selectivity) is of a π -complex nature, and is then followed by σ -complex formation, determining positional selectivity.

Activation parameters, ΔH^\ddagger and ΔS^\ddagger , for thermolysis of the azide in TFA and in benzene did not differ much from each other. This shows that the thermolysis in TFA does not proceed *via* an azide conjugate acid, but *via* the nitrene. Thus, the nitrenium ion with its equilibrated keto- and enol forms would be formed not *via* the conjugate acid but by proton abstraction¹ by the nitrene from TFA (the 1,3-dipole from

Table 2. Relative reactivity (r) of cyclohexane or toluene with respect to benzene for reaction of ethyl azidoformate (0.5 M) in the presence of TFA (30% v/v) and that in the absence of TFA with subsequent addition of TFA (30% v/v) at 25 °C.^a

Substrate (70% v/v)	$T/^\circ\text{C}$	t/h	% of azide decomposed	r (cyclohexane)	r (toluene)	
					o_r	p_r
Benzene-cyclohexane	109	2	60(53)	0.36(1.9)		
Benzene-cyclohexane	79	24	35(21)	0.36(2.0)		
Benzene-toluene	109	2	59(41)		2.8(3.9)	3.0(3.1)
Benzene-toluene	79	24	35(15)		2.6(4.5)	2.9(3.7)

^a The data in parentheses refer to thermolysis (ii) (see the text).

the nitrene may abstract a proton at the negative oxygen to give the enol). The evidence that the thermolysis in TFA does not proceed *via* the conjugate acid eliminates the possibility that an acid-catalysed S_N2 -type reaction (attack of aromatics on the conjugate acid) is involved in the thermolysis. Therefore, the TFA-catalysed substitution of aromatics by the nitrenium ion proceeds in the usual way. The mechanism is shown in Scheme 1.

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