A Kinetic Study of the Thermolysis of *N*-Crotyl Substituted 1,2,4-Triazoles

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A kinetic study of the thermolysis of 4-crotyl-3,5-diphenyl-4*H*-1,2,4-triazole (**1**) in a melt of the neat compound was performed at temperatures in the range of 260-350 °C. The main products formed were 1-crotyl-3,5-diphenyl-1*H*-1,2,4-triazole (**3**) and 1-(1-methylallyl)-3,5-diphenyl-1*H*-1,2,4-triazole (**4**) together with 3-methyl-2,6-diphenylpyridine (**2**) and 3,5-diphenyl-1,2,4-triazole (**5**). Products **2** and **5** were both formed preferentially from **3** and **4**. In the melt was observed first order kinetics. Activation parameters for formation of **3** and **4** were determined. Product **3**: E_a = 95 kJ/mole. Product **4**: E_a = 145 kJ/mole.

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A study of the thermolysis of a number of neat allylic 4*H*-1,2,4-triazoles at 315-320 °C has recently been reported [1]. The main products formed in these reactions were the corresponding 1-allyl substituted triazoles formed in rearrangements involving competing S_N2 and S_N2' pathways. There were, however, indications of [2,3]-allylic shift reactions taking place between the *N*1 and *N*2 ring positions. Thermolysis of triazoles also gave substituted pyridines. For example, 4-crotyl-3,5-diphenyl-4*H*-1,2,4-triazole (**1**) was converted to 3-methyl-2,6-diphenylpyridine (**2**). The same product was also obtained on thermolysis of 1-crotyl-3,5-diphenyl-1*H*-1,2,4-triazole (**3**) and 1-(1-methylallyl)-3,5-diphenyl-1*H*-1,2,4-triazole (**4**). Formation of pyridine was suggested to proceed *via* nitrile ylid intermediates after extrusion of N_2 followed by intramolecular ring closure and subsequent aromatization [1].

Results and Discussion.

The elimination of the allyl group leading to triazole **5** and pyridine **2** may take place from either the 1- or the 4-allyl substituted triazoles **1**, **3** or **4**. The distribution of products was found to be temperature dependent. In order to gain further insight into the details of the mechanisms involved, a careful product analysis was done together with a kinetic investigation of the thermolysis of neat 4-crotyl-3,5-diphenyl-4*H*-1,2,4-triazole (**1**), at temperatures in the range of 260-350 °C. Typical reaction profiles at the lower temperatures are shown in Figure 1 (260 °C) and in Figure 2 for reactions at 350 °C. Product distribution from thermolysis of **1**, **3** and **4** at 320 °C is shown in Table 1. Synthesis and thermal rearrangement of allyl substituted triazoles has been described in an earlier publication [1]. Formation of pyridine **2** was observed at the higher temperatures only, *i.e.* higher than 317 °C. The data also indicated that the pyridine **2** was preferably formed from the 1-allyl species **3** and **4**. The 3,5-diphenyl-1,2,4-triazole (**5**) appeared to be formed from **4** only in a slow elimination reaction. The information above in combination with earlier results indicated reaction pathways as illustrated in Scheme 1.

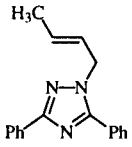
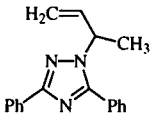
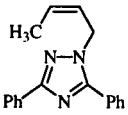
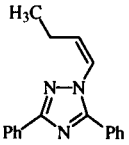
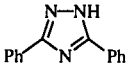
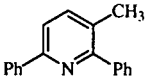
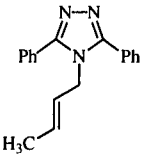
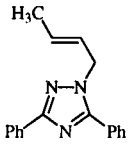
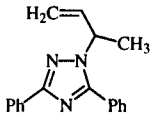
Compound **1** initially contained approximately 2% of the *cis*-crotyl isomer. During thermolysis, the amount of the *cis*-crotyl isomer of **6** was 2-3% at 317 °C increasing somewhat at higher temperatures to 6% at 350 °C. Thermolysis of **3** also resulted in double bond migration to form **7**. The migration product corresponding to, which would have been **4**, 1-(1-methyl-1-propenyl)-3,5-diphenyl-1,2,4-triazole (**8**), was not detected in the product mixtures. For reference purpose **8** was prepared by base catalyzed isomerization of **4**. Compounds **3** and **6** were difficult to separate chromatographically. In the following the amount applied for 1-crotyl substituted triazole is represented by the combined amounts of *cis*- and *trans*-isomers **3** and **6**. The "[2,3]-allyl walk" rearrangement of **3** to **4**, was of little importance and much slower than the S_N2/S_N2' driven rearrangement reactions. The equilibrium was displaced towards **3** for steric reasons.

Kinetic Measurements.

The rates of conversion and product formation in the thermolysis of the neat compounds was investigated at different temperatures, *i.e.*, 260, 290, 317 and 350 °C. The experimental technique applied in these high temperature kinetic experiments with the neat triazoles has been applied previously [2] for the solid state thermolysis of 4-methyl- and 4-ethyl-3,5-diphenyl-4*H*-1,2,4-triazole. Assuming the proposed S_N2-type mechanism is valid, second-order kinetics may be expected.

Kinetic experiments are usually performed in dilute solutions in order to avoid non-ideality. The kinetic work performed in the present investigation, however, is carried out in a melt of the neat substrate. In concentrated non-ideal systems activities are used instead of concentrations. The activities are related to concentrations by activity coefficients. The rate expressions will then be adjusted with the activity coefficients of the reactants and the acti-

Table 1

	 **3**	 **4**	 **6**	 **7**	 **5**	 **2**
 **1**	56	31	2	—	2	9
 **3**	6	81	1	—	2	9
 **4**	92	1	4	1	—	2

Thermolysis of **1**, **3** and **4** at 320 °C for 20 minutes.

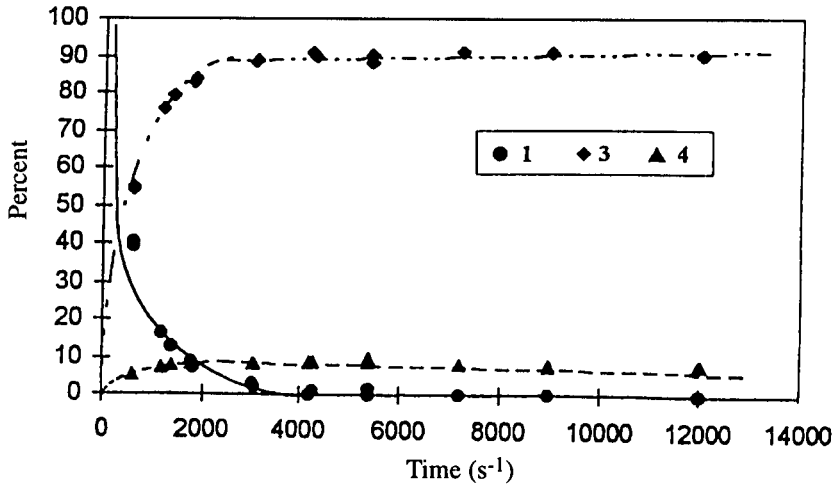


Figure 1. Thermolysis of **1** at 260 °C.

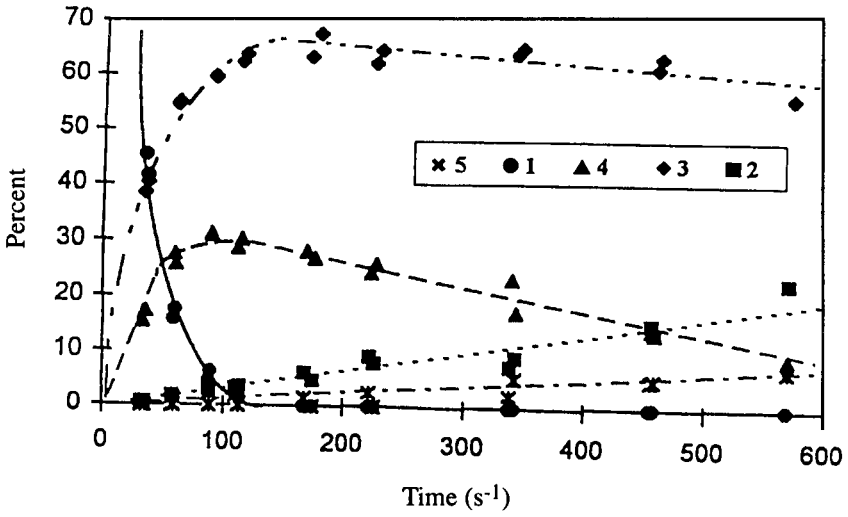
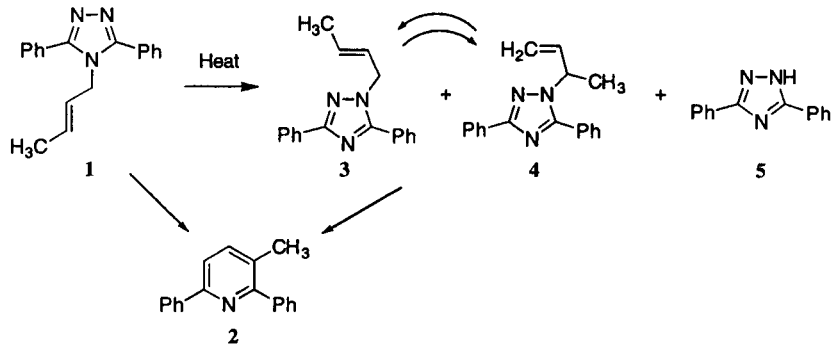


Figure 2. Thermolysis of **1** at 350 °C.

Scheme 1



vated complex. The reason for this has been discussed by Laidler [3]. In the melted phase the reaction can be viewed as a solvent reacting with itself, and the validity of the theory based on the reactants coming together and reacting after physically being separated can by good reasons be questioned. Connecting concentration and activity, the activity coefficients will also change as the reaction progresses. Thus, any observed reaction order can no longer be expected to reflect the mechanism, as in the conventional kinetic systems. In melts and the solid state the concept of bulk concentration will not be valid. As a consequence of the restricted movement within the medium, large concentration differences may occur at the microscopic level relevant for the reaction [4]. Usually the over-all processes of the solid state reactions are complicated and involve several steps. Thus, only the apparent rate constants can be determined, and reaction order, generally has no significance [5]. Similar consideration may be valid for reactions in melts.

The variable fractional conversion (α_a) is a convenient variable often used instead of concentration, Equation 1, where N is the number of molecules.

$$\alpha_a = (N_{ao}-N_a)/N_{ao} \quad \text{Equation 1}$$

First order reactions will then give Equation 2:

$$-ln(1-\alpha_a) = k.t \quad \text{Equation 2}$$

This corresponds to the Prout-Tompkins equation for solid state reactions [6]. Substitution will give the following expression for the first order rate equation, Equation 3:

$$-ln\,(N_a/N_{ao}) = k.t \quad \text{Equation 3}$$

where (N_a/N_{ao}) corresponds to (C_a/C_{ao}) in the first order rate equation based on concentration. (N_a/N_{ao}) is the *mole fraction*, X_a. A brief review of the theory of kinetics in the condensed and solid phase has been presented [5,7].

The limitations described above for kinetics in melts will naturally limit the insight into the mechanism based on the kinetic data alone. The kinetic experiments were performed by heating a number of separate samples (4-5 mg) in sealed capillary tubes at the appropriate temperature in an oven. It was necessary to use this technique to avoid loss of material due to sublimation and to hinder exposure to air. At certain intervals, tubes were selected, cooled and the contents analysed. To minimize possible errors due to effects of the reaction vessels, great care was observed with respect to loading, size and closure of the capillary tubes.

The over-all rate of reaction was determined from the disappearance of **1** and appeared to followed first order kinetics, as has previously been observed for 4-alkyl substituted triazoles [2]. As **1** was rapidly disappearing few data points were available to calculate individual reaction rates for the S_N2 and S_N2' reactions. However, plots of the *ln* of the molar fractions, X_a, of the triazoles *vs.* time exhibited good linear relationship, allowing us to determine "first order" rate constants for the reactions. These reaction rates were calculated from the available data, using a model for two competing reactions. The kinetic data for the reaction in the melt appeared to be in good agreement with an apparent pseudo-first order rate law.

To a good approximation, **1** was converted to **3** and **4** only, and since these species were formed from a common starting material following similar rate laws, the rate Equations 4 and 5 can be combined to yield the individual rate constants. In repeated experiments, the calculated rate constants usually deviated less than 10%.

$$-dX_1/dt = (k_3 + k_4)\, X_1 \qquad \text{Equation 4}$$

$$r_3/r_4 = dX_3/dX_4 = k_3/k_4 = X_3/X_4 \qquad \text{Equation 5}$$

Analysis of product compositions were done by GC measurements without the use of internal standard. However, experiments to elucidate the mass balance using internal standard technique gave satisfying results. Response factors for GLC–analysis (using FI-detector) of all compounds were all found to be close to unity. Deviations from unity were less than the general experimental errors.

There were insufficient data to study the kinetics for the pyridine formation in the full range of temperatures as **2** was only formed in sufficient amounts at the higher temperatures. We note that **3** and **4** were readily formed (in approximately 100 seconds at 350 °C) and only slowly interconverted under the reaction conditions. Thus, the combined amounts of these species may be considered as starting materials for the formation of triazole **5** and pyridine **2**. Reaction kinetics was carried out at 317 and 350 °C. This model ignores that **5** and **2** were formed with different rates from **3** and **4**. However, these calculations gave a reasonable estimate of the rate of reaction for the formations of these products.

The reaction rates are shown in Table 2. At 350 °C the S_N2 reaction (leading to product **3**) was approximately twice as fast as the S_N2' pathway (leading to product **4**), and about 100 times faster than the formation of **2** and **5**. The temperature dependency of the rate constants also agreed well with the Arrhenius equation, allowing the estimation of the activation parameters. These were calculated using LSTSQ [8] and are listed in Table 3. The activation energies were in the same range as those determined for the rearrangement of 4-methyl and 4-ethyl substituted 1,2,4-triazoles [2]. The activation energy for the S_N2' pathway was approximately 1.5 times higher than for the corresponding S_N2 reaction. The large negative activation entropies for these reactions indicates highly ordered transition states. However, when using these data, it should be kept in mind the limitation of the methods applied. The kinetic data alone do not give information about the details in the mechanism, but elucidate what mechanistic pathways are important in the reaction scheme.

Table 2

Temperature (°C)	k_2 cm^{-1}	k_3 cm^{-1}	k_4 cm^{-1}	k_5 cm^{-1}
260		$1.34*10^{-3}$	$1.27*10^{-4}$	
		$1.38*10^{-3}$	$1.34*10^{-4}$	
290		$4.32*10^{-3}$	$6.24*10^{-4}$	
		$4.30*10^{-3}$	$6.41*10^{-4}$	
317	$6.6*10^{-5}$	$1.68*10^{-2}$	$4.86*10^{-3}$	
	$5.1*10^{-5}$	$1.58*10^{-2}$	$4.43*10^{-3}$	
350	$4.4*10^{-4}$	$2.79*10^{-2}$	$1.34*10^{-2}$	$1.6*10^{-4}$
	$2.1*10^{-4}$	$2.42*10^{-2}$	$1.08*10^{-2}$	$2.0*10^{-4}$

First order rate constants for thermolysis of **1** at different temperatures. The subscripts indicate the reaction product.

Table 3

Reaction Product	*log* A (sec^{-1})	E_a (kJ/mol)	$\Delta H^{\neq}$ (kJ/mol)	$\Delta S^{\neq}$ (J/molK)
3 (S_N2)	6.4 (0.6)	94.6 (7.2)	89.8 (7.2)	-135 (12)
4 (S_N2')	10.3 (0.7)	144.5 (8.5)	139.7 (8.5)	-62 (15)

Activation parameters for the formation of **3** and **4** from thermolysis of **1**. The standard deviations are shown in parentheses.

EXPERIMENTAL

General.

The nmr spectra are recorded on a JEOL JNM-EX 400 FT NMR system with tetramethylsilane (TMS) as the internal standard. CG-FTIR spectra were obtained on a Nicolet 20-SXC FT-IR spectrometer connected to a Carlo Erba HRGC 5160 Mega Series gas chromatograph equipped with a CP-Sil 5 CB capillary column (25 m). GC-measurements were performed on a Perkin-Elmer Autosystem gas chromatograph equipped with a CP-Sil 5 CB capillary column (25 m). The different compounds were identified by comparing their spectroscopic properties with those of authentic samples previously characterized [1].

Kinetic Measurements in Capillary Tubes.

Capillary tubes were loaded with 4-5 mg of the substrate. The capillary tubes were then closed and placed in a heated metal block. As sample holder and heat sink was used a metal block (6 x 6 x 7 cm) with bore holes into which the capillary tubes were closely fit. The block was placed in an oven. Temperatures were measured using a thermocouple probe (chromel-constantan) inserted into the middle of the metal block. The thermocouple probe was calibrated in ice/water and boiling nonadecane (bp 330 °C) and assumed linear in that temperature range. Temperatures used in the calculations were average temperatures. Due to variations in the net-power the temperatures varied with +/- 1 °C. The experimental technique are described in an earlier publication [2].

At certain intervals capillary tubes were selected, cooled to room temperature, broken and the content dissolved in dichloromethane. Conversion was measure by GC-analysis.

Cis/trans-1-(1-Methyl-1-propene)-3,5-diphenyl-1*H*-1,2,4-triazole (**8**).

1-(1-Methylallyl)-3,5-diphenyl-1*H*-1,2,4-triazole [1] (0.15 g) was dissolved in tetrahydrofuran (4 ml) to which was added potassium *t*-butoxide (0.04 g). The mixture was stirred at room temperature under nitrogen for 7 days. Then the mixture was poured into water (20 ml) and evaporated under reduced pressure and then dissolved in dichloromethane (50 ml), washed with water (25 ml) and brine (25 ml), dried over anhydrous sodium sulfate and the solvent evaporated under reduced pressure. The resulting oil (0.1308 g) contained a *cis/trans* mixture of 1-(1-methyl-1-propene)-3,5-diphenyl-1*H*-1,2,4-triazole. The compounds were separated by preparative thin layer chromatography. Assignment of *cis* or *trans* stereochemistry of the isolated products was not possible due to inconclusive spectroscopic data.

Major product (62%): ^{1}H nmr (deuteriochloroform) δ: 1.33 (dd, J = 1.5, 6.8 Hz, 3H), 2.17 (m, 3H), 5.64-5.73 (m, 1H), 7.37-7.46 (m, 6H), 7.84-7.87 (m, 2H), 8.21-8.23 (m, 2H); ^{13}C nmr (deuteriochloroform) δ (DEPT): 13.0(CH_3), 22.1(CH_3), 124.7(CH), 126.5(CH), 128.4(CH), 128.5(CH), 129.2(CH), 130.0(CH), 131.0(C), 134.0(C), 154.5(C), 161.9(C); GC-FTIR (280 °C): 3073, 2991, 2958, 2932, 1518, 1478, 1444, 1399, 1352, 1296, 1175, 1122, 1071, 1029, 1011, 979, 907, 827, 766, cm^{-1}.

Minor product (37%): ^{1}H nmr (deuteriochloroform) δ: 1.73 (dd, J = 1.0, 7.3 Hz, 3H), 2.11 (m, 3H), 5.64-5.73 (m, 1H), 7.37-7.46 (m, 6H), 7.77-7.79 (m, 2H), 8.19-8.21 (m, 2H); ^{13}C nmr (deuteriochloroform) δ (DEPT): 13.1(CH_3), 16.4(CH_3), 125.5(CH), 127.8(CH), 128.2(C), 128.6(CH), 128.7(CH), 129.2(CH), 129.8(CH), 133.7(C), 154.0(C), 161.2(C); GC-FTIR (280 °C): 3073, 2933, 2873, 1519, 1478, 1445, 1396, 1347, 1300, 1176, 1154, 1123, 1068, 1029, 1018, 839, 767 cm^{-1}.

REFERENCES AND NOTES

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