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# Synthesis and Thermolysis of a Chiral, Non-Racemic Iminoaziridine<sup>[1]</sup>

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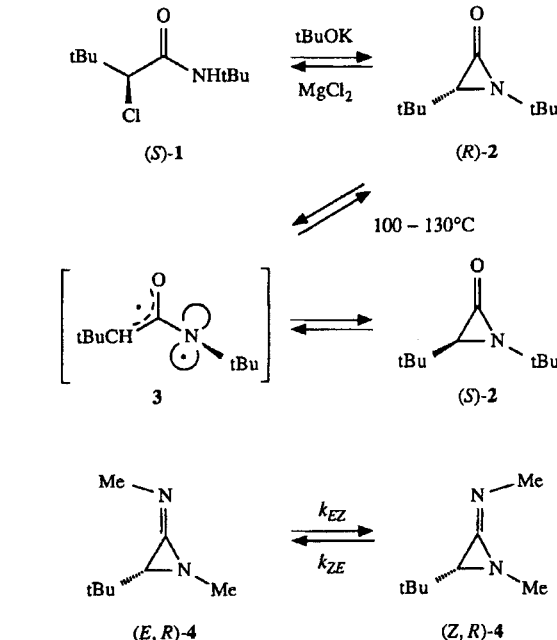
The 2-halo imidoyl chlorides **7** are obtained from the amide **5** and the 2-halo amides **6** by the action of phosphorus pentachloride and thionyl chloride, respectively. Non-racemic (*S*)-**6a** is converted into **7a** which is racemic, however. The reaction of Lawesson's reagent with **6a** furnishes the diastereomeric 1,3,2-thiazaphospholidine derivatives **15**. Treatment of (*S*)-**6a** (98% ee) with methyl triflate affords 2-chloro imidate **8** (95% ee) which reacts with methanamine in the presence of methan ammonium chloride to yield the 2-chloro amidine (*S*)-**9a** (90% ee). The 2-halo imidoyl halides **7a** and **b** react with methanamine to produce the 2-halo amidines **9a** and **b**. Strong bases, e.g. potassium *tert*-butoxide or sodium hydride in the presence of catalytic amounts of *tert*-butyl alcohol, eliminate hydrogen chloride or bromide from the 2-halo amidines **9a** and **b** and (*S*)-**9a** to yield mixtures of

the 2-iminoaziridines (*E*)- and (*Z*)-**4**, and (*E,R*)- and (*Z,R*)-**4** (83% ee), respectively. The 1,3-elimination of hydrogen bromide from **9b** is diastereoselective at  $-30$  to  $-40^{\circ}\text{C}$  [(*E*)-**4**:(*Z*)-**4** = <10:>90]. The diastereomers equilibrate at  $36^{\circ}\text{C}$  with  $(k_{EZ} + k_{ZE}) = (5.92 \pm 0.08) \cdot 10^{-5} \text{ s}^{-1}$  ( $K = k_{EZ}/k_{ZE} = 0.428 \pm 0.013$ ). The thermolysis of (*E*)- and (*Z*)-**4** in [*D*<sub>6</sub>]benzene solution yields the imine **16** and methyl isocyanide (**17**). The decomposition follows the first-order rate law. The following Arrhenius and Eyring parameters are calculated from five rate constants obtained in the temperature range of  $70$ – $110^{\circ}\text{C}$ :  $E_a = (115.2 \pm 0.4) \text{ kJmol}^{-1}$ ,  $\lg A = (12.06 \pm 0.28)$ ,  $\Delta H^{\ddagger} = (112.1 \pm 0.4) \text{ kJmol}^{-1}$ ,  $\Delta S^{\ddagger} = (-23.9 \pm 0.7) \text{ JK}^{-1} \text{ mol}^{-1}$ ,  $\Delta G_{373\text{K}}^{\ddagger} = 121 \text{ kJmol}^{-1}$ . The enantiomeric excess of the surviving fraction of (*E,R*)- and (*Z,R*)-**4** is unchanged after two half-lives at  $80^{\circ}\text{C}$ .

Recently, we demonstrated that the formation of the chiral non-racemic aziridinone (*R*)-**2** from the  $\alpha$ -chloro amide (*S*)-**1** by base-promoted dehydrochlorination<sup>[2]</sup> as well as the nucleophilic cleavage of the N–C(3) bond of (*R*)-**2**<sup>[3,4]</sup> occur with inversion of configuration, thus excluding the intervention of achiral (acyclic) intermediates. In the temperature range of  $100$ – $170^{\circ}\text{C}$ , however, slow racemization accompanies the thermolysis of (*R*)-**2** and indicates the existence of an achiral or a racemic transient, e.g. (*M*)-**3** + (*P*)-**3**. Indeed, high-level quantum-chemical calculations reveal that an activation energy of  $(170 \pm 25) \text{ kJmol}^{-1}$  is required for the unimolecular ring opening of the parent aziridinone which affords a species of high diradical character<sup>[4]</sup>. Subsequently, the unstable *N*-phenylaziridinone invoked in the decomposition of the (*S*)-2-bromopropananilide anion was shown to react with *tert*-butylamine or dimethylformamide with inversion of configuration at C(3)<sup>[5]</sup>. Thus, the stereochemical evidence in the series of 3-alkylaziridinones excludes achiral (acyclic) aziridinone isomers as intermediates at low temperatures<sup>[6]</sup>. Similar stereochemical studies are still missing in the related series of iminoaziridines. Therefore, we report on the synthesis and thermolysis of the diastereomeric chiral racemic (*E*)- and (*Z*)-**4**<sup>[7]</sup> and non-racemic iminoaziridines (*E,R*)- and (*Z,R*)-**4**.

## Racemic Iminoaziridines (*E*)- and (*Z*)-**4**

Though a photochemical route to the iminoaziridines (*E*)- and (*Z*)-**4** has been devised more recently, i.e. the pho-



toextrusion of molecular nitrogen from the 5-alkylenedihydro-1,2,4-triazole **10**<sup>[8]</sup>, the base-induced dehydrohalogenation of the  $\alpha$ -chloro (**9a**) or  $\alpha$ -bromo amidine **9b**<sup>[7]</sup> remains the

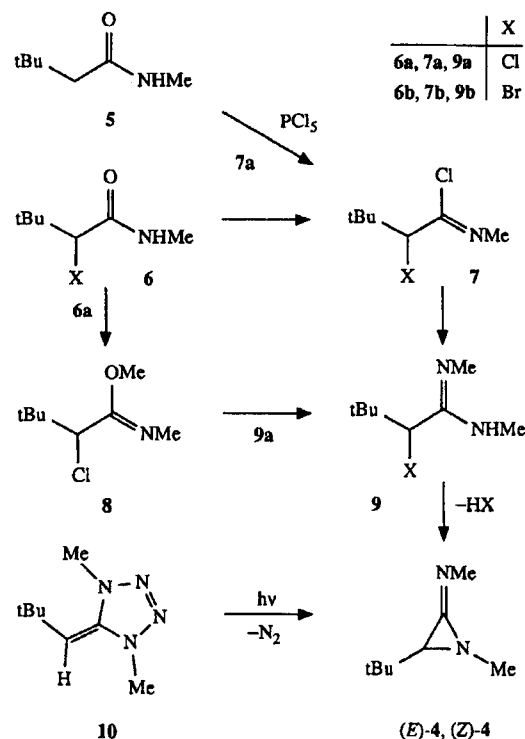
method of choice if substantial amounts of product are required. Even more important, (*S*)-2-chloro-3,3-dimethylbutanoic acid of high enantiomeric excess ( $\geq 97\%$ ) has become conveniently available<sup>[2]</sup>, and several established routes starting from this  $\alpha$ -chloro acid promised to lead to the non-racemic (*S*)-2-chloro amidine (*S*)-**9**. For these reasons, the synthesis of the racemic iminoaziridines (*E*)- and (*Z*)-**4**, required for preliminary studies, started from the *N*-methyl amides of 3,3-dimethylbutanoic acid (**5**), 2-chloro-3,3-dimethylbutanoic acid (**6a**), or 2-bromo-3,3-dimethylbutanoic acid (**6b**) which were converted into the  $\alpha$ -halo imidoyl chlorides **7a** and **b**, respectively, by the action of phosphorus pentachloride (**5**  $\rightarrow$  **7a**) or thionyl chloride (**6a**  $\rightarrow$  **7a**, **6b**  $\rightarrow$  **7b**<sup>[9]</sup>). Treatment of the  $\alpha$ -halo imidoyl chlorides **7** with an excess of methanamine at low temperature afforded the  $\alpha$ -halo amidines **9** in high yields as colourless oils distillable in vacuo (Table 1). Sealed in glass tubes and kept at  $-25^\circ\text{C}$ , they can be stored for long periods of time. Alternatively, they may be converted into the crystalline perchlorates **9**·HClO<sub>4</sub> which are shelf-stable. As expected<sup>[10]</sup>, both amidinium perchlorates **9**·HClO<sub>4</sub> exist in the *E,Z* configuration as shown by the proton (Table 2) and carbon-13 NMR spectra (Table 3) which exhibit signals originating from two different *N*-methyl groups.

The 1,3-dehydrohalogenation of the  $\alpha$ -halo amidines **9a** and **b** is induced by strong bases in diethyl ether or tetrahydrofuran, e.g. potassium *tert*-butoxide or sodium hydride in the presence of catalytic amounts of *tert*-butyl alcohol, to yield mixtures of the diastereomeric iminoaziridines (*E*)- and (*Z*)-**4** as colourless, volatile, typically smelling oils (Table 1), which are stable for long times in sealed tubes at low temperatures.

The formation of the iminoaziridines (*E*)- and (*Z*)-**4** from the  $\alpha$ -halo amidines **9a** and **b** can be conveniently monitored by IR spectroscopy because the IR spectra of the former are characterized by a strong absorption at  $1805\text{ cm}^{-1}$ , while the latter absorb in the usual range of amidine C=N frequencies<sup>[10]</sup>. By analogy with the interpretation of the IR spectrum of methylenecyclopropane<sup>[11]</sup>, the very high wave-number of the C=N absorption of iminoaziridines has to be ascribed to a strong coupling of the C=N vibration with a vibration of the aziridine ring<sup>[12]</sup>. The assignment of configuration for (*E*)- and (*Z*)-**4** is based on the extent of the long-range coupling between the ring proton and the methyl protons of the C=NCH<sub>3</sub><sup>[8]</sup> moiety and an asymmetric solvent-induced shift (tetrachloromethane or [D]trichloromethane vs. [D<sub>6</sub>]benzene). This high-field shift, which is caused by the asymmetric solvation of the C=NCH<sub>3</sub> moiety by [D<sub>6</sub>]benzene molecules, is larger for protons *cis* to the imino methyl group than for *trans* protons<sup>[8,13]</sup>.

The ratio of the diastereomers (*E*)- and (*Z*)-**4** in the mixture produced and isolated at or slightly below room temperature is 57:43. When the dehydrobromination of **9b** is carried out at  $-40^\circ\text{C}$  followed by workup at low temperatures, the *Z* diastereomer (*Z*)-**4** is preferred [(*E*)-**4**:(*Z*)-**4** = < 10: > 90]. The *E/Z* equilibration can be monitored conveniently by proton spectroscopy leading to ( $k_{EZ} + k_{ZE}$ ) =  $(5.92 \pm 0.08) \cdot 10^{-5}\text{ s}^{-1}$  and  $K = k_{EZ}/k_{ZE} = (\text{Z})\text{-4}/(\text{E})\text{-4} =$

$(0.428 \pm 0.013)$  at  $36^\circ\text{C}$  in the absence of solvent,  $\Delta G^\ddagger = 97.5\text{ kJ mol}^{-1}$ . In contrast to the dehydrobromination of **9b**, photoextrusion of molecular nitrogen from the neopentylidenedihydrotetrazole **10** at low temperatures produces predominantly the *E* diastereomer [(*E*)-**4**:(*Z*)-**4** = 95:5 at  $-60^\circ\text{C}$ ]<sup>[8]</sup>. By analogy with the formation of aziridinones from  $\alpha$ -bromo amide anions<sup>[5]</sup>, anions of the  $\alpha$ -halo amidines **9a** and **b** are probably involved in the base-induced dehydrohalogenation which decompose into the halide ion and the iminoaziridine (*Z*)-**4**. Thus, the high *Z* diastereoselectivity may be traced back to the relative stability of diastereomeric  $\alpha$ -bromo amidine anions. Apparently, the anion with the *Z,Z* configuration, which leads to (*Z*)-**4**, is more stable because repulsion of the nitrogen lone pairs is minimized in this particular configuration.



#### Non-Racemic Iminoaziridines (*E,R*)- and (*Z,R*)-**4**

Since the non-racemic  $\alpha$ -chloro amide (*S*)-**6a** (98% ee) is readily available from (*S*)-*tert*-leucin<sup>[2]</sup>, the synthesis of the non-racemic iminoaziridines (*E,R*)- and (*Z,R*)-**4** appeared to be straightforward on the route via the  $\alpha$ -chloro imidoyl chloride followed in the preparation of racemic (*E*)- and (*Z*)-**4**. Treatment of (*S*)-**6a** with thionyl chloride yielded the  $\alpha$ -chloro imidoyl chloride **7a** which was racemic, however, as shown by the proton spectrum obtained in the presence of Pirkle's alcohol **11** as chiral shift reagent<sup>[14]</sup> which was employed throughout this work. Presumably, deprotonation/reprotonation at the  $\alpha$ -carbon atom had occurred in a step of the sequence. In order to shed some light on this process, we treated in separate experiments racemic **6a** and [D]**6a**, the amide proton of which had been replaced

Table 1. Precursors, reagents, solvents, reaction conditions, yields, ratios of *E/Z* diastereomers, boiling points, and spectroscopic data (recorded from solutions in tetrachloromethane) of some 3,3-dimethylbutanoic acid derivatives and the iminoaziridines (*E*)-4 and (*Z*)-4

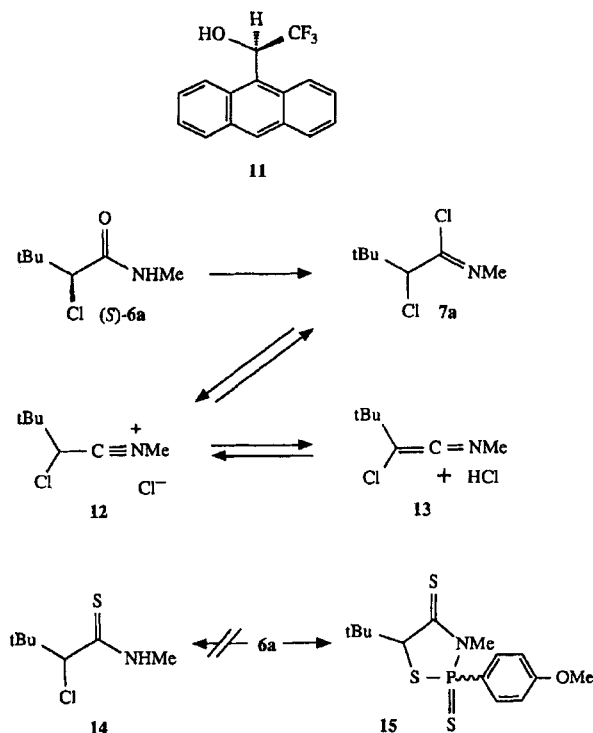
Cpd.	Pre-cursor	Reagent, Solvent	Condition [°C/h]	Yield [%]	( <i>E</i> )-4 : ( <i>Z</i> )-4	b. p. [°C/Torr]	IR [cm <sup>-1</sup> ] C=N	(CCl <sub>4</sub> ) NH
7a	5	PCl <sub>5</sub> , cyclohexane	85/7	72		85 – 87/23	1680, 1710	
6a		SOCl <sub>2</sub> , trichloromethane	65/1.5	65		83 – 84/16		
8	6a	1. F <sub>3</sub> CSO <sub>2</sub> Me 2. KHCO <sub>3</sub> , H <sub>2</sub> O	20–25/240	83		33 – 34/10 <sup>-2</sup>	1683	
15	6a	[(4-MeOC <sub>6</sub> H <sub>4</sub> PS <sub>2</sub> ) <sub>2</sub> ] toluene	95/2	55		85 – 86 <sup>[a]</sup>	1580, 1565 (C=C)	
9a	7a	MeNH <sub>2</sub> , pentane	–20/1	68		48 – 50/10 <sup>-2</sup>	1642	3450
	8	MeNH <sub>2</sub> , MeNH <sub>3</sub> <sup>+</sup> Cl <sup>–</sup> MeOH	65/5	88		30 – 31/10 <sup>-3</sup>		
9b	7b	MeNH <sub>2</sub> , petroleum ether	–20 → 25/20	84		30 – 31/5·10 <sup>-4</sup>	1642(s)	3445 (m) 3380 (br) <sup>[b]</sup>
( <i>E</i> )-4, ( <i>Z</i> )-4	9a	<i>t</i> BuOK, Et <sub>2</sub> O	0/10	49	57 : 43	20 – 25/10 <sup>-2</sup>	1805	
		NaH ( <i>t</i> BuOH), THF	20–25/40	71	57 : 43			
	9b	NaH, THF	20–25/70	65				
		<i>t</i> BuOK, Et <sub>2</sub> O	–40 → –30/3	23	<10 : >90			

<sup>[a]</sup> Melting point. – <sup>[b]</sup> Recorded in the absence of solvent.

by deuterium, in sealed NMR sample tubes at 65°C with a mixture of thionyl chloride and [D]trichloromethane (3:1) and monitored the course of the reaction by proton spectroscopy. The amide **6a** reacted somewhat faster than its isotopomer [D]**6a** (82% vs. 62% conversion after three hours). The  $\alpha$ -proton of the  $\alpha$ -chloro imidoyl chloride obtained from [D]**6a** had been replaced by deuterium to a considerable extent (> 50%). A probable mechanism of this exchange involves equilibration of **7a** with the nitrilium chloride **12** and the ketene imine **13** plus hydrogen chloride<sup>[15]</sup> followed by the addition to **13** of deuterium chloride which was formed from [D]**6a** and thionyl chloride.

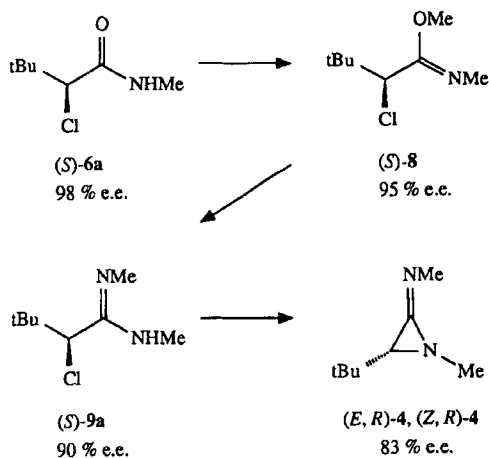
A second attempt to convert the  $\alpha$ -chloro amide (*S*)-**6a** into a reactive non-racemic derivative suitable for the reaction with methanamine failed likewise. Treatment of **6a** at 95°C in toluene as solvent with Lawesson's reagent did not yield the expected  $\alpha$ -chloro thioamide **14** but a chlorine-free, phosphorus-containing product as a mixture of two diastereomers (6:1, proton NMR analysis). The 1,3,2-thiazaphospholidine structure was assigned to the components of this mixture on the basis of analytical and spectroscopic evidence. The relative configurations were not determined, however.

Eventually, the long-known imidate route to amidines<sup>[16]</sup> was followed. Because the chlorine atom in the  $\alpha$ -position reduces the reactivity of **6a** toward methylating agents, even methyl triflate in the absence of solvent reacted only slowly with **6a**. Nevertheless, after several days at ambient temperature and workup with aqueous potassium hydrogen carbonate, a high yield of the imidate **8** was realized which was obtained as a colourless oil distillable in vacuo. It was



even more gratifying that, when the reaction started from non-racemic (*S*)-**6a** (98% ee), the enantiomeric excess of the product (*S*)-**8** was still as high as 95%.

While the imide **8** was very reluctant toward methanamine in the absence of acid catalysis<sup>[17]</sup>, an excess of methanamine in boiling methanol in the presence of one mol of methan ammonium chloride smoothly converted (*S*)-**8** into the amidinium chloride (*S*)-**9a**·HCl from which the free base (*S*)-**9a** was obtained in 88% yield with only little racemization (90% ee).



The 1,3-dehydrochlorination of the non-racemic  $\alpha$ -chloro amidine (*S*)-**9a** was carried out as before by means of the preferred base-solvent combination, i.e. sodium hydride in tetrahydrofuran in the presence of a catalytic amount of *tert*-butyl alcohol. The mixture of diastereomeric iminoaziridines (*E,R*)- and (*Z,R*)-**4** was isolated in 71% yield. Both diastereomers possessed an enantiomeric excess of 83%. Rigorous proof of the absolute configuration of the diastereomers was not attempted. Because it is reasonable to assume that the steric course of aziridine ring formation is the same, i.e. inversion, in both the 3-alkylaziridin-2-one and the 3-alkyl-2-iminoaziridine series, we assign the *R* configuration to the iminoaziridines obtained from (*S*)-**9a**. Thus, a consistent mechanistic picture describes the sequence of events: Deprotonation by a strong base affords the  $\alpha$ -bromo amide and the  $\alpha$ -chloro amidine anion, respectively, which decompose on a semi-W path<sup>[18]</sup> into the aziridine derivative and a halide ion.

#### Thermolysis of the Iminoaziridines (*E*)- and (*Z*)-**4**

Iminoaziridines decompose thermally into imines and isocyanides at temperatures that depend on the nature of the alkyl groups attached to the ring nitrogen atom and the imino group<sup>[7]</sup>. This thermolysis poses an upper limit on the temperature range suitable for a study of reagent-induced ring opening reactions. The question whether the decomposition is a truly unimolecular process has not been answered as yet, neither is any quantitative information available concerning rate constants and the activation barrier. Furthermore, monitoring the enantiomeric excess of (*R*)-**4** at higher temperatures would perhaps uncover a thermal generation of achiral or racemic transients as has been the case in the thermolysis of the aziridinone (*R*)-**2**<sup>[4]</sup>.

Therefore, we embarked on a kinetic study of the thermolysis of racemic **4** and non-racemic (*R*)-**4**. To this end, carefully degassed solutions in [D<sub>6</sub>]benzene were heated in evacuated, sealed NMR sample tubes to temperatures between 70 and 110°C. In a very clean process, the imine **16** and methyl isocyanide (**17**) emerged as the sole products within the limits of detection (1%). Integration of the proton signals of the *tert*-butyl groups during 2–3 half-lives demonstrated a perfect first-order behaviour for the decomposition (Figure 1) and yielded the rate constants summarized in Table 4 which were calculated by the non-linear least-squares method<sup>[19]</sup>.

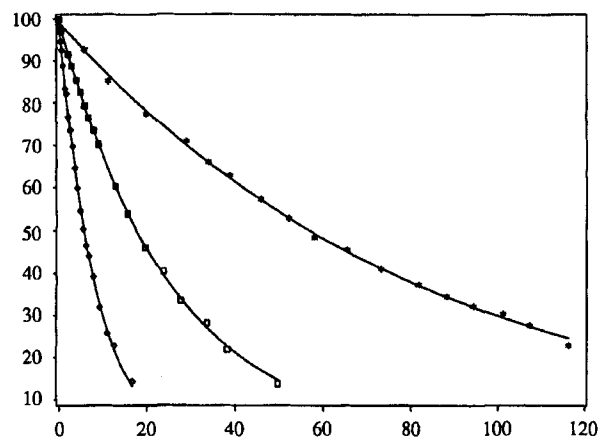
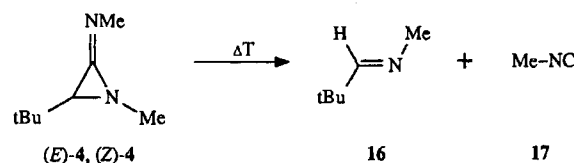


Figure 1. Conversion [%] vs. time [h] in the thermal decomposition of (*E*)- and (*Z*)-**4** in [D<sub>6</sub>]benzene solution at 343.16 (\*), 353.16 (□), and 363.16 K (◇)

From the temperature dependence of the rate constants according to the Arrhenius equation,  $\ln k = \ln A - E_a/RT$  (Figure 2), and the Eyring equation,  $\ln k/T = \ln k_B/h + \Delta S^\ddagger/R - \Delta H^\ddagger/RT$ , the following parameters of activation are obtained:  $E_a = (115.2 \pm 0.4) \text{ kJ mol}^{-1}$ ,  $\lg A = (12.06 \pm 0.28)$ , and  $\Delta H^\ddagger = (112.1 \pm 0.4) \text{ kJ mol}^{-1}$ ,  $\Delta S^\ddagger = (-23.9 \pm 0.7) \text{ JK}^{-1} \text{ mol}^{-1}$ ,  $\Delta G^\ddagger_{373\text{K}} = 121 \text{ kJ mol}^{-1}$ .

The iminoaziridines (*E*)- and (*Z*)-**4** are thermally rather labile. The free enthalpy of activation for the decomposition, extrapolated to 36°C ( $\Delta G^\ddagger_{309\text{K}} = 119.5 \text{ kJ mol}^{-1}$ ), is higher than that of the *E/Z* isomerization by only 22 kJ mol<sup>-1</sup>. A few kinetic studies<sup>[4,20]</sup> of thermal [2+1] cycloeliminations have been carried out, but accurate parameters of activation are scarce. We note that the entropy of activation for the thermolysis of (*E*)- and (*Z*)-**4** is different from what is to be expected for normal unimolecular thermal reactions ( $\Delta S^\ddagger \approx 0$ <sup>[21]</sup>), i.e. it is relatively large and negative. This is indicative of a constrained transition state

which may be explained in terms of the mode of decomposition following the non-linear cheletropic reaction path as predicted by Woodward and Hoffmann<sup>[22]</sup>.

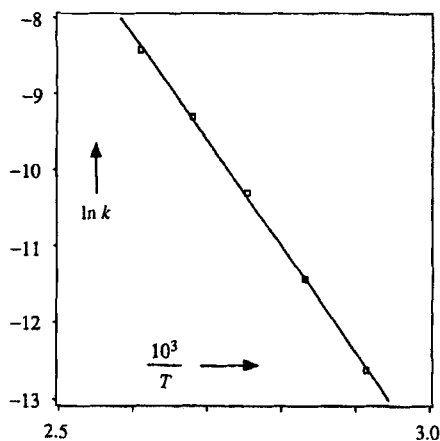


Figure 2. Temperature dependence of the rate constants according to the Arrhenius equation for the thermolysis of the iminoaziridines (E)- and (Z)-4

Attempts to detect a thermal racemization of (E,R)- and (Z,R)-4 were frustrated by their lability at higher temperatures. After carefully degassed samples of a [D<sub>6</sub>]benzene solution had been kept at 80°C for up to 2 half-lives, the enantiomeric excess of the surviving fractions of the iminoaziridines (E,R)- and (Z,R)-4 had not been diminished. Therefore, the search for achiral or racemic (acyclic) transients in the iminoaziridine series has to await the advent of non-racemic examples of higher thermal stability.

Nucleophilic ring-opening reactions of racemic and non-racemic (E)- and (Z)-4 will be the subject of a separate report.

We are indebted to the *DEGUSSA AG*, Hanau, for generous gifts of valuable chemicals. We thank Mrs. E. Ruckdeschel and Dr. D. Scheutzw for recording high-field proton and carbon-13 NMR spectra, Mrs. M. Schäfer for taking phosphorus-31 NMR spectra, and Dr. G. Lange and Mr. F. Dadrich for running the mass spectra. Financial support by the *Deutsche Forschungsgemeinschaft* and the *Fonds der Chemischen Industrie*, Frankfurt am Main, is gratefully acknowledged.

## Experimental

Starting materials, reagents, solvents, reaction conditions, yields, physical and IR data: Table 1. – <sup>1</sup>H-NMR data: Table 2. – <sup>13</sup>C-NMR data: Table 3. – Details of the kinetic investigation and results: Table 4. – Molecular formulae and masses, and elemental analyses: Table 5. – Melting points: Sealed capillary tubes, apparatus from Büchi, Flawil, Switzerland. – IR: Beckman IR 10 and Perkin-Elmer 1420. – <sup>1</sup>H NMR: Bruker AC 250 (0.305 Hz/pt.), Varian A60, Enantiomeric excesses (ee) were calculated from 5 integrations of 250-MHz <sup>1</sup>H-NMR spectra recorded in the presence of 2 equivalents of 11<sup>[14]</sup>. – <sup>13</sup>C NMR: Bruker AC 200 and AC 250. The assignments are based on DEPT spectra or <sup>13</sup>C,<sup>1</sup>H COSY spectra [9a, (E)- and (Z)-4]. – <sup>31</sup>P NMR: Jeol FX 90Q, (external standard: 85% phosphoric acid). – MS (70 eV): Finnigan MAT 8200.

Ether and tetrahydrofuran were distilled under Ar from sodium-potassium alloy. Under N<sub>2</sub>, pentane, petroleum ether, and toluene were distilled from sodium hydride, dichloromethane and trichloromethane from diphosphorus pentoxide. – Sodium hydride was freed from paraffin oil by repeated washings with pentane and dried in a stream of N<sub>2</sub>. Gaseous methanamine was dried with potassium hydroxide pellets. Thionyl chloride was distilled under N<sub>2</sub> before use. Potassium *tert*-butoxide was sublimed three times at 200°C/5 · 10<sup>–2</sup> Torr and kept under Ar. (S)-2-Chloro-3,3-dimethylbutanoyl chloride<sup>[2]</sup>, 5<sup>[23]</sup>, 7b<sup>[9]</sup>, and methyl triflate<sup>[24]</sup> were prepared according to literature procedures.

(S)-2-Chloro-N,3,3-trimethylbutanamide [(S)-6a]: A solution of (S)-2-chloro-3,3-dimethylbutanoyl chloride (13.3 g, 79 mmol) in dichloromethane (240 ml) and a solution (250 ml) of methanamine (0.72 M, 0.18 mol) in the same solvent were added simultaneously dropwise during 2 h to stirred dichloromethane (400 ml) cooled to –10°C. Stirring was continued for 0.5 h without cooling. The reaction mixture was extracted with hydrochloric acid (2 M, 200 ml) followed by an aqueous solution of potassium carbonate (2 M, 200 ml) and dried with magnesium sulfate. Distillation of the solvent in vacuo afforded colourless crystals (12.4 g, m.p. 112–113°C). Recrystallization from cyclohexane (70 ml) yielded colourless needles (10.3 g, 80%, m.p. 118–119°C, ref.<sup>[2]</sup> 118–119°C, ee 98%).

Racemic 2-Chloro-N,3,3-trimethylbutanamide (6a) was obtained as described in the preceding experiment from 2-chloro-3,3-dimethylbutanoyl chloride and methanamine in 80% yield as colourless needles (m.p. 106–108°C) after recrystallization from cyclohexane.

2-Chloro-N-deuterio-N,3,3-trimethylbutanamide ([D]6a): Repeated recrystallizations from a 1:1 mixture of deuterium oxide and [D<sub>4</sub>]methanol of 5.0 g 6a with strict exclusion of moisture yielded colourless crystals (3.7 g, m.p. 106°C) which were dried at 10<sup>–2</sup> Torr over diphosphorus pentoxide. – IR (CCl<sub>4</sub>): 2570 cm<sup>–1</sup> (ND).

### 2-Chloro-N,3,3-trimethylbutanimidoyl Chloride (7a)

a) According to the method by von Braun et al.<sup>[25]</sup>, phosphorus pentachloride (16.6 g, 80 mmol) was added under N<sub>2</sub> in several portions to a stirred solution of 5 (5.2 g, 40 mmol) in cyclohexane (15 ml), and the resulting mixture was heated under reflux for 7 h while the conversion was monitored by <sup>1</sup>H-NMR spectroscopy. Petroleum ether (30–50°C, 50 ml) was added to the cooled reaction mixture, and the solution was decanted from inorganic material. The solvent was distilled in vacuo at a bath temp. below 50°C. Distillation of the residue afforded a colourless oil (5.0 g, 72%, b.p. 85–87°C/23 Torr).

b) Thionyl chloride (65 g, 0.55 mol) was added under N<sub>2</sub> to a stirred solution of 6a (9.00 g, 55 mmol) in trichloromethane (20 ml). The mixture was heated to 65°C for 1.5 h while the conversion was monitored by <sup>1</sup>H-NMR spectroscopy. The solvent and excess thionyl chloride were distilled in vacuo. Distillation of the remaining pale brown oil yielded a colourless oil (6.50 g, 65%, b.p. 83–84°C/16 Torr).

c) A solution of (S)-6a (1.0 g, 6.1 mmol) and thionyl chloride (4.4 ml, 60 mmol) in trichloromethane (4 ml) was heated to 65°C for 2 h. Workup as described under b) yielded a colourless oil (0.98 g, 88%) which afforded completely racemized 9a after treatment with methanamine.

Methyl 2-Chloro-N,3,3-trimethylbutanimidate (8): A stirred suspension of 6a (40.8 g, 0.25 mol) in methyl triflate (49.1 g, 0.30 mol) was heated to 45°C for 1.5 h and subsequently kept at 20–25°C for 10 d. A saturated aqueous solution of potassium hydrogen carbonate (200 ml) was added to the reaction mixture followed by

extraction with ether (2 × 200 ml). The combined organic layers were washed with water (200 ml) and dried with potassium carbonate. Distillation of the solvent in vacuo afforded a pale yellow oil (47.1 g, quant.) which was distilled to yield a colourless oil (36.6 g, 83%, b.p. 30–31°C/10<sup>-2</sup> Torr).

*Methyl (S)-2-Chloro-N,N',3,3-trimethylbutanimidate [(S)-8]* was obtained as described for **8** from (S)-**6a** (7.71 g, 47 mmol) and methyl triflate (9.21 g, 56 mmol) as a colourless oil (6.88 g, 83%, b.p. 30–31°C/10<sup>-2</sup> Torr, ee 95%).

*5-tert-Butyl-2-(4-methoxyphenyl)-3-methyl-1,3,2-thiazaphospholidine-4-thione 2-Sulfide (15, 6:1 Mixture of Diastereomers):* Lawesson's reagent<sup>[26]</sup> (4.19 g, 10.4 mmol) was added to a stirred solution of **6a** (2.26 g, 13.8 mmol) in toluene (30 ml). The mixture was heated to 95°C for 2 h. Water (20 ml) was added to the cooled, clear solution followed by stirring of the mixture for 0.5 h. The phases were separated, and the aqueous layer was extracted with ether (5 × 20 ml). The combined organic layers were dried with magnesium sulphate. Distillation of the solvent in vacuo followed by flash chromatography of the residue [50 × 5 cm glass column packed with silica gel 32–63 µm (ICN Biomedicals), petroleum ether (30–75°C)/ethyl acetate (9:1), 1.8 bar N<sub>2</sub>] and recrystallization from ether/pentane (1:1) yielded yellow crystals (2.63 g, 55%, m.p. 85–86°C). – MS; *m/z* (%): 345 (18) [M<sup>+</sup>], 289 (100), 87 (62), 86 (34), 63 (38), 57 (30), 43 (30), 42 (79), 41 (44). – *Major diastereomer*: <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ = 1.29 (tBu), 2.99 (<sup>3</sup>J<sub>PH</sub> = 8.3 Hz, NMe), 3.89 (OMe), 4.73 (<sup>3</sup>J<sub>PH</sub> = 12.2 Hz, CH), 6.99 (H<sub>A</sub>H'<sub>A</sub>, <sup>4</sup>J<sub>PH</sub> = 8.9 Hz), 7.28 (H<sub>B</sub>H'<sub>B</sub>, <sup>3</sup>J<sub>PH</sub> = 15.3 Hz, AA'BB'X spectrum). – <sup>13</sup>C NMR (CDCl<sub>3</sub>): δ = 28.6, 38.1 (tBu), 33.4 (<sup>2</sup>J<sub>PC</sub> = 8.2 Hz, NMe), 55.6 (OMe), 74.2 (<sup>2</sup>J<sub>PC</sub> = 2.0 Hz, CH), 114.2 (<sup>2</sup>J<sub>PC</sub> = 16.3 Hz, o-C), 124.3 (<sup>1</sup>J<sub>PC</sub> = 108.1 Hz, P–C=), 134.2 (<sup>3</sup>J<sub>PC</sub> = 15.0 Hz, m-C), 163.5 (<sup>4</sup>J<sub>PC</sub> = 3.3 Hz, C–OMe), 202.3 (<sup>2</sup>J<sub>PC</sub> = 12.1 Hz, C=S). – <sup>31</sup>P NMR (CDCl<sub>3</sub>): δ = 89.9. – *Minor diastereomer*: <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ = 1.31 (tBu), 3.10 (<sup>3</sup>J<sub>PH</sub> = 8.9 Hz, NMe), 3.90 (OMe). – <sup>31</sup>P NMR (CDCl<sub>3</sub>): δ = 85.8.

#### 2-Chloro-N,N',3,3-tetramethylbutanimidine (9a)

a) A solution of methanamine (4.4 ml, 100 mmol) in pentane (20 ml) was added dropwise during 1 h to a stirred solution of **7a** (9.1 g, 50 mmol) in pentane (30 ml) cooled to –20°C. The suspension was allowed to attain 20°C. The precipitated methan ammonium chloride was filtered and washed with pentane. Distillation of the solvent from the combined filtrates and subsequently of the pale yellow residue in vacuo yielded a colourless oil (6.0 g, 68%, b.p. 48–50°C/10<sup>-2</sup> Torr).

b) According to ref.<sup>[27]</sup>, gaseous methanamine was introduced during 4 h into a boiling solution of **8** (7.00 g, 39.5 mmol) and methan ammonium chloride (2.70 g, 39.5 mmol) in methanol (50 ml). After the conversion was virtually complete (<sup>1</sup>H NMR), the solvent was distilled in vacuo. A cold aqueous solution of sodium hydroxide (2 M, 50 ml) was added to the residue, and the mixture was quickly extracted with petroleum ether (30–50°C, 100 ml). Small amounts of unchanged **8** were removed by extraction with a mixture (100 ml) of a saturated aqueous solution of potassium dihydrogen phosphate and water (1:3) immediately followed by the addition to the aqueous layer of a cold aqueous solution of sodium hydroxide (2 M, 50 ml). By rapid extraction with petroleum ether (30–50°C, 100 ml), **9a** was recovered. The organic layer was dried with potassium carbonate. The solvent and the colourless residue were distilled in vacuo to afford a colourless oil (6.20 g, 88%, b.p. 48–50°C/10<sup>-2</sup> Torr).

*(S)-2-Chloro-N,N',3,3-tetramethylbutanimidine [(S)-9a]:* According to procedure b) given for **9a**, a colourless oil (3.54 g, 87%, ee 90%) was obtained from (S)-**8** (4.32 g, 24.3 mmol).

*2-Chloro-N,N',3,3-tetramethylbutanimidinium Perchlorate (9a · HClO<sub>4</sub>):* An aqueous solution of perchloric acid (85%, 0.40 g, 3.54 mmol) was added to a stirred solution of **9a** (0.50 g, 2.83 mmol) in ethanol (3 ml) cooled to 0°C. After the addition of ether (10 ml) the mixture was stirred for 10 min, and the solid was filtered to yield colourless crystals (0.76 g, 96%, m.p. 198–199°C). Recrystallization from ethanol afforded colourless crystals (0.71 g, 90%, m.p. 199–200°C).

*(S)-2-Chloro-N,N',3,3-tetramethylbutanimidinium Perchlorate [(S)-9a · HClO<sub>4</sub>]* was obtained as described for **9a · HClO<sub>4</sub>** from (S)-**9a** (0.50 g, 2.83 mmol) as colourless crystals (0.71 g, 90%, m.p. 201–202°C).

*2-Bromo-N,N',3,3-tetramethylbutanimidine (9b):* An excess of gaseous methanamine was introduced under N<sub>2</sub> into a stirred solution of **7b** (41.0 g, 181 mmol) in petroleum ether (30–50°C, 400 ml) cooled to –20°C. The mixture was allowed to attain room temp. overnight. The white precipitate (methan ammonium chloride, 11.8 g, 96%) was filtered under N<sub>2</sub> and washed with petroleum ether. Distillation of the solvent from the combined filtrates and subsequently of the pale yellow residue in vacuo yielded a colourless oil (33.5 g, 84%, b.p. 30–31°C/5 · 10<sup>-4</sup> Torr).

*2-Bromo-N,N',3,3-tetramethylbutanimidinium Perchlorate (9b · HClO<sub>4</sub>):* An aqueous solution of perchloric acid (70%, 1.5 ml, 17.4 mmol) was added dropwise to a stirred solution of **9b** (2.21 g, 10 mmol) in ethanol (3 ml) cooled to 0°C. After the addition of ether (20 ml) the mixture was stirred at 0°C for 10 min to afford colourless crystals (3.19 g, 99%, m.p. 208–210°C). Recrystallization from ethanol raised the m.p. to 210–210.5°C.

*N-(3-tert-Butyl-1-methyl-2-aziridinylidene)methanamine, Mixture of Diastereomers [(E)- and (Z)-4]*

a) Potassium *tert*-butoxide (13.8 g, 123 mmol) was added under Ar to a stirred solution of **9a** (10.9 g, 61.7 mmol) in ether (400 ml) cooled to 0°C. Stirring at 0°C was continued for 10 h followed by the addition of pentane (100 ml). The mixture was quickly extracted with iced water (3 × 50 ml) and dried with potassium carbonate. Distillation of the solvent and the remaining pale yellow oil in vacuo yielded a colourless oil (4.02 g, 49%, b.p. 20–25°C/10<sup>-2</sup> Torr) consisting of (E)- and (Z)-**4** (57:43, <sup>1</sup>H NMR).

b) Sodium hydride (6.09 g, 250 mmol) and *tert*-butyl alcohol (0.3 ml, 4.4 mmol) were added under Ar to a stirred solution of **9a** (5.32 g, 30.1 mmol) in tetrahydrofuran (100 ml). Stirring was continued at 20–25°C for 40 h while the conversion was monitored by IR spectroscopy. After the addition of pentane (100 ml), the white precipitate was filtered and washed with pentane. The filtrate and the washing were combined, quickly extracted with iced water (3 × 50 ml), and dried with potassium carbonate. Distillation of the solvent and the remaining pale yellow oil in vacuo yielded a colourless oil (2.99 g, 71%) consisting of (E)- and (Z)-**4** (57:43, <sup>1</sup>H NMR).

c) Sodium hydride (3.80 g, 158 mmol) was added under N<sub>2</sub> to a solution of **9b** (5.51 g, 25 mmol) in tetrahydrofuran (50 ml). The mixture was stirred at 20–25°C for 70 h. Workup as described under b) and distillation in vacuo yielded a colourless oil (2.26 g, 65%).

d) Potassium *tert*-butoxide (18.4 g, 164 mmol) was dissolved in ether (260 ml) with stirring for 1 h, and the solution was filtered under Ar and cooled to –40°C. **9b** (8.84 g, 40 mmol) was added followed by stirring at –40°C for 3 h. Most of the solvent was distilled at –30 to –35°C (bath temp.)/14 → 10<sup>-1</sup> Torr. Hexane (100 ml, cooled to –50°C) was added, and the mixture was stirred at –30°C for 5 min followed by evaporation of the solvent at –30 to –35°C/10<sup>-1</sup> Torr. After the addition of pentane (80 ml, cooled

Table 2. Chemical shifts ( $\delta$  values) in  $^1\text{H}$ -NMR spectra of some 3,3-dimethylbutanoic acid derivatives. The  $^1\text{H}$ -NMR spectra of solutions of **6a**, **8**, **9a**, and the iminoaziridines (*E*)- and (*Z*)-**4** were also recorded in the presence of 2 equivalents of (*R*)-1-(9-anthryl)-2,2,2-trifluoroethanol (**11**); the average of the chemical shifts of the enantiomers [ $\delta(R) + \delta(S)$ ]/2 and (in *italics*) the differences of resonance frequencies  $\nu(R) - \nu(S)$  [Hz] are listed

Cpd.	<i>t</i> Bu	CH	=NMe	Me—N—H <sup>[a]</sup>	<sup>3</sup> <i>J</i>	[b]	
<b>5</b>	1.03	2.07 (CH <sub>2</sub> )		2.79	6.1	4.8	CDCl <sub>3</sub>
<b>6b</b>	1.15	4.18		2.84	6.6	4.8	CDCl <sub>3</sub>
( <i>E</i> )- <b>4</b>	0.80 4.4	1.66 7.6	2.89	2.36 -27.6			B
( <i>Z</i> )- <b>4</b>	0.66 3.5	1.39 9.2	2.54	2.47 -20.2			B
<b>7a</b>	0.99	4.38	2.91				CDCl <sub>3</sub>
	0.93 [1.1]	4.43 [5.8]	2.81 [1.0]				B
<b>8</b> <sup>[c]</sup>	0.99	4.43	2.85				C <sub>6</sub> D <sub>6</sub>
	0.97 -4.6	4.33 4.4	2.84 -5.8				C
<b>9a</b>	0.97	4.43	2.98 <sup>[d]</sup>	2.61 <sup>[d]</sup>	4.1		C <sub>6</sub> D <sub>6</sub>
	0.89 -5.2	4.53	2.55 <sup>[d]</sup>	2.55 <sup>[d]</sup>	4.1		B
<b>9a</b> · HClO <sub>4</sub>	1.13	4.97		2.95 3.14	7.4 7.6	5.3 5.3	CD <sub>3</sub> CN
<b>9b</b>	1.13	4.82	3.02 <sup>[d]</sup>	2.70 <sup>[d]</sup>	4.1		CCl <sub>4</sub>
	1.13	4.88		2.80 <sup>[d]</sup>	5.4		[CD <sub>3</sub> ] <sub>2</sub> SO
<b>9b</b> · HClO <sub>4</sub>	1.17	4.95 <sup>[d]</sup>		2.96 3.13 <sup>[d]</sup>	7.5		CD <sub>3</sub> CN

[a] Broad signal. — [b] Solvent: B = [D<sub>6</sub>]benzene/tetrachloromethane (1:3); C = [D<sub>12</sub>]cyclohexane/tetrachloromethane (1:12). — [c] OMe:  $\delta$  = 3.49; 3.45, 2.0. — [d] Broadened singlet.

to  $-50^\circ\text{C}$ ) to the residue and stirring for 10 min, the suspension was filtered at  $-30^\circ\text{C}$  under N<sub>2</sub> into a precooled flask ( $-50^\circ\text{C}$ ), and the filtrate was concentrated at  $-50$  to  $0^\circ\text{C}/12 \rightarrow 10^{-2}$  Torr. The remaining oil was distilled at  $0$ – $20^\circ\text{C}/10^{-3}$  Torr to afford a colourless oil (1.31 g, 23%) consisting of (*E*)- and (*Z*)-**4** ( $<10$  :  $>90$ ,  $^1\text{H}$  NMR) which was kept at dry-ice temperature.

(*E,R*)- and (*Z,R*)-**4**: According to the preceding procedure b), (*S*)-**9a** (3.10 g, 17.5 mmol) was allowed to react with sodium hydride (3.67 g, 153 mmol) and *tert*-butyl alcohol (0.3 ml, 4.4 mmol) in tetrahydrofuran (100 ml) to afford a colourless oil (1.75 g, 71%, ee 83%).

Equilibration (*E*)-**4**  $\rightleftharpoons$  (*Z*)-**4**: A mixture of neat (*E*)- and (*Z*)-**4** (1:9) and tetramethylsilane was sealed in a degassed, evacuated NMR sample tube and kept at  $36^\circ\text{C}$  in the insert of a Varian A60 NMR spectrometer. The equilibrium constant  $K = k_{EZ}/k_{ZE}$  was determined after 22 h. From 15 integrations during the first 7 h, the sum ( $k_{EZ} + k_{ZE}$ ) was calculated by the least-squares method according to the (non-linear) equation<sup>[28]</sup>  $[m_E K - m_Z] = [(m_E)_0 K - (m_Z)_0] \exp - (k_{EZ} + k_{ZE})t$ ;  $m_E$ ,  $m_Z$  = mole fractions of (*E*)- and (*Z*)-**4**, respectively;  $(m_E)_0$ ,  $(m_Z)_0$  = mole fractions at the beginning.

Thermolysis of (*E*)- and (*Z*)-**4**: The mixture of (*E*)- and (*Z*)-**4** (samples of 40 mg, 0.29 mmol) was placed into NMR sample tubes which had been dried at  $200$ – $300^\circ\text{C}/10^{-1}$  Torr and flushed with

Table 3. Chemical shifts ( $\delta$  values) in  $^{13}\text{C}$ -NMR spectra of some 3,3-dimethylbutanoic acid derivatives

Cpd.	Me <sub>3</sub> C		CH	C=O	=NMe	NHMe	Solvent
<b>5</b>	29.7	30.7	50.3	172.5		26.0	CDCl <sub>3</sub>
			(CH <sub>2</sub> )				
<b>6b</b>	27.4	34.9	63.4	168.8		26.6	CDCl <sub>3</sub>
				C=N			
<b>7a</b>	26.8	36.4	74.5	143.1	39.9		CDCl <sub>3</sub>
<b>8</b> <sup>[a]</sup>	26.9	35.3	52.2	159.7	35.3		C <sub>6</sub> D <sub>6</sub>
<b>9a</b>	27.0	36.3	61.9	155.3	36.0 <sup>[b]</sup>	28.2 <sup>[b]</sup>	C <sub>6</sub> D <sub>6</sub>
<b>9a</b> · HClO <sub>4</sub>	26.0	38.0	61.3	164.8		29.0 31.6	CD <sub>3</sub> CN
<b>9b</b> <sup>[c]</sup>	27.6	35.8	55.6	155.7	35.8 <sup>[b]</sup>	28.7 <sup>[b]</sup>	C <sub>6</sub> D <sub>6</sub>
<b>9b</b> · HClO <sub>4</sub>	26.7	37.2	51.6	165.3		29.1 31.5	CD <sub>3</sub> CN

[a] OMe:  $\delta$  = 59.2. — [b] Broad signal. — [c] 100.6-MHz spectrum (1.526 Hz/pt.).

Table 4. Experimental details and results of the kinetic investigation of the thermolysis of (*E*)- and (*Z*)-**4** in [D<sub>6</sub>]benzene solution

Temp. [K] ( $\pm 0.2$ )	No. of points	conversion [%]		$10^5 \cdot k$ [s <sup>-1</sup> ]	$t_{\frac{1}{2}}$ [min]
343.16	18	77	116	$0.334 \pm 0.003$	3500
353.16	22	86	50	$1.08 \pm 0.01$	1070
363.16	19	75	11	$3.38 \pm 0.03$	342
373.16	21	81	5	$9.18 \pm 0.09$	126
383.16	18	75	1.5	$22.0 \pm 0.5$	53

Ar while being attached to a high-vacuum line. [D<sub>6</sub>]Benzene (0.5 ml) was dried with LiAlH<sub>4</sub>, repeatedly degassed at  $10^{-5}$  Torr, and condensed into the NMR sample tubes which were flame-sealed at  $10^{-5}$  Torr. The sample tubes were completely immersed in a Lauda Ultrathermostate NS-S15/22/SP, the temperature of which was measured with calibrated thermometers. The identity of the products **16** and **17** was confirmed by  $^1\text{H}$ - and  $^{13}\text{C}$ -NMR spectra. The conversion was monitored by 200-MHz  $^1\text{H}$ -NMR spectra and calculated from integrations of the *tert*-butyl signals at 10 Hz/cm scale expansion. The rate constants were calculated by the non-linear least-squares method<sup>[19]</sup> according to  $I = I_0 \exp(-kt)$ ;  $I$  = sum of the integrations of (*E*)- and (*Z*)-**4**;  $I_0$  = sum of the integrations of (*E*)- and (*Z*)-**4** and **16**. Details and results are listed in Table 4.

[1] Iminoaziridines, part 4. — For part 3 see ref.<sup>[12]</sup>. — The results are taken from the Dissertations by S. Aldenkortt (1995) and P. Schäfer (1977), and the Diploma Thesis by E. Heller (1991), University of Würzburg.

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Table 5. Molecular formulae, masses, and elemental analyses for some 3,3-dimethylbutanoic acid derivatives, the iminoaziridines (*E*)- and (*Z*)-4 and the diastereomeric 1,3,2-thiazaphospholidines 15

Cpd.		Molecular Mass	Elemental Analysis		
			C	H	N
( <i>E</i> )-4, ( <i>Z</i> )-4	C <sub>8</sub> H <sub>16</sub> N <sub>2</sub>	140.2	Calcd. 68.52 Found 68.36	11.50 11.77	19.98 19.87
7a	C <sub>7</sub> H <sub>13</sub> Cl <sub>2</sub> N	182.1	Calcd. 46.17 Found 46.58	7.20 7.77	7.69 8.09
8	C <sub>8</sub> H <sub>16</sub> ClNO	177.7	Calcd. 54.08 Found 54.27	9.08 9.30	7.88 7.98
9a	C <sub>8</sub> H <sub>17</sub> ClN <sub>2</sub>	176.7	Calcd. 54.38 Found 54.38	9.70 10.02	15.87 16.05
( <i>S</i> )-9a · HClO <sub>4</sub>	C <sub>8</sub> H <sub>18</sub> Cl <sub>2</sub> N <sub>2</sub> O <sub>4</sub>	277.2	Calcd. 34.67 Found 34.70	6.55 6.33	10.11 9.99
15	C <sub>14</sub> H <sub>20</sub> NOPS <sub>3</sub>	345.5	Calcd. 48.67 Found 48.38	5.83 5.76	4.05 4.14
Br					
9b	C <sub>8</sub> H <sub>17</sub> BrN <sub>2</sub>	221.1	Calcd. 36.14 Found 36.28		12.67 12.77
Br + Cl					
9b · HClO <sub>4</sub>	C <sub>8</sub> H <sub>18</sub> BrClN <sub>2</sub> O <sub>4</sub>	321.6	Calcd. 35.87 Found 36.27		8.71 8.73

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[6] This statement does not refer to photochemical reactions, of course, neither to reactions of 3,3-disubstituted aziridinones, whose acyclic isomers still remain popular subjects of mechanistic speculations. For a collection of relevant examples see ref.[5].

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[94/94]