Pergamon

Tetrahedron 58 (2002) 2729–2733

TETRAHEDRON

Highly diastereoselective thermal decomposition of 3-(azidomethylene)dihydrofuran-2-one

Ctibor Mazal,[a,*] Jaroslav Jonas[a] and Zdirad Žák[b]

[a]*Department of Organic Chemistry, Faculty of Science, Masaryk University, Kotlářská 2, 611 37 Brno, Czech Republic*
[b]*Department of Inorganic Chemistry, Masaryk University, Kotlářská 2, 611 37 Brno, Czech Republic*

Received 19 November 2001; accepted 21 February 2002

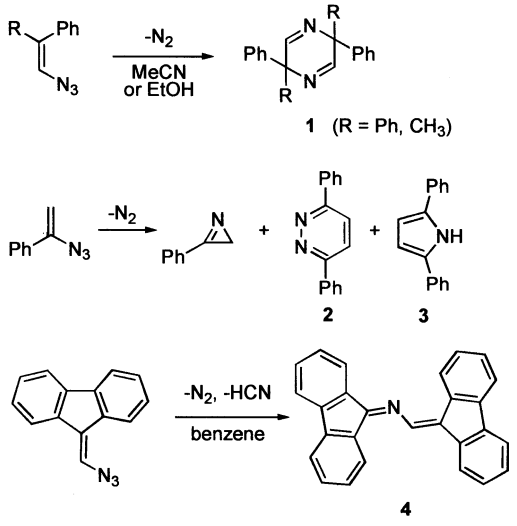
Abstract—Thermal decomposition of 3-(azidomethylene)dihydrofuran-2-one in various solvents at temperatures above 70°C gave a spiroaziridine derivative with an excellent diastereoselectivity. A mechanism of this new kind of substituted vinyl azide decomposition has been suggested based mainly on the stereochemistry and kinetic data of the reaction. A spiroazirine derivative proposed as a reaction intermediate was trapped by the decomposition of title azide in acetic anhydride.

1. Introduction

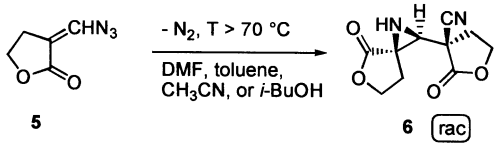
In the early sixties, Smolinsky[1] first investigated pyrolysis of α-substituted vinyl azides, which yielded 2*H*-azirines together with small amount of ketene imines. Although, since that time, thermal as well as photochemical decomposition of vinyl azides became a common route to azirines,[2] especially after Hassner's discovery of a general synthesis of vinyl azides,[3] an exceptional behavior of α-unsubstituted, terminal, vinyl azides was recognized soon after.[4] They failed to form isolable azirines, but depending on the constitution of their molecules a variety of products resulted instead. Indoles or isoxazoles have been isolated when neighboring groups were phenyl and carbonyl, respectively; in many cases rearranged nitriles or ketene imines were isolated, too.[5] On the other hand, only a few examples of dimerization during the decomposition processes of vinyl azides have been observed most probably due to a high reactivity of intermediates preferring intramolecular reactions or interactions with solvents instead. A recombination of intermediate nitrenes was assumed to explain formation of heterocyclic compounds **1** and **2**, whereas two different manners of 1,3-dipolar cycloaddition were suggested in the reaction mechanism leading to diphenylpyrrole **3**.[6] Formation of an unusual 'dimer' **4** was rationalized by coupling of nitrene and carbene, both formed from corresponding intermediate spiroazirine; the former by a ring opening and the later by an expulsion of HCN (Scheme 1).[7] Some interesting dimerizations of intermediates were observed also during photolytic decompositions of vinyl azides.[8]

2. Results and discussion

Thermal decomposition of 3-(azidomethylene)dihydrofuran-2-one[9] (**5**) yields the compound **6** when heated above 70°C in various solvents such as DMF, toluene, acetonitrile, and *iso*-butanol (Scheme 2). Since none of the previously reported mechanisms of vinyl azide dimerization



Scheme 1.



Scheme 2.

Keywords: vinyl azides; azirines; aziridines; methylene lactones.

* Corresponding author. Tel.: +420-5-41129303; fax: +420-5-41211214; e-mail: mazal@chemi.muni.cz

0040–4020/02/$ - see front matter
PII: S0040-4020(02)00184-9

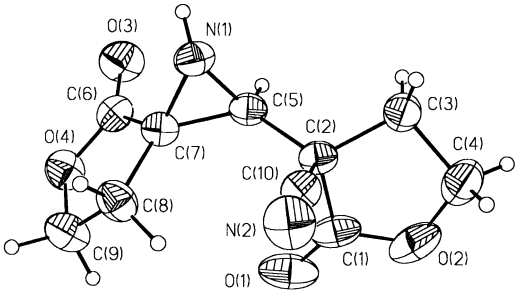


Figure 1. An ORTEP representation of **6**.

were able to rationalize this process, the reaction represents, to our best knowledge, a new kind of dimerization in the course of vinyl azide decomposition. As the product **6** was obtained in good yield and, moreover, with an outstanding stereoselectivity, an elucidation of the mechanism of its formation seemed to be appropriate.

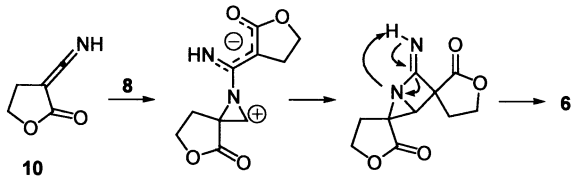
The structure of **6** was unambiguously determined by X-ray analysis (Fig. 1). Both the isomers of **5** gave the same product, a (2′*R**,3*S**,3′*S**)-2-oxo-3-(4′-oxo-5′-oxa-1′-aza-spiro[2,4]hept-2′-yl)tetrahydrofuran-3-carbonitrile. The exclusivity of this diastereomer formation was proved by high resolution ^{1}H NMR of crude reaction mixture, as well as by HPLC. Moreover, neither NMR spectroscopy, nor HPLC detected any sufficiently stable intermediate in the course of the reaction. The formation of a dimeric intermediate has to be taken into account due to a well-known 1,3-dipolar reactivity of organic azides[10] and its application in some related processes.[6]

The lack of any stable intermediate together with kinetic data obtained by volumetric measurements of nitrogen expulsion (Table 1), which fit first-order kinetics, supported a suggestion that **6** is created by a prompt interaction of reactive intermediates after nitrogen expulsion. Any interaction of such intermediates with azide **5** could also be ruled out. The different rates of decomposition of pure isomers of **5**, where the (*Z*)-isomer decomposes twice as fast as (*E*)-**5**, remained unchanged when observed in an *E*/*Z* mixture by HPLC (Table 1). This proved clearly that the decomposition of **5** is a unimolecular reaction and that the final product **6** is formed in subsequent reactions of some unstable intermediates. The faster decomposition of (*Z*)-**5** is easily understood by an assistance of the neighboring lactone carbonyl

Table 1. Rate constants *k*, Arrhenius activation energy E_a, and activation entropy ΔS^* of thermal decomposition of vinyl azides **5** in DMF

Isomer	*T* (°C)	$k\times10^4$ (s^{-1})	E_a (kJ mol^{-1})	ΔS^*_{100} (J K^{-1} mol^{-1})
E	96.4±0.1	4.49±0.02	131±5	36±12
	101.1±0.1	8.49±0.03		
	106.1±0.1	14.90±0.11		
	110.2±0.2	21.22±0.15		
	114.7±0.1	34.99±0.14		
	110.2±0.2	21.7±0.2[a]		
Z	96.2±0.2	12.34±0.14	126±6	30±16
	100.0±0.2	19.81±0.06		
	105.6±0.2	32.84±0.38		
	110.2±0.2	54.98±0.83		
	110.2±0.2	56.2±0.3[a]		

[a] Determined by HPLC from decomposition of *E*/*Z*-mixture (1:1).



Scheme 3.

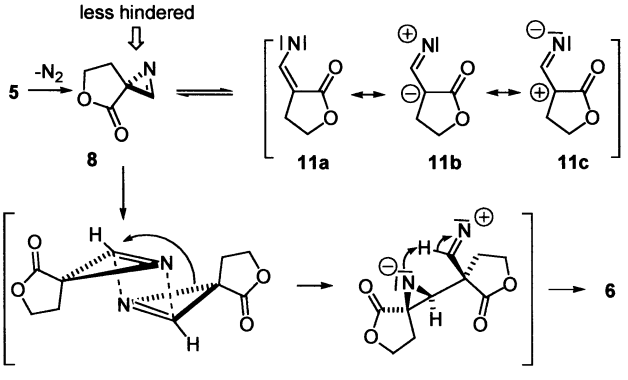
group. Such assistance is well documented by an easy isoxazole formation from β-azido-α,β-unsaturated esters and ketones,[11] or by pyrolysis of (*Z*)-isomer of homologous azidomethylene valerolactone **7** which gives, contrary to **5**, the corresponding isoxazole.[12] No evidence of similar isoxazole or oxazole formation was found during the decomposition of **5**.

Structural features suggest that **6** could be formed by a reaction of azirine **8** and nitrile **9**, which are reasonable products of terminal vinyl azide decomposition. Indeed, when the thermolysis of **5** was carried out in acetic acid, the nitrile **9** was obtained in good yield as the only product. However, when **5** was decomposed in the presence of **9** in the above mentioned less protic solvents, the nitrile remained unreacted after the reaction yielding, again, the dimer **6**. Clearly, the nitrile **9** does not participate in the reaction.

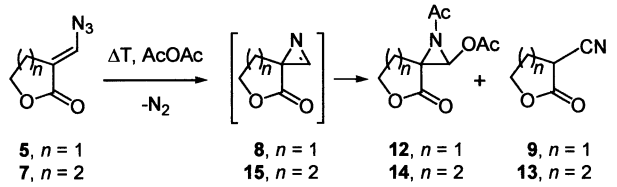
Another possible way to **6** can involve a recombination of the azirine **8** with a ketenimine **10** that is a reasonable intermediate of vinyl azide thermal decomposition, too (Scheme 3).[13] Since a stepwise pathway initiated by an azirine nitrogen attack to the electrophilic ketimine carbon was suggested in similar 'thermal' processes,[14] we suspect that the reaction would hardly run with the excellent selectivity observed in our case. On the other hand, a concerted [2+2]cycloaddition of 3-phenyl-2*H*-azirine to the corresponding ketenimine was indeed observed in a 'photochemical' decomposition of α-azidostyrene.[8b]

Concerning the facts mentioned above, we proposed the mechanism assuming the key role of the intermediate azirine **8** (Scheme 4).

According to this mechanism, the vinyl azide **5** loses nitrogen forming the azirine **8** that can open to **11a–c** in an azirine–nitrene equilibrium.[15] Since we, however, were



Scheme 4.



5, n = 1 **8**, n = 1 **12**, n = 1 **9**, n = 1
7, n = 2 **15**, n = 2 **14**, n = 2 **13**, n = 2

Scheme 5.

not able to prove **11** in the reaction mixture, the equilibrium, if exists at all, was shifted to the azirine **8**.[16] The interaction of two molecules of **8**, approaching each other from the less hindered side, results in formation of a dimeric product **6** with the configuration detected.

We tried to prove the intermediacy of the azirine **8**, but none of the methods commonly used for entrapping such an unstable azirine[17] succeeded. When, conversely, the azide **5** was decomposed in acetic anhydride, a compound identified by ^{1}H NMR to be the adduct **12** was detected in the reaction mixture besides the nitrile **9**. A similar adduct was isolated also by Sato et al. from reaction of 2-phenylazirine with acetic anhydride;[18] therefore, we consider **12** to be formed by the addition of acetic anhydride on the intermediate azirine **8**.

Unfortunately, this highly diastereoselective conversion seems to be limited to five membered lactone derivatives. When (*E*)-isomer of azidomethylene valerolactone **7** was heated in DMF or in *iso*-butanol above 70°C, only the corresponding nitrile **13** was detected as the major product. However, in the ^{1}H NMR spectrum of complex mixture of products obtained after the decomposition in acetic anhydride, three characteristic signals were detected (δ 5.35 (s, 1H) 2.25 (s, 3H) 2.19 (s, 3H)) and assigned to spiroaziridine **14**. This again suggests the intermediacy of the azirine **15** (Scheme 5). As mentioned above, (*Z*)-**7** decomposed already at room temperature giving the corresponding fused isoxazole.[12]

Some uniqueness of the butyrolactone derivative stems from the fact that its five membered ring would make the corresponding fused isoxazole too strained, whereas the geometry of the azirine **8** seems to be just the right one for the successful dimerization as shown in Scheme 4.

In conclusion, we have found a new, highly diastereoselective transformation of simple azidomethylene butyrolactone **5** into a more complex spiroderivative **6**. Our suggestion of mechanism of this interconversion is based on its stereochemistry as well as on the product of the acetic anhydride addition onto the intermediate azirine **8** proposed. The reaction referred to seems to be limited to five membered ring derivatives, but its high stereoselectivity provokes further study of its limits.

Table 2. Crystallographic data and refinement parameters of **6**

Empirical formula	$C_{10}H_{10}N_2O_4$
Formula weight	222.20
Temperature (K)	298(2)
Wavelength (Å)	0.71073
Crystal system, space group	Monoclinic, $P2(1)/c$
a (Å)	8.421(2)
b (Å)	9.826(2)
c (Å)	12.344(2)
α (°)	90.00
β (°)	104.97(3)
γ (°)	90.00
Volume (Å^3)	986.7(3)
Z, Calculated density D (g cm^{-3})	4, 1.496
Absorption coefficient (mm^{-1})	0.118
F_{000} (e)	464
Crystal size (mm^3)	0.70×0.40×0.20
Θ range for data collection (°)	2.50–25.06
Range of *hkl*	0→10, −11→0, −14→14
Reflections collected/unique	1749/1327 (R_{int}=0.0199)
Completeness to 2Θ=25.06 (%)	93.8
Max. and min. transmission	0.9768 and 0.9221
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	1749/1/149
Goodness-of-fit on F^2	1.035
Final R indices [$I>2\sigma(I)$]	$R1$=0.0346, $_wR2$=0.0948
R indices (all data)	$R1$=0.0547, $_wR2$=0.1033
Extinction coefficient	0.017(3)
Largest diff. peak and hole (e A^3)	0.246 and −0.160

3. Experimental

3.1. General

^{1}H NMR spectra were obtained in $CDCl_3$ at 300 or 500 MHz with TMS as an internal standard. ^{13}C NMR were obtained in $CDCl_3$, if not stated otherwise, at 75 or 125 MHz. IR spectrum of **6** was measured in a KBr pellet. Melting points are uncorrected. CI mass spectrum of **6** was obtained using *iso*-butane. Elemental analysis was done at Lachema, a.s., Brno.

3.2. General procedure for decomposition of vinyl azides

A solution of vinyl azide **5** or **7** (0.01 mol) in appropriate solvent (40 mL) was heated to 100–120°C with stirring until the evolution of nitrogen was complete. After evaporation of solvent the crude product was recrystallized or separated by flash chromatography.

3.2.1. (2′*R,3*S**,3′*S**)-2-Oxo-3-(4′-oxo-5′-oxa-1′-azaspiro-[2,4]hept-2′-yl)tetrahydrofuran-3-carbonitrile (6).** Thermolysis of **5** in *i*-BuOH gave **6** (600 mg, 54%) as white crystals, mp 158–159°C; (Found: C, 53.93; H, 4.52; N, 12.39. $C_{10}H_{10}N_2O_4$ requires C, 54.05; H, 4.54; N, 12.61%); ν_{max} (KBr) 3222, 2240 (very weak), 1765, 1485, 1445, 1395, 1380, 1210, 1175, 1020, 740, 698, 680 cm^{-1}; δ_H (500 MHz) 4.65–4.49 (4H, m, 2×CH_2O), 2.89 (1H, d, J=9.9 Hz, CH), 2.78–2.59 (4H, m, 2×OCH_2CH_2), 1.91 (1H, bd, J=9.9 Hz, NH); δ_C (100 MHz, DMF-d$_7$) 175.7, 170.4, 115.9, 67.1, 65.8, 43.8, 42.5, 39.0, 31.3, 24.3; *m/z* (CI, *iso*-butane) 223 (100, MH$^+$), 196 (18), 179 (30), 161 (12), 135 (6), 112 (39), 85 (28), 69 (42%).

3.2.2. 2-Oxotetrahydrofuran-3-carbonitrile (9). Thermolysis of **5** in acetic acid gave nitrile **9** after flash chromatography on silica gel as colorless oil (940 mg, 85%); ν_{max} (liquid film) 2916, 2256, 1778, 1483, 1456, 1380, 1255, 1222, 1165, 1020, 975, 950, 870, 806, 703, 665; δ_H (500 MHz) 4.56–4.50 (1H, m, OCH_aH$_b$), 4.36 (1H, dt, J=6.7, 9.3 Hz, OCH_aH$_b$), 3.76 (1H, dd, J=9.2, 10.4 Hz, CH), 2.79–2.72 (1H, m, CH_aH$_b$CH), 2.68–2.59 (1H, m, CH_aH$_b$CH) (cf. Ref. 19).

3.2.3. 2-Oxotetrahydropyran-3-carbonitrile (13). Thermolysis of **7** in acetic acid gave nitrile **13** after flash chromatography on silica gel as colorless oil (1.025 g, 82%); δ_H (300 MHz) 4.47–4.35 (2H, m, CH_2O), 3.75 (1H, dd, J=10.4, 9.2 Hz, CH), 2.54–2.39 (1H, m, $CHCH_aCH_b$), 2.30–1.93 (3H, m, $CH_2CH_aCH_bCH$) (cf. Ref. 20).

3.2.4. Thermolysis of vinyl azide 5 in acetic anhydride; 1-acetyl-4-oxo-5-oxa-1-azaspiro[2.4]hept-2-yl acetate (12). The vinyl azide **5** (70 mg, 0.5 mmol) was heated in acetic anhydride (4 mL) after the above general procedure yielding a crude mixture of products (90 mg) consisting mainly of two compounds, the nitrile **9** and the aziridine derivative **12** (4:5), which were separated by preparative TLC on precoated TLC plates RP-8 F254 s, layer thickness 0.25 mm, using 30% aqueous methanol as an eluent. The aziridine **12** was isolated as colorless oil (46 mg, 43%); (Found: C, 50.94; H, 5.07; N, 6.29. $C_9H_{11}NO_5$ requires C, 50.70; H, 5.20; N, 6.57 %); R_f (30% MeOH/water) 0.30; ν_{max} (liquid film) 2987, 2925, 1778, 1720, 1678, 1435, 1371, 1323, 1286, 1201, 1136, 1093, 1059, 1014, 955, 903, 665; δ_H (300 MHz) 5.24 (1H, s, CH), 4.64 (1H, dt, J=5.6, 8.9 Hz, OCH_aCH_b), 4.50 (1H, dt, J=6.9, 8.9 Hz, OCH_aCH_b), 2.60–2.39 (2H, m, OCH_2CH_2), 2.26 (3H, s, $NCOCH_3$), 2.18 (3H, s, $OCOCH_3$); δ_C (75 MHz) 176.3, 170.6, 170.1, 66.2, 64.6, 46.1, 24.3, 22.9, 20.5.

3.2.5. Decomposition of vinyl azide 7 in acetic anhydride. Following the general procedure, thermolysis of 50 mg of **7** in 5 mL of acetic anhydride gave a mixture of products, which was analyzed by ^{1}H NMR. Two main system of peaks were detected besides of the other minor peaks: signals of nitrile **13** and signals resembling the spiroazirine **12** (δ 5.35 (1H, s) 2.25 (3H, s) 2.19 (3H, s)). The later were assigned to homologous azirine **14**. The **13/14** ratio was approximately 6:1.

3.3. Kinetic measurements

Small sample tubes charged with vinyl azide **5** (ca. 0.40 mmol) were introduced to preheated stirred DMF (5 mL) in a thermostated round bottom flask connected to a gasometric burette. The observed rate constants k were determined from $\ln(V_{max}-V_t)$ vs. t plot where V_{max} and V_t were the volumes of nitrogen expelled at the end and in the time t of the reaction, respectively. The measurements were performed at the temperatures given. The activation parameters E_a and A were obtained from the Arrhenius plot. ΔS^* was determined from $\Delta S^*=8.314(\ln(A/T)-24.76)$.

3.3.1. HPLC determination of rate constants. The same setup as for volumetry was used also for thermolysis of a mixture of (*E*)- and (*Z*)-azide **5** (43.4 mg and 42.2 mg) in DMF (5 mL) with β-naphthol as an internal standard. Aliquots (20 μL) were diluted with 30% MeOH (5 mL) and analyzed by HPLC (3×150 mm C 18 column, 30% MeOH, UV detection at 280 nm).

3.4. X-Ray crystallographic analysis

Suitable crystals were obtained by recrystallization from EtOH. Experimental data were collected with a KUMA K4 kappa-axis four-circle diffractometer with graphite-monochromatized radiation. The data were corrected for L_p-factor but no absorption (μ=0.118 mm^{-1}) correction was applied. The structure was solved and refined using the SHELX97[21] program system and the drawing was prepared by ORTEP.[22] Hydrogen atoms were inserted from geometry consideration using HFIX option of the program, except the H atom attached to N1, which was introduced from its localization in the difference electron density map. All hydrogens were refined on an assumption of a 'ride-on' model except atom H which positional parameters were refined freely. The structure is built from isolated molecules arranged into layers parallel to (011) planes. The layers are bound by hydrogen bonds among H's and O2′s (O2···H 2.420 Å). All interatomic distances and angles are normal. Crystal data and other details concerning the data collection are summarized in Table 2.

Crystallographic data (excluding structure factors) for the structure **6** in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 174351. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1 EZ, UK (fax: +44-1223-336033 or e-mail: deposit@ccdc.cam.ac.uk).

Acknowledgements

We are grateful to Professor T. Głowiak of University of Wroclaw, Poland, for help with X-ray structure analysis.

References

1. Smolinsky, G. *J. Org. Chem.* **1962**, *27*, 3557–3559.
2. Padwa, A.; Woolhouse, A. D. *Comprehensive Heterocyclic Chemistry*; Katritzky, A., Rees, C. W., Eds.; Pergamon: New York, 1987; Vol. 7, p. 47 Part 5, Lwowski, W., Ed.
3. Hassner, A.; Fowler, F. W. *J. Org. Chem.* **1968**, *33*, 2686–2691.
4. Smolinsky, G.; Pryde, C. A. *J. Org. Chem.* **1968**, *33*, 2411–2416.
5. For reviews covering decomposition of vinyl azides see (a) L'abbé, G. *Angew. Chem.* **1975**, *87*, 831–838 *Angew. Chem., Int. Ed. Engl.* **1975**, *14*, 775. (b) Hassner, A. In *Azides and Nitrenes*, Scriven, E. F. V., Ed.; Academic: New York, 1984; p. 35. (c) Soderberg, B. C. G. *Curr. Org. Chem.* **2000**, *4*, 727–764.
6. Boyer, J. A.; Krueger, W. E.; Modler, R. *Tetrahedron Lett.* **1968**, *57*, 5979–5982.
7. Bauer, W.; Hafner, K. *Angew. Chem.* **1969**, *81*, 787–788.
8. (a) Meth-Cohn, O.; Williams, N. J. R.; MacKinnon, A.; Howard, J. A. K. *Tetrahedron* **1998**, *54*, 9837–9848. (b) Woerner, F. P.; Reimlinger, H.; Arnold, D. R. *Angew. Chem.* **1968**, *80*, 119–120 *Angew. Chem., Int. Ed. Engl.* **1968**, *7*, 130.
9. Mazal, C.; Jurka, Z.; Jonas, J. *Collect. Czech. Chem. Commun.* **1984**, *49*, 2509–2519.
10. For 1,3-dipolar reactivity of organic azides see: Lwowski, W. *1,3-Dipolar Cycloaddition Chemistry*; Padwa, A., Ed.; Wiley: New York, 1984; Vol. 1, p. 559.
11. (a) Friedrich, K.; Thieme, H. K. *Chem. Ber.* **1970**, *130*, 1982–1989. (b) Nesmeyanov, A. N.; Rybinskaya, M. I.; Kelkhsaeva,

T. G. *Izv. Acad. Nauk SSSR, Ser. Khim.* **1969**, 866–870 *Bull. Acad. Sci. USSR Div. Chem. Sci.* (Engl. Transl.) **1969**, 787. (c) L'Abbé, G.; Van Stappen, P. *Bull. Soc. Chim. Belg.* **1981**, *90*, 1073–1077. (d) Sauers, R. R.; Van Arnum, S. D. *Tetrahedron Lett.* **1987**, *28*, 5797–5800.

12. Mazal, C.; Jonas, J. *Collect. Czech. Chem. Commun.* **1993**, *58*, 1607–1623.
13. Gazit, A.; Rappoport, Z. *J. Org. Chem.* **1988**, *53*, 679–681.
14. (a) Woerner, F. P.; Reimlinger, H.; Merényi, R. *Chem. Ber.* **1971**, *104*, 2786–2792. (b) Schaumann, E.; Brabley, S. *Liebigs Ann. Chem.* **1981**, 290–305.
15. For an excellent example of such azirine–nitrene equilibrium see: Isomura, K.; Ayabe, G.-I.; Hatano, S.; Taniguchi, H. *J. Chem. Soc., Chem. Commun.* **1980**, 1252–1253.
16. It is also possible that the nitrene **11** is an intermediate of **8**. Our suggestion of **8** to be the first formed intermediate is based only on the relatively low temperature of decomposition as well as the rather low activation energy E_a. This corresponds to an anchimeric assistance of double bond (as well as the carbonyl group in the case of (*Z*)-**5**) in nitrogen expulsion. cf. (a) Hassner, A.; Wiegand, N. H.; Gottlieb, H. E. *J. Org. Chem.* **1986**, *51*, 3176–3180. (b) L'abbé, G.; Mathys, G. *J. Org. Chem.* **1974**, *39*, 1778–1780.
17. (a) Hassner, A.; Anderson, D. J. *J. Org. Chem.* **1973**, *38*, 2565. (b) Anderson, D. J.; Hassner, A. *Synthesis* **1975**, 483–495. (c) Tamura, Y.; Yoshimura, Y.; Nishamura, T.; Kato, S. *Tetrahedron Lett.* **1973**, 351–354. (d) Isomura, K.; Kobayashi, S.; Taniguchi, H. *Tetrahedron Lett.* **1968**, 3499–3502.
18. (a) Sato, S.; Kato, H. *Bull. Chem. Soc. Jpn* **1967**, *40*, 2938–2942. See also (b) Hassner, A.; Burke, S. S. *J. Am. Chem. Soc.* **1975**, *97*, 4692–4700.
19. (a) Feofilaktov, V. V.; Onishchenko, A. S. *J. Gen. Chem. USSR* **1938**, *9*, 304. (b) Fristad, W. E.; Peterson, J. R.; Ernst, A. B. *J. Org. Chem.* **1985**, *50*, 3143–3148.
20. Morgenlie, S. *Acta Chem. Scand.* **1970**, *24*, 365–366.
21. Sheldrick, G. M.; *SHELX97*, Program for Structure Solution and Refinement; University of Göttingen: Göttingen, 1997.
22. Johnson, C. K. *ORTEP*; Report ORNL-3794; Oak Ridge National Laboratory: Oak Ridge, TN, 1965.