Grant 04-00117 from the U.S.-Israel Binational Science Foundation, Jerusalem, Israel.

Registry No. **1a**, 947-91-1; **1b**, 112-31-2; **1d**, 123-38-6; **1e**, 78-84-2; **3a**, 111238-39-2; **3b**, 111238-40-5; **3c**, 111238-41-6; **3d**, 111238-42-7; **3e**, 111238-43-8; **3f**, 91633-37-3; **3i**, 111238-45-0; **4a**, 51936-06-2; **4b**, 7779-41-1; **5b**, 111238-44-9; **7c**, 933-40-4; **8**, 54-95-5; **9**, 5129-73-7; **10a**, 96-22-0; **10b**, 563-80-4; **10c**, 108-94-1; **10d**, 98-86-2; **11a**, 87272-11-5; **11b**, 111238-47-2; **11c**, 111238-46-1; **11d**, 65501-11-3; **12d**, 20258-22-4; **12e**, 41796-01-4; **12f**, 111238-49-4; **13f**, 1125-70-8; **14d**, 107-12-0; **14e**, 78-82-0; **14f**, 1823-91-2; **15a**, 24433-77-0; **15b**, 111238-50-7; **15c**, 2525-16-8; **15d**, 1775-61-7; **16b**, 111238-51-8; **16d**, 24433-81-6; HN_3, 7782-79-8; $Ph_2CHCH(OEt)_2$, 67820-48-8; $Me(CH_2)_8CH(OEt)_2$, 34764-02-8; Pr_2CO, 123-19-3; $Et_2C(OMe)_2$, 25636-49-1; *i*-PrC(Me)$(OMe)_2$, 59554-08-4; PhC(OMe)$(CH_2N_3)N_3$, 111238-48-3.

Intramolecular Azide-Olefin Cycloadditions. A Novel Synthesis of 2,5-Dihydrooxazoles[1]

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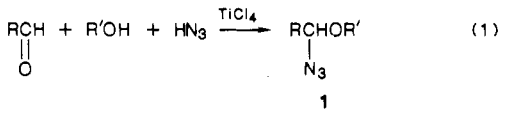
A facile synthetic route from aldehydes to allyl α-azidoalkyl ether **2** is described. Thermolysis of **2** proceeds by intramolecular azide-olefin cycloaddition via triazolines and provides a novel synthesis of 2,5-dihydrooxazoles **6**. The use of silica gel in the chemoselective conversion of the intermediate triazolines to bicyclic aziridines **7** is described.

Introduction

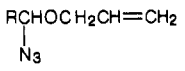
In the accompanying paper,[2] we have shown that α-azido ethers **1** can be prepared from an aldehyde, an alcohol, and hydrazoic acid using titanium tetrachloride as the catalyst (eq 1).



(1)

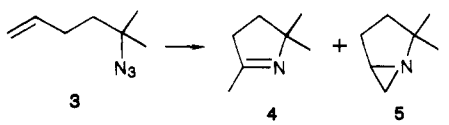
1

We reasoned that by employing an unsaturated alcohol such as allyl alcohol as the R'OH component, it should be possible to prepare allyl α-azidoalkyl ethers of type **2**, if the olefinic double bond can be made to survive the acid-catalyzed reaction conditions.



2

Such unsaturated azido ethers are molecules that set the stage for an intramolecular 1,3-dipolar cycloaddition.[3] In fact, Logothetis[4] had studied the thermal intramolecular azide-olefin cycloaddition (IAOC) of 5-azido-5-methyl-1-hexene (**3**) and observed the formation of a mixture of imine **4** and aziridine **5**. Recently we showed that IAOC



3 **4** **5**

reactions of azido vinyl β-lactams lead primarily to fused triazolines.[5] Thermolysis of azido ethers in the absence of a double bond produces imidates.[2] Hence, allyl α-azidoalkyl ethers **2** on cyclization should result either in fused triazolines, in imidates, in aziridines, or in the title compounds **6**.

While Δ^2-oxazolines are well-known, their Δ^3-isomers, the 2,5-dihydrooxazoles **6**, are a rare class of compounds, and there are only few methods known for their preparation.[6] A synthetic approach to this class of molecules is also desirable since various substituted 2,5-dihydrooxazoles have been used as artificial flavors.[7]

Results and Discussion

We herewith report the synthesis of allyl α-azidoalkyl ethers **2** and their utility in a new approach to 2,5-dihydrooxazoles. The reaction of an aldehyde with an allyl alcohol and HN_3 in a ratio of 1:3:9 was carried out in the presence of $TiCl_4$, as a catalyst and produced azido ethers **2** in yields of 70–90%. The ratio of reagents is critical[2] to ensure a high yield of azido ether and prevent formation of acetal and diazide side products. These reaction conditions do not affect the olefinic double bond.

The allyl azido ethers **2** were somewhat unstable compounds, but chromatography on basic alumina provided analytically pure samples in many cases. Yields of 70–88% were achieved before chromatography, and the products were pure enough for the cycloaddition step. Intramolecular cycloaddition was studied in chloroform, benzene, and toluene at reflux temperature. Benzene was found to be the solvent of choice, because it gave cleaner products.

Thermolysis of azidoalkenes **2a–g** in benzene for 6–20 h led to 2,5-dihydrooxazoles **6** as the major products in 66–90% yield. In some cases triazolines **8** were observed (by NMR) as byproducts.

Structure proof for oxazolines **6** was provided by ^1H and ^{13}C NMR, mass spectra, and elemental analysis. For instance, **6a** showed the imino methyl signal at δ 2.08 with

(1) Cycloadditions. 34. For paper 33, see: Amarasekara, A. S.; Hassner, A. *Tetrahedron Lett.* **1987**, *28*, 3151.
(2) Hassner, A.; Fibiger, R.; Amarasekara, A. S. *J. Org. Chem.*, preceding paper in this issue.
(3) Padwa, A. *1,3 Dipolar Cycloadditions*; Padwa, A., Ed.; Wiley: New York, 1984; Vol. II, Chapter 12, p 327.
(4) Logothetis, A. L. *J. Am. Chem. Soc.* **1967**, *87*, 749.
(5) Hassner, A.; Murthy, K. *Tetrahedron Lett.* **1987**, *28*, 97.
(6) (a) Nair, V. *Small Ring Heterocycles*; Hassner, A., Ed.; Wiley: New York, 1983; Vol. 42, Part 1, (b) Kitamura, T.; Kobayashi, S.; Taniguchi, H. *Heterocycles* **1985**, *23*, 193.
(7) (a) Maga, J. A. *J. Agric. Food Chem.* **1978**, *26*, 1049. (b) International Flavors and Fragrances, Inc. U.S. Patent 3 627 540 (C1. 99-140R; A231), 1971; *Chem. Abstr.* **1972**, *76*, 57964r.

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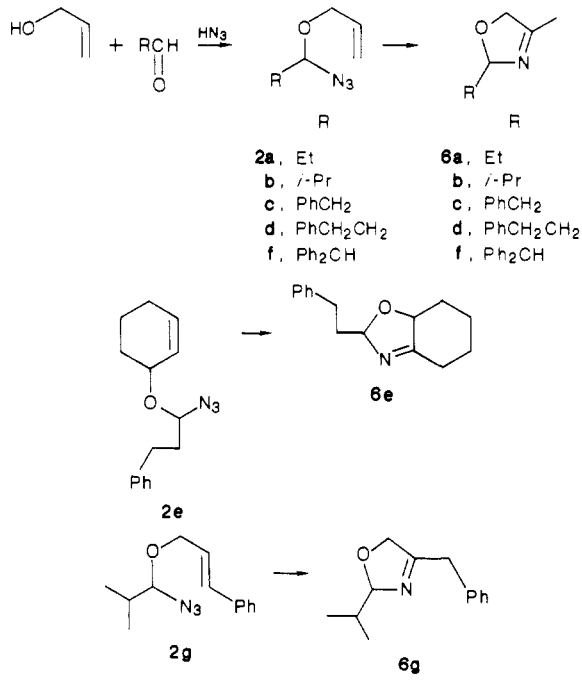
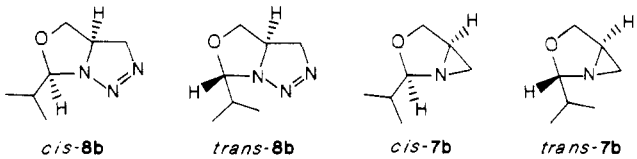


long-range coupling (J = 2 Hz) to one of the protons at C-5 and correlated with the ^{13}C methyl absortion at 15.86 ppm. The C-2 proton appeared as a multiplet at 5.45 ppm. Interestingly, the spectrum of **6** showed a large long-range coupling (J = 4.5–6 Hz) between the C-5 methylene and the C-2 methine protons. This homoallylic coupling of the HCC=NCH system is reminiscent of homoallylic 1,4-coupling in cyclohexadienes.[8]

The imino carbon in **6a** appeared at 169 ppm. The C-2 absorption, identified as a methine by off-resonance decoupling was at 105.4 ppm; all consistent with a 3-oxazoline rather than a 2-oxazoline structure.

In order to determine whether oxazolines **6** are formed via an independent nitrene pathway or via triazolines **8**, the thermolysis of **2b** was followed by ^1H NMR in hexadeuteriobenzene at 70 °C. First formation of both oxazoline **6b** and triazoline **8b** was observed at partial conversion. After 3 h of heating only oxazoline **6b** was present. The same behavior was observed for **2a**, **2c**, and **2e**. On the other hand if a mixture of **6b** and **8b** after 50% conversion was chromatographed on silica gel only oxazoline **6b** and the fused aziridine **7b** (cis and trans mixture) were isolated in addition to starting material. The aziridine **7b** was stable in refluxing benzene for 4 h and was not converted to **6b**.



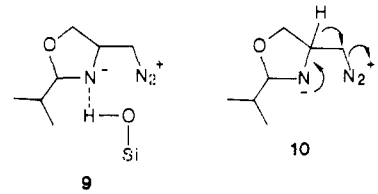
We succeeded in converting **2b** to triazoline **8b** as a 2.9:1 mixture of trans and cis isomers, without appreciable presence of oxazoline **6b** or aziridine **7b**, by heating at 50 °C in $CDCl_3$ for 1 h and following the reaction by ^1H NMR (up to 80% conversion). Isolation of pure **8b** was not possible since it was unstable to chromatography.

The structure of triazolines **8b** follows from NMR data and from their conversion to aziridine **7b**, as a 2.9:1 mixture of diastereomers on treatment with silica gel. We assign the cis structure to the minor isomer of **8b** on the basis of an unusually low-field absorption of its isopropyl methine at 2.49 ppm, while the corresponding proton in the trans isomer appears at 1.85 ppm. A possible explanation is that this proton lies in the deshielding cone of the π-electrons of the N=N. Similarly the isopropyl methine carbon is shifted in the cis isomer to 29.67 vs 32.47 ppm in the trans isomer. The C-5 protons (CH_2O) are found as doublets of doublets near 4.2 ppm in *trans*-**8b** and near 4.5 ppm in *cis*-**8b**. The C-6 protons (CH_2N) are also clearly distinguishable doublets of doublets (3.11 and 3.90 ppm in the trans isomer and 3.4 and 3.75 ppm in the cis isomer).

^1H and ^{13}C NMR permitted clear differentiation between the isomeric oxazoline **6b** and the cis and trans aziridines **7b**. The aziridine methylene protons have characteristic absorption at 1.76 (d,d) and 1.37 (d) ppm in *trans*-**7b** and at 1.48 (d,d) and 1.52 (d) ppm in *cis*-**7b**. In each case both hydrogens exhibit a small coupling (3.5 Hz) to the vicinal methine proton, while one of these hydrogens shows long-range coupling to one of the C-5 protons (J = 1.2–1.5 Hz); no geminal coupling was observed.[9] The absorption of the C-2 proton at 4.12 and 3.99 ppm for *trans*- and *cis*-**7b**, respectively reflects the changed hybridization on nitrogen in **7** vs **6**. Similarly the ring methylene protons were shifted downfield in the oxazoline (4.47 ppm) compared to the aziridine (3.7–4.0 ppm). In the ^{13}C spectrum of **7b** no signal below 102 ppm was observed, indicating the absence of an sp^2 carbon. The aziridine methine and methylene carbons are found in the 33 and 30 ppm region, typical of such rings.[9a]

The overall pathway for the conversion of the unsaturated azido ether **2** to 2,5-dihydrooxazoles **6** involves first formation of the dipolar cycloaddition product **8**, which thermolyzes to oxazoline **6** or is converted to silica gel to oxazolinoaziridine **7**.

The utilization of silica gel in the decomposition of triazoline **8** leading exclusively to formation aziridine is intriguing. While thermolysis or acid-catalyzed decomposition of triazolines to a mixture of imine and aziridine is well documented,[10] this is the first example[11] in which clear differentiation of products is observed depending on whether thermolysis or exposure to silica gel is used. The role of the silica in this chemoselective reaction is still obscure, but it is likely that acidic surface sites catalyze the triazoline decomposition via an intermediate resembling **9**, which prefers to close to an aziridine (**7**). On the other hand, thermolysis of **8** may proceed via **10** (or the corresponding diradical) in which hydrogen migration is favored over ring closure.



Experimental Section

The NMR spectra were recorded on a Bruker AM 300 instrument; ^1H at 300.1 MHz and ^{13}C at 75.5 MHz in $CDCl_3$ with

(8) Gunther, H. *NMR Spectroscopy*; Wiley: New York, 1980; p 118.

(9) A lack of geminal coupling was also noted for other bicyclic aziridines: (a) Berges, D. A.; Schmidt, S. J. *J. Org. Chem.* **1984**, *49*, 4555. (b) Horning, D. E.; Muchowski, J. M. *Can. J. Chem.* **1974**, *52*, 1321. (c) Brois, S. J.; Beardsky, G. P. *Tetrahedron Lett.* **1966**, 5113.

(10) Scheiner, P. *Selective Organic Transformations*; Thyagarajan, B. S., Ed.; Wiley-Interscience: New York, 1970; pp 327–362.

(11) The first case of utilization of SiO_2 in the selective decomposition of triazolines is apparently our report in ref 5.

TMS as an internal standard. Chemical shifts are reported in δ downfield from TMS, and coupling constants in proton spectra are given in hertz (Hz). The following notations are used for multiplicity; s, singlet; d, doublet, t, triplet; sept, septet; m, multiplet. Mass spectra were recorded in a Finnigan 4021 instrument and reported as M (relative abundance). Elemental analyses were performed at Hebrew University, Jerusalem. Hydrazoic acid in methylene chloride solution was prepared according to the previously described method[12] and standardized by titrating against 0.10 M sodium hydroxide with phenolphthalein as the indicator. All the aldehydes and allyl alcohols were distilled before use. Benzene used for the thermolysis was distilled over sodium.

Preparation of Allyl Azidoalkyl Ethers 2 (General Procedure) Aldehyde (2.0 mmol) was dissolved in 12.0 mL of 1.51 M hydrazoic acid in methylene chloride (18.1 mmol) and was added to allyl alcohol (6.0 mmol) in 3 mL of dry methylene chloride followed by titanium tetrachloride (20 mg, 0.1 mmol). The mixture was stirred at room temperature for 4 h, passed through a 2.5 × 4.5 cm column of basic alumina, and concentrated under reduced pressure to give the crude product. Usually this material was pure enough for the next reaction, otherwise it was chromatographed on basic alumina, eluting with ethyl acetate/hexane, to obtain analytical samples.

Thermolysis of Allyl Azidoalkyl Ethers 2 (General Procedure). Allyl azido ether **2** (1.0 mmol) was dissolved in 10 mL of dry benzene and refluxed. The reaction was monitored on TLC (alumina, ethyl acetate/hexane) and stopped after the two products first formed were converted to a single product, usually 6–20 h. The solvent was evaporated under reduced pressure and the residue chromatographed (silica, ethyl acetate/hexane) to give the 2,5-dihydrooxazoles **6** as colorless oils.

1-Azidopropyl allyl ether (2a) was prepared from propanal and allyl alcohol as a colorless liquid (85%): ^{1}H NMR 0.99 (t, J = 7.5 Hz, CH_3), 1.78 (m, CH_2), 4.16 (m, N_3CHO), 4.06 and 4.28 (2 m, CH_2O), 5.25 (m, CH_2=), 5.98 (m, CH=); ^{13}C NMR 9.12 (CH_3), 27.87 (CH_2), 69.79 (CH_2O), 93.03 (N_3CHO), 117.92 (CH_2=), 133.58 (CH=); MS (EI), m/e (relative intensity) 127 (M – N, 5), 114 (M – N_2, 24), 100 (M – N_3, 100).

1-Azido-2-methylpropyl allyl ether (2b) was prepared from isobutyraldehyde and allyl alcohol as a colorless liquid (88%): ^{1}H NMR 1.00 (d, J = 7 Hz, 2 CH_3), 1.96 (d, sept, J = 6, 7 Hz, C*H*(CH_3)$_2$), 4.18, (d, J = 6 Hz, N_3CHO), 4.06 and 4.29 (2 m, CH_2O), 5.28 (m, CH_2=), 5.91 (m, CH=); ^{13}C NMR 17.73 (2-CH_3), 33.62 (*C*H(CH_3)$_2$), 70.21 (CH_2O), 96.58 (N_3CHO), 117.77 (CH_2=), 133.57 (CH=); MS (EI), m/e (relative intensity) 152 (M, 2), 142 (0.5, 124 (M – N_2, 58), 100 (6), 84 (100).

Anal. Calcd for $C_7H_{13}ON_3$: C, 54.17; H, 8.44. Found: C, 54.40; H, 8.32.

1-Azido-2-phenylethyl allyl ether (2c) was prepared from phenyl acetaldehyde and allyl alcohol as a colorless liquid (78%): ^{1}H NMR 2.98 (d, d, J = 6, 14 Hz, CH_2Ph, 1 H), 3.08 (d, d, J = 6, 14 Hz, CH_2Ph, 1 H), 4.01 and 4.23 (2 m, CH_2O), 4.57 (t, J = 6 Hz, N_3CHO), 5.19 (m, CH_2=), 5.82 (m, CH=), 7.20– 7.30 (m, Ph, 5 H); ^{13}C NMR 41.17 (Ph*C*H_2), 69.83 (CH_2O), 92.11 (N_3CHO), 117.77 (CH_2=), 126.83 (Ph), 128.34 (Ph), 129.46 (Ph), 133.25 (CH=); MS (EI), m/e (relative intensity) 176 (M – N_2, 1), 161 (M – N_3, 10), 143 (13), 131 (4), 91 (100).

1-Azido-3-phenylpropyl allyl ether (2d) was prepared from dihydrocinnamaldehyde and allyl alcohol as a colorless liquid (80%): ^{1}H NMR 2.05 (m, C*H*$_2$CHN$_3$), 2.72 (m, CH_2Ph), 4.02 and 4.23 (2 m, CH_2O), 4.37 (t, J = 6 Hz, N_3CHO), 5.18 (m, CH_2=), 5.88 (m, CH=); MS (EI), m/e (relative intensity) 189 (M – N_2, 5), 175 (M – N_3, 5), 158 (4), 144 (2), 131 (13), 117 (22), 84 (100).

1-Azido-3-phenylpropyl 2-cyclohexenyl ether (2e) was prepared from dihydrocinnamaldehyde and 2-cyclohexenol as a coloroless liquid (72%): ^{1}H NMR 1.55–2.20 (m, cyclohexenyl + C*H*$_2$CHN$_3$, 8 H), 2.70 (m, CH_2Ph), 4.15 (m, OC*H*CH=), 4.43 (m, N_3CHO), 5.68–5.96 (m, CH=CH), 7.10–7.30 (m, Ph, 5 H); MS (EI), m/e (relative intensity) 229 (M – N_2, 4), 215 (M – N_3, 1), 138 (5), 124 (18), 97 (40), 81 (100).

Anal. Calcd for $C_{15}H_{19}ON_3$; C, 70.00; H, 7.44. Found: C, 70.84; H, 7.56.

(12) Hassner, A.; Fibiger, R.; Andisik, D. *J. Org. Chem.*, **1984**, *49*, 4237.

1-Azido-2,2-diphenylethyl allyl ether (2f) was prepared from diphenylacetaldehyde and allyl alcohol as a colorless liquid (70%): ^{1}H NMR 4.05 and 4.25 (2 m, CH_2O), 4.27 (d, J = 8 Hz, N_3CHO), 5.06 (d, J = 8 Hz, $CH(Ph)_2$, 5.17 (m, CH_2=), 5.74 (m, CH=), 7.20–7.32 (m, Ph); MS (EI), m/e (relative intensity) 251 (M – N_2, 6), 237 (M – N_3, 14), 222 (45), 196 (100).

1-Azido-2-methylpropyl *trans*-cinnamyl ether (2g) was prepared from isobutyraldehyde and *trans*-cinnamyl alcohol as a colorless liquid (75%): ^{1}H NMR 0.99 and 1.01 (2 d, J = 7 Hz, 2 CH_3), 1.99 (d, q, J = 6, 7 Hz), 4.22 (d, d, d, J = 13, 6, 2 Hz), 4.23 (d, J = 6 Hz), 4.44 (d, d, d, J = 13, 6, 2), 6.26 (d, d, d, J = 16, 6, 6 Hz), 6.63 (d, J = 16 Hz), 7.23–7.42 (m, Ph, 5 H); MS (EI), m/e (relative intensity (203 (M – N_2, 6), 189 (M – N_3, 10), 126 (46), 70 (100).

2-Ethyl-4-methyl-2,5-dihydrooxazole (6a) was prepared from 1-azido-1-propyl allyl ether (**2a**) as a colorless oil (90%): ^{1}H NMR 1.04 (t, J = 7.5 Hz, CH_3CH_2), 1.43 (d, q, J = 6, 7.5 Hz, CH_2), 2.08 (t, J = 2 Hz, CH_3), 4.40 (d, d, J = 4.5, 14.5 Hz, C-5, CH_2), 5.45 (m, C_2H); ^{13}C NMR 14.82 (*C*H_3CH_2), 15.86 (C-4, CH_3), 24.64 (CH_3CH_2), 75.46 (C-5), 105.41 (C-2), 169.02 (C-4); MS (EI), m/e (relative intensity) 114 (M + 1, 4), 112 (2), 86 (28), 84 (100), 82 (6).

2-Isopropyl-4-methyl-2,5-dihydrooxazole (6b) was prepared from 1-azido-2-methylpropyl allyl ether (**2b**) as a colorless liquid (82%): ^{1}H NMR 0.94 (d, J = 6 Hz, CH_3), 0.96 (d, J = 6 Hz, CH_3), 1.92 (d, sept, J = 4.5, 7 Hz, (CH_3)$_2$C*H*), 2.08 (d, t, J = 2, 0.5 Hz, CH_3), 4.47 (d, d, q, J = 14.5, 4.5, 0.5 Hz, C-5 CH_2), 5.45 (d, t, q, J = 6, 4.5, 2 Hz); ^{13}C NMR 16.68 (CH_3), 15.78 (C-4, CH_3), 17.31 (CH_3), 33.52 ((CH_3)$_2$*C*), 76.56 (C-5), 111.02 (C-2), 168.91 (C-4); MS (EI), m/e (relative intensity) 128 (M + 1, 6), 126 (1), 88 (7), 86 (45), 84 (100), 83 (10). Anal. Calcd for $C_7H_{13}ON$: C, 66.10% H, 10.30. Found: C, 66.08; H, 10.56.

2-Benzyl-4-methyl-2,5-dihydrooxazole (6c) was prepared from 1-azido-2-phenylethyl allyl ether (**2c**) as a colorless liquid (80%): ^{1}H NMR 196 (d, J = 2 Hz, CH_3), 2.92 (d, d, J = 6, 16 Hz, CH_2, 1 H), 3.08 (d, d, J = 6, 16 Hz, CH_2, 1 H), 4.22 (d, d, d, J = 0.5, 5.14 Hz, C-5, 1 H), 4.34 (d, d, d, J = 0.5, 5.14 Hz, C-5, 1 H), 5.89 (m, C-2, 1 H), 7.16–7.30 (m, Ph, 5 H); ^{13}C NMR 15.52 (CH_3), 41.98 (CH_2), 76.27 (C-5), 106.53 (C-2), 126.18 (Ph), 127.88 (Ph), 129.78 (Ph), 136.41 (Ph), 169.26 (C-4); MS (EI), m/e (relative intensity), 176 (M + 1, 6), 130 (3), 98 (13), 92 (22), 91 (21), 84 (100), 57 (24), 49 (67). Anal. Calcd for $C_{11}H_{13}ON$: C, 75.40; H, 7.48. Found: C, 7.58; H, 7.31.

2-(2-Phenylethyl)-4-methyl-2,5-dihydrooxazole (6d) was prepared from 1-azido-3-phenylpropyl allyl ether (**2d**) as a colorless liquid (84%): ^{1}H NMR 2.03 (m, PhCH_2C*H*$_2$, 2 H), 2.07 (d, J = 2 Hz, CH_3), 2.73 (t, J = 8 Hz, PhC*H*$_2$, 2 H), 4.43 (d, d, d, J = 0.5, 5, 18 Hz, C-5, 1 H), 4.53 (d, d, d, J = 0.5, 5, 18 Hz, C-5, 1 H), 5.65 (m, C-2, 1 H), 7.15–7.30 (m, Ph, 5 H); ^{13}C NMR 15.81 (CH_3), 30.48 (PhCH_2C*H*$_2$), 37.37 (Ph*C*H$_2$), 76.24 (C-5), 106.0 (C-2), 125.73 (Ph), 128.34 (Ph), 131.67 (Ph), 168.92 (C-4); MS (EI), m/e (relative intensity) 189 (M, 5), 158 (3), 131 (7), 117 (17), 104 (32), 99 (20), 91 (57), 84 (97), 68 (25), 57 (100).

2-(2-Phenylethyl)-1-oxa-3-aza-3,4-bicyclo[4.3.0]nonene (6e) was prepared from 1-azido-3-phenylpropyl 2-cyclohexenyl ether (**2e**) as a thick colorless oil (66%), in a 1:1 mixture of diastereomers: ^{1}H NMR 1.30–2.40 (m, 10 H, C-5,6,7,8 and ethyl C-1, 10 H), 2.75 (m, ethyl C-2, 2 H), 4.49 (m, C-9, 1 H) 5.50–5.80 (m, C-2, 1 H), 7.10–7.30 (m, Ph, 5 H); ^{13}C NMR 26.39, 26.65, 29.99, 30.12, 30.56, 30.61, 34.78, 35.36, 37.65, 38.08, 83.27, 83.55, 104.12, and 104.87 (C-2), 125.69, 128.26, 128.32, 128.37, 128.51, 141.72, 141.79, 173.87, and 173.98 (C-4); MS (EI), m/e (relative intensity) 229 (M, 13), 138 (14), 117 (14), 97 (100), 91 (36), 79 (20), 69 (45).

2-(Diphenylmethyl)-4-methyl-2,5-dihydrooxazole (6f) was prepared from 1-azido-2,2-diphenylethyl allyl ether (**2f**) as a thick pale yellow oil (76%): ^{1}H NMR 1.78 (d, J = 2 Hz, CH_3), 3.82 (d, d, d, J = 0.5, 6, 14 Hz, C-5, 1 H), 4.21 (d, d, d, J = 0.5, 3, 14 Hz, C-5, 1 H), 4.36 (d, J = 4 Hz, Ph_2CH), 6.36 (m, C-2, 1 H), 7.11–7.38 (m, 2 Ph, 10 H); ^{13}C NMR, 15.22 (CH_3), 56.06 (Ph_2C), 76.43 (C-5), 107.81 (C-2), 126.16 (Ph), 127.61 (Ph), 129.03 (Ph), 139.77 (Ph), 169.61 (C-4); MS (EI), m/e (relative intensity) 251 (M, 18), 174 (22), 98 (24), 97 (22), 57 (100).

2-Isopropyl-4-benzyl-2,5-dihydrooxazole (6g) was prepared from 1-azido-2-methylpropyl cinnamyl ether (**2g**) as a thick oil (71%): ^{1}H NMR 0.92 (d, J = 7 Hz, CH_3), 0.95 (d, J = 7 Hz, CH_3), 1.97 (d, q, J = 6, 7 Hz, (CH_3)$_2$C*H*), 3.73 (AB q, J = 14 Hz, C*H*$_2$Ph),

4.37 (AB x, J = 5, 14 Hz, C-5, 2 H), 5.51 (m, C-2, 1 H), 7.20–7.33 (m, Ph, 5 H); ^{13}C NMR 16.48 (CH_3), 17.20 (CH_3), 33.42 ((CH_3)$_2$CH), 37.13 (CH_2Ph), 74.80 (C-5), 110.66 (C-2), 126.87 (Ph), 128.64 (Ph), 135.26 (Ph), 170.88 (C-4); MS (EI), m/e (relative intensity) 203 (M, 8), 112 (M - PhCH$_2$, 48), 97 (20), 82 (4), 76 (2), 57 (100).

Formation of Triazoline Intermediates. Azido allyl ether **2b** (40 mg, 0.26 mmol) in 0.5 mL of $CDCl_3$ in an NMR tube was heated at 50 °C, and the reaction was monitored by ^{1}H NMR. After 1.0 h the heating was stopped, and the mixture was analyzed by ^{1}H and ^{13}C NMR; 80% of the starting material had cyclized to the triazolines *trans*- and *cis*-**8b**, while only traces of 2,5-dihydrooxazole **6b** had formed.

***trans*-8b (major isomer)**: ^{1}H NMR 1.05 and 1.06 (2 d, J = 6.7 Hz, 2 CH_3), 1.85 (d, sept, J = 7.2, 6.7 Hz, C-7, 1 H), 3.11 (d, d, J = 7.4, 7.4 Hz, C-6, 1 H), 3.76 (m, C-4, 1 H), 3.90 (d,d, J = 7.2, 7.4 Hz, C-6, 1 H), 4.17 (d, d, J = 8.8, 9.0 Hz, C-5, 1 H), 4.25 (d, d, J = 6.7, 8.8 Hz, C-5, 1 H), 5.33 (d, J = 7.2 Hz, C-2, 1 H); ^{13}C NMR 17.70 (CH_3), 17.87 (CH_3) 32.47 (C-7), 55.10 (C-4), 68.69 (C-6), 71.29 (C-5), 98.61 (C-2).

***cis*-8b (minor isomer)**: ^{1}H NMR 1.11 and 1.34 (2 d, J = 6.5 Hz, 2 CH_3), 2.49 (d, sept, J = 2.2, 6.5 Hz, C-7, 1 H), 3.41 (d, d, J = 4.0, 7.8 Hz, C-6, 1 H), 3.75 (m, C-6, 1 H), 3.77 (m, C-4, 1 H, 4.46 (d, J = 2.2 Hz, C-2, 1 H), 4.47 (d, d, J = 2.5, 5.5 Hz, C-5, 1 H), 4.52 (d, d, J = 2.3, 5.5 Hz, C-5, 1 H); ^{13}C NMR 18.91 (CH_3), 19.75 (CH_3), 29.67 (C-7), 54.75 (C-4), 69.80 (C-6), 74.48 (C-5), 99.97 (C-2).

Triazoline Decomposition on Silica Gel. The triazoline mixture in $CDCl_3$ from the above experiment was transfered to a small flask, 10 mg of 230–400 mesh silica gel (E. Merck) was added and the mixture stirred at room temperature for 2 h. Evolution of nitrogen was observed. The contents were filtered into an NMR tube, washing with 0.2-mL of $CDCl_3$. The NMR showed the quantitative decomposition of triazolines to aziridines *trans*- and *cis*-**7b**.

***trans*-7b (major isomer)**: ^{1}H NMR 0.93 and 1.03 (2 d, J = 7.2 Hz, CH_3), 1.37 (d, J = 3.5 Hz, C-6, 1 H), 1.67 (d, sept. J = 7.5, 7.2 Hz, C-7, 1 H), 1.76 (d, d, J = 3.5, 1.2 Hz, C-6, 1 H), 2.60 (m, C-4, 1 H), 3.76 (d, d, d, J = 1.2, 3.2, 8.2 Hz, C-5, 1 H), 3.98 (d, J = 8.2 Hz, C-5, 1 H), 4.12 (d, J = 7.5 Hz, C-2, 1 H); ^{13}C NMR 18.11 (CH_3), 18.49 (CH_3), 28.31 (C-6), 32.74 (C-4), 38.36 (C-7), 65.00 (C-5), 102.11 (C-2).

***cis*-7b (minor isomer)**: ^{1}H NMR 1.01 and 1.13 (2 d, J = 7.2 Hz, 2 CH_3), 1.48 (d, d, J = 3.5, 1.5 Hz, C-6, 1 H), 1.52 (d, J = 3.5 Hz, C-6, 1 H), 1.65 (d, sept, J = 8.0, 7.2 Hz, C-7, 1 H), 2.54 (m, C-4, 1 H), 3.70 (d, d, d, J = 1.5, 3.0, 8.6 Hz, C-5, 1 H), 3.99 (d, J = 8.0 Hz, C-2, 1 H), 4.02 (d, J = 8.6 Hz, 1 H); ^{13}C NMR 17.80 (CH_3), 19.39 (CH_3), 30.50 (C-6), 33.64 (C-4), 36.78 (C-7), 66.31 (C-5), 100.30 (C-2).

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Registry No. **2a**, 111209-39-3; **2b**, 111209-40-6; **2c**, 111209-41-7; **2d**, 111209-42-8; **2e**, 111209-43-9; **2f**, 111209-44-0; **2g**, 111209-45-1; **6a**, 111209-46-2; **6b**, 111209-47-3; **6c**, 111209-48-4; **6d**, 111209-49-5; **6e** (isomer 1), 111209-50-8; **6e** (isomer 2), 111209-51-9; **6f**, 111209-52-0; **6g**, 111209-53-1; *trans*-**7b**, 111209-56-4; *cis*-**7b**, 111209-57-5; *trans*-**8b**, 111209-54-2; *cis*-**8b**, 111209-55-3; allyl alcohol, 107-18-6; propanal, 123-38-6; isobutryaldehyde, 78-84-2; phenylacetaldehyde, 122-78-1; dihydrocinnamaldehyde, 104-53-0; 2-cyclohexenol, 822-67-3; diphenylacetaldehyde, 947-91-1; (*E*)-cinnamyl alcohol, 4407-36-7.

Formation of Six Cyclic 1,N^2-Hydroxybromopropanodeoxyguanosine Isomers upon Reaction of 2-Bromoacrolein with 2′-Deoxyguanosine

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As a preliminary study in the investigation of reactions of the genotoxin 2-bromoacrolein (2-BA) with DNA, we treated the aldehyde with 2′-deoxyguanosine (2′-dG). Six isomeric cyclic 1,N^2-propano-2′-deoxyguanosine adducts were isolated and characterized by UV, LSIMS, and ^{1}H NMR spectral techniques. The adducts **1a–1d** were identified as diastereomeric 3-(2-deoxy-β-D-*erythro*-pentofuranosyl)-5,6,7,8-tetrahydro-6-hydroxy-7-bromopyrimido[1,2-*a*]purin-10(3*H*)-ones. Adducts **2a** and **2b** were regioisomeric 7-bromo-8-hydroxy diastereomers. At physiological pH (7.4) and temperature (37 °C), adducts **1a–1d** are hydrolyzed to 6,7-dihydroxypropano-2′-deoxyguanosines. These can be transformed to stable 6,7-dihydroxypropanoguanines by removal of the deoxyribose moiety. The resulting bases can be used as standards for further investigations of reactions of 2-BA with DNA.

2-Bromoacrolein (2-BA) is a genotoxic metabolite of the flame retardant tris(2,3-dibromopropyl) phosphate (Tris-BP) that is formed in incubations of Tris-BP with mammalian microsomes.[1,2] As a preliminary study in the investigation of reactions of the genotoxin 2-BA with DNA, we treated the aldehyde with 2′-deoxyguanosine (2′-dG).

Reaction of carcinogens can take place at many sites in DNA. Unstable metabolites of carcinogenic arylamines and arylamides predominately react with the C-8 atom of deoxyguanosine, but reaction with the O^6 and N^2 atoms of deoxyguanosine and the N^6 atom of deoxyadenosine also takes place.[3] The N-7 of deoxyguanosine is a major target atom of reactive metabolites formed from a variety of other carcinogens, e.g., aflatoxin B$_1$, 1,2-dibromoethane, and *N*-nitroso compounds.[4–6] However, minor reactions can take place at other atoms as well, and the mutagenic and

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