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1,3-DIPOLAR CYCLOADDITION OF NITRONES TO SUGAR ENLACTONES

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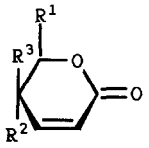
Abstract - It was found that 1,3-dipolar cycloaddition of nitrones derived from formaldehyde and acetaldehyde to sugar enlactones proceeds regio- and stereospecifically to afford *anti* - *endo* adducts.

Isoxazolidines, readily available *via* 1,3-dipolar cycloaddition of nitrones to olefins, represent an attractive class of compounds which can be utilized in synthesis of other heterocyclic systems and substituted alkanes.[1,2]

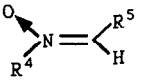
Recently we have reported on the cycloaddition of nitrones to α,β-unsaturated sugar lactones 1-4.[3,4,5] As the bicyclic system is highly functionalized, the adducts offer wide possibilities of formation of selected structures. These possibilities have been exemplified by the synthesis of β-lactams having a polyol side chain at the C-3 carbon atom of the azetidinine ring. The full reaction sequence, based on the known Tufariello approach,[6] has been accomplished, however, only for nitrones bearing aromatic substituents.[4,5] Owing to the low reactivity of such nitrones, reactions have been performed in boiling toluene. In the case of D-glycero 2 and D-threo 3 lactones, nitrone 5 enters into the double bond exclusively *anti* with respect to the terminal acetoxymethyl group, whereas in the case of D-erythro lactone 4 the addition proceeds from both sides of the six-membered ring[3]. On the ground of the large values of the vicinal coupling constants $J_{3,3a}$ and $J_{3a,7a}$, found in the ^{1}H-NMR spectra of the main diastereoisomer formed, we erroneusly assigned the relative *cis* arrangement to these protons, and thereby the R-configuration at the C-3 carbon atom in compound 11*, 12*, and 13*[3]. This wrong assignment was not corrected when the adducts 11 and 12 were transformed into azetidinones 14*[4] and 15*[5], respectively. Consequently the wrong trans configuration of the azetidinone ring was assigned to 14 and 15.

In this paper we would like to present the cycloaddition reactions between lactones 1, 2, and 3, and the more reactive nitrones derived from formaldehyde 7, 9, and acetaldehyde 8, 10. As these reactions are directly related to our previous work[3,4,5], we feel that this is the proper time to introduce the necessary corrections to the wrong configurational assignments made in the past.

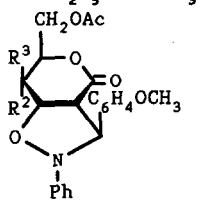
Chart 1



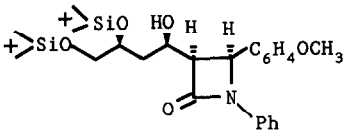
1: R^1=R^2=R^3=H
2: R^1=CH_2OAc, R^2=R^3=H
3: R^1=CH_2OAc, R^2=H, R^3=OAc
4: R^1=CH_2OAc, R^2=OAc, R^3=H
5: R^1=C_2H_5, R^2=CH_3, R^3=H



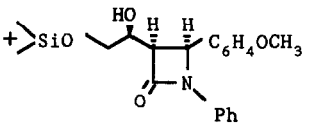
6: R^4=Ph, R^5=*p*-$CH_3OC_6H_4$
7: R^4=Bn, R^5=H
8: R^4=Bn, R^5=CH_3
9: R^4=*p*-$CH_3OC_6H_4CH_2$, R^5=H
10: R^4=*p*-$CH_3OC_6H_4CH_2$, R^5=CH_3



11*: R^2=R^3=H
12*: R^2=H, R^3=OAc
13*: R^2=OAc, R^3=H



14*



15*

Nitrones **7** and **9** derived from formaldehyde were used *in situ* according to the known procedure,[7] whereas those derived from acetaldehyde **8** and **10** were isolated and subsequently used as pure compounds. According to the NMR spectra, nitrones **8** and **10** exist as single *z* isomers only.[1]

Methylene nitrones **7** and **9** enter a lactone molecule regiospecifically and *anti* to the existing substituents to give cycloadducts **18**, and **20** with a good yield. Nitrones **8** and **10** react with lactones **1**, **2**, and **3**, affording with the same regiochemistry the respective *anti-endo* diastereoisomers **17**, **19**, **21**, and **22** as the only isolated products. The gross structures of the adducts were assigned on the basis of the ^1H and ^{13}C NMR spectra (Table 1).

The configuration of adduct **19** was proved by X-ray crystallography, thus confirming

Table 1. ^{13}C NMR chemical shifts of.tetrahydropyrano-[3,4-d]- isoxazolidines **17**, **18**, **19**, **22**, and tetrahydrofurano[3,4-d]isoxazolidines **23**, and **24**; Pyridine-d_5; 100°C.

Comp.	C-3	C-3a	C-4	C-6	C-7	C-7a	CH_2OAc	CH_2Ar	CH_3
18	47.43	59.68	170.04	73.85	29.81	72.88	65.78	61.29	-
19	58.88	55.00	169.63	73.60	29.25	71.75	65.78	66.73	16.64
20	46.47	59.68	169.63	75.23	67.14	74.78	62.82	61.32	-
22	58.62	53.81	169.90	74.47	66.37	74.30	62.88	66.20	16.50
23	50.72	58.91	176.17	77.18	71.12	81.22	63.22	61.55	-
24	58.75	57.81	175.91	77.10	71.03	80.32	63.02	64.74	16.36

* Formulae **11** - **15** presented in this paper refer to the corrected configuration at C-3 of the tetrahydropyrano[3,4-d]isoxazolidine skeleton or at C-4 of the azetidinone ring.

also the configuration of other cycloadducts (Fig 1; Table 2.). The relative configuration of compound **19** was assigned using its sugar moiety as internal standard. A PLUTO diagram of the proper enantiomer is shown in Fig. 1, together with the numbering scheme adopted during the X-ray structure determination. In the above picture the two H-atoms at C-3a and C-7a carbons and the methyl group at carbon C-3 are mutually cis located. The shape of the sugar ring is approximated by the twist-boat (S) conformation[8], with a two-fold axis of symmetry relating the torsion angles, located in the middle of the C-4 - C-3a bond [asymmetry parameter ΔC_2 = 5(2)°], whereas the five-membered ring has an *envelope* conformation, with atom N-2 0.71Å above the least-squares plane containing the C-3, C-3a, C-7a, O-1 atoms.

The stereospecificity of cycloaddition of nitrones **7** - **10** is noteworthy, particularly since the nitrones investigated earlier[3,4,5,9] have given mixtures of *exo* and *endo* adducts. The low stereoselectivity of addition in the case of diaromatic nitrones was not a consequence of the *exo* : *endo* approach of lactones 1-3 and z-nitrones, but rather of the fact that the temperature of reaction (boiling toluene) caused equilibration of the z and E isomers of the 1,3-dipole.[1,9]

Nitrones were added to the conformationally stable lactones **2**, **3**, and **5** exclusively *anti* to the acetoxymethyl[3,4] or ethyl[9] substituent. It can be explained in terms of the axial approach[10,11] of the nitrone oxygen atom, and in consequence the formation of the C-O bond prior to the C-C bond. Owing to the allylic effect[12] of the acetoxy substituent at C-4, the conformation of the lacton **4** is more liabile (J_{45}=7.9[13]), and therefore nitrones or nitrile oxides[14] can be added to both sides of the lactone ring.

Deacetylation of adducts **17** and **20** in the presence of an acid catalyst led to the contraction of the δ-lactone ring into the more stable γ-lactone, and after acetylation compounds **23**, and **24** were obtained. The NMR spectra of the compounds having an isoxazolidine ring display line broadening at room temperature, owing to the slow inversion process at the nitrogen atom, and therefore they have to be recorded at 70-100°C. The ^{1}H-NMR spectra of **18**, **19**, **20**, **22**, **23**, and **24** recorded at -80°C in CD_2Cl_2 display lines characteristic of definite single nitrogen invertomers. Adducts **18** and **20** show the presence of two invertomers in a ratio of 1:1.5 and 1:3.1, respectively; both, *endo* and *exo* positions of the *p*-methoxybenzyl group are possible. Introduction of the *exo* methyl substituent at the C-3 carbon atom (adducts **19** and **21**) caused a shift of the equilibrium towards only the isomers having relative *trans* arrangement of the methyl and *p*-methoxybenzyl substituent. This prefered configuration of the nitrogen atom is well visible in the crystalline state (Fig. 1). The contraction of the δ-lactone ring into a γ-lactone ring in compounds **23** and **24** caused *endo* location of the $CHOAcCH_2OAc$ group and therefore forced an exclusively *exo* position of the *p*-methoxybenzyl group in **23**. The effect of the *exo* methyl substituent at the C-3 carbon atom (adduct **24**) differs from that found for **19** and **21**. Both the *exo* and *endo* position of the *p*-methoxybenzyl group in **24** are similarily disfavored and consequently both nitrogen invertomers occur in a proportion of 1:1.2.

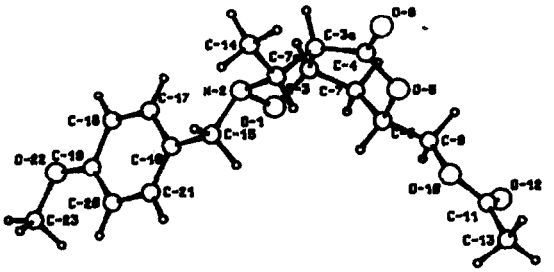
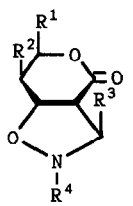
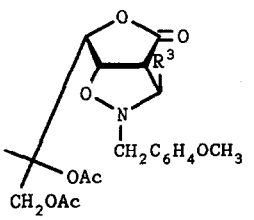


Fig. 1. PLUTO diagram showing conformation of compound **19**.

Chart 2





16: $R^1=R^2=R^3=H$, $R^4=CH_2Ph$

17: $R^1=R^2=H$, $R^3=CH_3$, $R^4=CH_2Ph$

18: $R^1=CH_2OAc$, $R^2=R^3=H$, $R^4=p\text{-}CH_3OC_6H_4CH_2$

19: $R^1=CH_2OAc$, $R^2=H$, $R^3=CH_3$, $R^4=p\text{-}CH_3OC_6H_4CH_2$

20: $R^1=CH_2OAc$, $R^2=OAc$, $R^3=H$, $R^4=p\text{-}CH_3OC_6H_4CH_2$

21: $R^1=CH_2OAc$, $R^2=OAc$, $R^3=CH_3$, $R^4=CH_2Ph$

22: $R^1=CH_2OAc$, $R^2=OAc$, $R^3=CH_3$, $R^4=p\text{-}CH_3OC_6H_4CH_2$

23: $R^3=H$

24: $R^3=CH_3$

Experimental.

X-ray structure determination of compound 19.

A crystal (0.1 x 0.13x 0.3 mm) was used for data collection at a four-circle CAD4 diffractometer. The orthorhombic $P2_12_12_1$ space group was assigned on the basis of systematic extinctions. Unit cell parameters: a = 7.119(4), b = 8.966(3), c = 27.708(6)Å^3, were obtained during theprocedure of centering of 25 reflections; V = 1769(1) Å^3, Z = 4, d_x=1.149 g·cm^{-3}. A total of 1732 reflections were measured within the θ range 0-24° in the $\omega/2\theta$ scanning mode. Among 1667 unique reflections only 1071 were observed. Intensities were corrected for Lorentz polarization and for the empirical absorption factors (program DIFABS, minimum and maximium corrections 0.63 and 1.216).

The structure was solved by direct methods (SHELXS, 1986) and refined by the full-matrix least-squares procedure (SHELX76) to a R-factor 0.055, R_w=0.051 (statistical weights) with anisotropic temperature factors, and H-atoms at their calculated and not refined positions. Refined atomic coordinates are presented in Table 2.

Melting points are uncorrected. Optical rotations were measured with a Perkin-Elmer 141 spectropolarimeter. I.R. spectra were recorded with a Beckman 4240 spectrophotometer.

^{1}H NMR and ^{13}C NMR spectra were obtained with a Bruker AM 500 spectrometer. Column chromatography was performed on Merck KIeselgel 60 (70-230 mesh).

Nitrones **8** and **10** were obtained according to the Torssell and Zeuthen procedure[15] from an appropriate hydroxylamine and acetaldehyde in methylene chloride at room temperature.

(Z)-Methyl-N-benzylnitrone (8): m.p. 80-82°C; I.R. (CH_2Cl_2): 1610, 1500 cm^{-1}; ^{1}H NMR (CD_2Cl_2): 1.93 (d, 3H, *J* 5.8 Hz, CH_3), 4.84 (s, 2H, CH_2), 6.79 (q, 1H, CH), 7.38 (m, 5H, Ph); MS m/z: M^+ 149. Anal. Calcd for $C_9H_{11}NO$: C, 72.48; H, 7.38; N, 9.39. Found: C, 72.2; H, 7.6; N, 9.5.

(Z)-Methyl-N-p-methoxybenzylnitrone (10): m.p. 87-89°C; I.R. (CH_2Cl_2): 1620, 1520 cm^{-1}; ^{1}H NMR (CD_2Cl_2): 1.92 (d, 2H, *J* 5.8 Hz, CH_3), 3.80 (s, 3H, OCH_3), 4.77 (s, 2H, CH_2), 6.73 (q,, 1H, CH), 6.90, 7.32 (2m, 4H, aromatic); MS m/z: M^+ 179. Anal. Calcd for $C_{10}H_{13}NO_2$: C, 67.03; H, 7.26; N, 7.82. Found: C, 66.9; H, 7.2; N, 7.8.

Cycloadditions using methylene nitrones 7 and 9. General procedure. A mixture of substituted hydroxylamine (3.0 mmol) and 37% aqueous formaldehyde (0.45 g, 5.0 mmol) in ethanol (5 mL) was warmed to 40°C and lactone **1-3** (3.0 mmol) was added. The mixture was refluxed for 1 h, whereupon the solvent was evaporated and the crude residue was purified on a silica gel column using hexane - AcOEt (1:1 v/v) as an eluent.

Table 2. Fractional atomic coordinates with e.s.d.'s in parentheses

	X/A	Y/B	Z/C	B_{eq}*
O1	1.0589(7)	-.0547(5)	.1079(2)	4.4(2)
O2	1.3590(7)	-.0786(6)	.0903(2)	4.7(2)
C1	1.209(1)	-.0254(7)	.0783(3)	3.8(2)
C2	1.1813(8)	.0612(7)	.0330(2)	3.1(2)
C3	1.0074(9)	.1651(7)	.0311(2)	3.4(2)
C4	.8948(9)	.1652(7)	.0764(2)	3.1(2)
C5	.8720(9)	.0079(7)	.0964(2)	3.3(2)
C6	.768(1)	.0048(7)	.1429(2)	3.8(2)
O7	.7334(7)	-.1465(5)	.1554(2)	3.9(1)
C8	.607(1)	-.168(1)	.1919(3)	4.1(2)
C9	.576(1)	-.3276(9)	.2021(2)	4.5(2)
O10	.5312(9)	-.0666(6)	.2118(2)	5.8(2)
O11	.8921(6)	.1044(5)	-.0064(1)	3.5(1)
N12	1.0280(8)	.0421(6)	-.0412(2)	3.5(2)
C13	1.1496(9)	-.0463(7)	-.0083(2)	3.1(2)
C14	1.329(1)	-.0907(8)	-.0345(3)	5.4(3)
C15	.916(1)	-.0533(8)	-.0723(2)	4.0(2)
C16	.808(1)	.0309(7)	-.1107(2)	3.7(2)
C17	.865(1)	.1700(8)	-.1283(3)	4.1(2)
C18	.779(1)	.2385(8)	-.1660(3)	4.2(2)
C19	.6247(9)	.1681(8)	-.1895(2)	3.5(2)
C20	.5669(9)	.0318(8)	-.1723(3)	4.1(2)
C21	.658(1)	-.0348(7)	-.1342(3)	3.9(2)
O22	.5481(7)	.2449(6)	-.2262(2)	4.9(2)
C23	.393(1)	.172(1)	-.2512(3)	6.0(3)

*Calculated from anisotropic thermal parameters as $B_{eq} = 8\pi^2 \cdot D_u$ where D_u is the determinant of the *U* matrix in orthogonal space.

(3aR*, 7aR*)-2-Benzyl-4-oxo-tetrahydropyrano[3,4-d]isoxazolidine (16). 67%; syrup; I.R. (film): 1730 cm^{-1}; ^1H NMR ($CDCl_3$): 1.94 (m, 1H, H-7), 2.10 (m, 1H, H-7'), 3.09 (bs, 1H, H-3), 3.44 (bt, 1H, *J* 9.5 and 8.2 Hz, H-3'), 3.57 (q, 1H, *J* 7.6, 8.2, and 8.5 Hz, H-3a), 3.95 (s, 2H, CH_2Ph), 4.20 (m, 1H, H-6), 4.49 (m, 1H, H-6'), 4.55 (m, 1H, H-7a); MS m/z: M^+ 233. Anal. Calcd for $C_{13}H_{15}NO_3$: C, 66.91; H, 6.43; N, 6.00. Found: C, 66.4; H, 6.3; N, 6.2.

(3aR, 6S, 7aR)-6-Acetoxymethyl-2-p-methoxybenzyl-4-oxo-tetrahydropyrano[3,4-d]isoxazolidine (18). 92%; m.p. 84-86°C; $[\alpha]_D$ +20.7° (*c* 1, CH_2Cl_2); I.R. (film): 1760 cm^{-1}; ^1H NMR (toluene-d_7, 100°C): 1.29 (ddd, 1H, *J* 3.8, 11.1, and 14.8 Hz, H-7), 1.60 (dt, 1H, *J* 2.1, 2.8, and 14.8 Hz, H-7'), 1.69 (s, 3H, OAc), 2.75 (bt, 1H, *J* 7.0 and 9.9 Hz, H-3), 3.06 (t, 1H, *J* 8.7 and 9.9 Hz, H-3'), 3.14 (ddd, 1H, *J* 7.0, 7.9, and 8.7 Hz, H-3a), 3.45 (s, 3H, OCH_3), 3.67 (bs, 2H, CH_2Ar), 3.90 (dd, 1H, *J* 4.3 and 11.9 Hz, CH_AH_BOAc), 3.93 (dd, 1H, *J* 5.5 and 11.9 Hz, CH_AH_BOAc), 4.06 (dt, 1H, *J* 2.8, 3.8, and 7.9 Hz, H-7a), 4.58 (m, 1H, H-6); MS m/z: M^+ 335. Anal. Calcd for $C_{17}H_{21}NO_6$: C, 60.89; H, 6.26; N, 4.17. Found: C, 60.7; H, 6.3; N, 4.3.

(3aR, 6R, 7R, 7aS)-7-Acetoxy-6-acetoxymethyl-2-p-methoxybenzyl-4-oxo-tetrahydropyrano[3,4-d]isoxazolidine (20). 88%; m.p. 99-100°C; $[\alpha]_D$ +56.5° (*c* 1, CH_2Cl_2); I.R. (film): 1755 cm^{-1}; ^1H NMR (C_6D_6, 70°C): 1.55, 1.60 (2s, 6H, 2OAc), 2.82, 2.90 (2bs, 2H, H-3,3'), 3.24 (q, 1H, *J* ~7.2 Hz, H-3a), 3.38 (s, 3H, OCH_3), 3.60, 3.67 (2bd, 2H, *J* 13.1 Hz, CH_2Ar), 4.14 (m, 3H, H-7a, CH_2OAc), 4.95 (bt, 1H, *J* 5.9 and 6.5 Hz, H-6), 5.15 (bd, 1H, *J* 1.5 and 3.2 Hz, H-7); MS m/z: M^+ 393. Anal. Calcd for $C_{19}H_{23}NO_8$: C, 58.01; H, 5.85; N, 3.56. Found: C, 58.0; H, 5.8; N, 3.5.

Cycloaddition using nitrones derived from acetaldehyde. General procedure. A solution of equimolar amounts of nitrone 8 or 10 (0.75 g, 5 mmol) and lactone (1 - 3) in boiling benzene (10 mL) was refluxed for 1 h. Subsequently the solvent was evaporated and the residue was purified on a silica gel column (70-230 mesh) using hexane - ethyl acetate 1:1 as an eluent to afford isoxazolidine 17, 19, 21, or 22, respectively.

(3R*, 3aR*, 7aR*)-2-Benzyl-3-methyl-4-oxo-tetrahydropyrano[3,4-d]isoxazolidine (17). 78%; 87-90°C; I.R. (film): 1730 cm^{-1}; ^1H NMR ($CDCl_3$): 1.37 (d, 3H, *J* 6.1 Hz, CH_3), 1.89 (dq, 1H, H-7), 2.03 (ddt, 1H, H-7'), 2.92 (bm, 1H, H-3), 3.07 (t, 1H, *J* 8.8 and 8.5 Hz, H-3a), 3.78, 4.08 (2d, 2H, *J* 14.2 Hz, CH_2Ph), 4.20 (dt, 1H, H-6), 4.43 (m, 2H, H-7a,6'); MS m/z: M^+ 247. Anal. Calcd for $C_{14}H_{17}NO_3$: C, 68.1; H, 6.88; N, 5.66. Found: C, 67.8; H,6.8; N, 5.7.

(3R, 3aR, 6S, 7aR)-6-Acetoxymethyl-2-p-methoxybenzyl-3-methyl-4-oxo-tetrahydropyrano[3,4-d]isoxazolidine (19). 83%; m.p. 123-125°C; $[\alpha]_D$ -90.0° (*c* 1, CH_2Cl_2); I.R. (CH_2Cl_2): 1740 cm^{-1}; ^1H NMR (toluene-d_7, 100°C): 1.15 (d, 3H, *J* 6.1 Hz, CH_3), 1.19 (ddd, 1H, *J* 3.8, 11.3, and 14.9 Hz, H-7), 1.52 (dt, 1H, *J* 2.3, 2.0, and 14.9 Hz, H-7'), 1.69 (s, 3H, OAc), 2.59 (dq, 1H, *J* 6.1 and 8.7 Hz, H-3), 2.73 (t, 1H, *J* 8.7 and 8.2 Hz, H-3a), 3.45 (s, 3H, OCH_3), 3.56, 3.78 (2d, 2H, *J* 14.0 Hz, CH_2Ar), 3.89 (dd, 1H, *J* 4.3 and 11.9 Hz, CH_AH_BOAc), 3.92 (dd, 1H, *J* 5.5 and 11.9 Hz, CH_AH_BOAc), 3.98 (ddd, 1H, *J* 2.3, 3.8, and 8.2 Hz, H-7a), 4.46 (m, 1H, H-6); MS m/z: M^+ 349. Anal. Calcd for $C_{18}H_{23}NO_6$: C, 61.89;

H, 6.59; N, 4.01. Found: C, 61.7; H, 6.6; N, 4.0.

(3R, 3aR, 6R, 7R, 7aS)-7-acetoxy-6-acetoxymethyl-2-benzyl- 3-methyl-4-oxo-tetrahydro pyrano[3,4-d]isoxazolidine (21). 82%; syrup; $[\alpha]_D$ -65.3° (*c* 1, CH_2Cl_2); ^1H NMR ($CDCl_3$): 1.37 (d, 3H, *J* 6.1 Hz, CH_3), 2.06, 2.07 (2s, 6H, 2OAc), 2.90 (bs, 1H, H-3), 3.18 (t, 1H, *J* 8.8 and 8.2 Hz, H-3a), 3.80, 4.10 (2d, 2H, *J* 14.3 Hz, CH_2Ph), 4.18 (dd, 1H, *J* 6.7 and 11.8 Hz, CH_AH_BOAc), 4.20 (dd, 1H, *J* 5.9 and 11.8 Hz, CH_AH_BOAc), 4.26 (dd, 1H, *J* 8.3 and 2.5 Hz, H-7a), 4.80 (dt, 1H, *J* 1.2, 5.9, and 6.7 Hz, H-6), 5.10 (dd, 1H, *J* 1.2 and 2.5 Hz, H-7), MS m/z: M^+ 377. Anal. Calcd for $C_{19}H_{21}NO_7$: C, 60.47; H, 6.10; N, 3.71. Found: C, 60.2; H, 6.1; N, 3.6.

(3R, 3aR, 6R, 7R, 7aS)-7-Acetoxy-6-acetoxymethyl-2-p-methoxybenzyl-3-methyl-4-oxo-tetrahydropyrano[3,4-d]isoxazolidine (22). syrup; $[\alpha]_D$ -46.5° (*c* 1, CH_2Cl_2); I.R. (film): 1755 cm^{-1}; ^1H NMR (C_6D_6, 70°C); 1.09 (d, 3H, *J* 6.1 Hz, CH_3), 1.51, 1.63 (2s, 6H, 2OAc), 2.62 (bs, 1H, H-3), 2.93 (t, 1H, *J* 8.7 and 8.3 Hz, H-3a), 3.39 (s, 3H, OCH_3), 3.52, 3.76 (2d, 2H, *J* 14.2 Hz, CH_2Ar), 4.05 (dd, 1H, *J* 2.6 and 8.3 Hz, H-7a), 4.13 (dd, 1H, *J* 6.0 and 11.7 Hz, CH_AH_BOAc), 4.15 (dd, 1H, *J* 6.6 and 11.7 Hz, CH_AH_BOAc), 4.75 (dt, 1H, *J* 1.5, 6.0, and 6.6 Hz, H-6), 5.09 (dd, 1H, *J* 2.6 and 1.3 Hz, H-7); MS m/z: M^+ 407. Anal. Calcd for $C_{20}H_{25}NO_8$: C, 58.96; H, 6.14; N, 3.43. Found: C, 58.9; H, 6.3; N, 3.4.

Isomerization of lactones 20 and 22. General procedure. Cycloadduct **20** or **22** (1 mmol) was dissolved in 5 ml of methanol and 3 drops of a saturated solution of HCl in ethyl ether were added. The mixture was refluxed for 5 min and then neutralized with Et_3N. Solvents were evaporated and the residue was dissolved in methylene chloride (5 mL), treated with acetic anhydride (0.5 mL) and pyridine (0.5 mL), and left overnight. Subsequently the solvents were evaporated and the product was purified on a silica gel column using hexane:ethyl acetate 1:1 as an eluent to give **23** and **24** respectively.

(3aR, 6R, 6aS, 1'R)-6-(1',2'-diacetoxyethyl)-2-p-methoxybenzyl-4-oxo-tetrafurano-[3,4-d]isoxazolidine (23). 90%; syrup; $[\alpha]_D$ -16.1° (*c* 1, CH_2Cl_2); I.R. (film): 1790, 1755 cm^{-1}; ^1H NMR (C_6D_6, 70°C): 1.70, 1.76 (2s, 6H, 2 OAc), 2.29 (bs, 1H, H-3), 2.74 (bt, 1H, H-3a), 3.22 (bd, 1H, H-3'), 3.40 (s, 3H, OCH_3), 3.58, 3.62 (2d, 1H, *J* 13.2 Hz, CH_2Ar), 4.20 (m, 3H, H-6,6a,CH_AH_BOAc), 4.31 (dd, 1H, CH_AH_BOAc), 5.65 (m, 1H, CHOAc); MS m/z: M^+ 393. Anal. Calcd for $C_{19}H_{23}NO_8$: C, 58.1; H, 5.85; N, 3.56. Found: C, 57.8; H, 5.7; N, 3.4.

(3R, 3aR, 6R, 6aS, 1'R)-6-(1',2'-diacetoxyethyl)-2-p-methoxybenzyl-3-methyl-4-oxo-tetrahydrofurano[3,4-d]isoxazolidine (24). 90%; syrup; $[\alpha]_D$ -94.0° (*c* 1, CH_2Cl_2); I.R. (film): 1795, 1760 cm^{-1}; ^1H NMR (C_6D_6, 70°C): 0.88 (d, 3H, *J* 6.3 Hz, CH_3), 1.68, 1.75 (2s, 6H, 2OAc), 2.51 (dd, 1H, *J* 3.3 and 6.3 Hz, H-3a), 3.25 (bs, 1H, H-3), 3.39 (s, 3H, OCH_3), 3.60, 3.63 (2d, 2H, *J* 13.4 Hz, CH_2Ar), 4.16 ((dd, 1H, *J* 4.4 and 12.4 Hz, CH_AH_BOAc), 4.20 (m, 2H, H-6,6a), 4.36 (dd, 1H, *J* 3.1 and 12.4 Hz, CH_AH_BOAc), 5.58 (m, 1H, *J* 8.5, 4.4, and 3.1 Hz, CHOAc); MS m/z: M^+ 407. Anal. Calcd for $C_{20}H_{25}NO_8$: C, 58.96; H, 6.14; N, 3.43. Found: C, 59.2; H, 6.3; N, 3.7.

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