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HIGH-PRESSURE [2+2]CYCLOADDITION OF TOLUENE-4-SULPHONYL ISOCYANATE TO GLYCALS

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Abstract - High-pressure [2+2]cycloaddition of toluene-4-sulphonyl isocyanate to glycals is examined. Reactions proceed regiospecifically to afford single products in case of all 3-substituted glycals. Upon heating or even after standing at room temperature adducts undergo retro-addition to give starting glycals. Various aspects of the cycloaddition are discussed, especially retro-reaction and rearrangement of β-lactams to α,β-unsaturated amides.

Recently we have reported on high-pressure [2+2]cycloaddition of toluene-4-sulphonyl isocyanate to glycals 1 - 4.[1] The reaction proceeds regio- and stereospecifically to afford a β-lactam ring in position *trans* to the acetoxy group at C-3 of the glycal moiety (5 - 8). Owing to the enol ether structure of glycals, cycloaddition offers an approach to various β-lactams, particularly to oxapenams and oxacephams.

Owing to the stereospecificity of the reaction, glycals of D-series 1 and 2 lead to S-configuration at the carbon atom attached to the nitrogen and oxygen atom, whereas glycals of L-series 3 and 4 lead to R-configuration at the C-1 carbon atom. This offers stereocontrol in formation of an appropriate configuration at the carbon atom crucial for the biological activity of β-lactam antibiotics.

Cycloaddition of tosyl isocyanate to dihydropyran 9 at low temperature (~0°C) and atmospheric pressure leads to formation of bicyclic β-lactam 15. Elevation of the temperature of cycloaddition causes a rearrangement of the four-membered ring to open-chain amide 21.[2] Recently Barrett et al.[3] have found that 2,2,2-trichloroethylsulphonyl, 2,2,2-trichloroethoxysulphonyl and trifluoroacetyl isocyanate react with dihydropyran 9 to give unsaturated amides 19 - 21, no β-lactam being isolated in all three cases. Similar results have been reported by Chan and Hall[4] for the addition of tosyl isocyanate to dihydropyrans 12 - 14. The 5-substituted dihydropyrans 10 and 11 have, however, been found to react with trifluoroacetyl isocyanate to give the expected β-lactams 16 and 17, respectively, obtained after cleavage of the trifluoroacetyl group with silica-gel.[3]

Attempts at adding chlorosulphonyl isocyanate to glucal 1 have failed to give the expected β-lactam; isocyanate acted only as a Lewis acid, causing the known dimerisation of the sugar substrate.[5]

The aim of the present work was to elucidate the stereochemistry of [2+2]cycloaddition of tosyl isocyanate to glycals, as well as to interpret the chemical properties of the bicyclic β-lactams synthetized. Therefore we selected a wide and representative group of glycals, namely 1 - 4 and 22 - 27.

RESULTS AND DISCUSSION

All cycloadditions, except that to 23, were performed in absolute ethyl ether either at room temperature or at 50°C, under 10 - 11 kbar pressure. Cycloaddition to glycals 1, 3, 4, 22, 23, 25 and 27 proceeded with formation of products which crystallized from the post-reaction mixture, whereas

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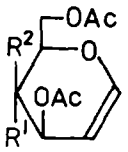
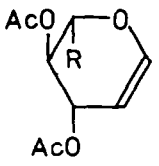
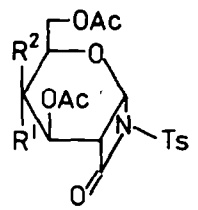
Chart 1



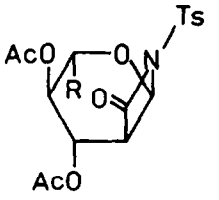
1: R^1=OAc, R^2=H
2: R^1=H, R^2=OAc



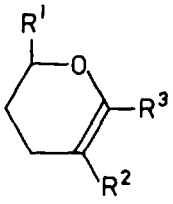
3: R=H
4: R=CH_3



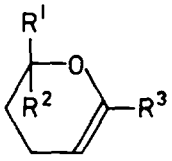
5: R^1=OAc, R^2=H
6: R^1=H, R^2=OAc



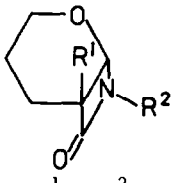
7: R=H
8: R=CH_3



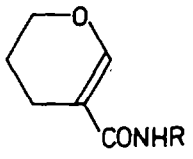
9: R^1=R^2=R^3=H
10: R^1=R^3=H, R^2=CH_3
11: R^1=R^3=H, R^2=CH_2Ph



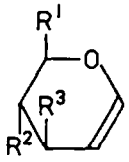
12: R^1=R^2=R^3=CH_3
13: R^1=R^3=H, R^2=OCH_3
14: R^1=R^3=CH_3, R^2=OCH_3



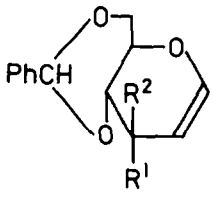
15: R^1=H, R^2=Ts
16: R^1=CH_3, R^2=H
17: R^1=CH_2Ph, R^2=H



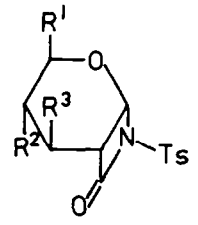
18: R=Ts
19: R=$CCl_3CH_2SO_2$
20: R=$CCl_3CH_2OSO_2$
21: R=$COCF_3$



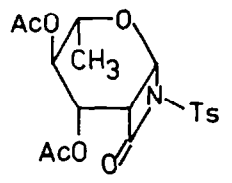
22: R^1=CH_2OAc, R^2=OAc, R^3=H
23: R^1=CH_2OAc, R^2=R^3=H
24: R^1=CH_2OSiMe_2t-Bu, R^2=R^3=$OSiMe_2t$-Bu



25: R^1=R^2=H
26: R^1=H, R^2=OAc
27: R^1=OAc, R^2=H



28: R^1=CH_2OAc, R^2=OAc, R^3=H
29: R^1=CH_2OAc, R^2=R^3=H
30: R^1=CH_2OSiMe_2t-Bu, R^2=R^3=$OSiMe_2t$-Bu



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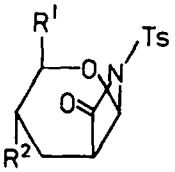
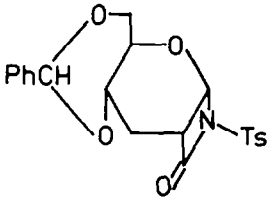


32: R^1=CH_2OAc, R^2=OAc
33: R^1=CH_2OAc, R^2=H



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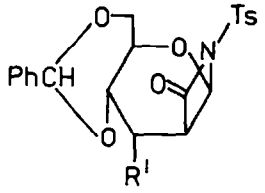
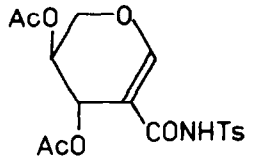


35: R^1=H
36: R^1=OAc



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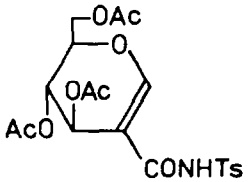

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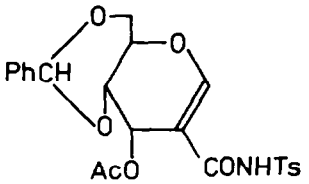


39

the products derived from galactal (2) and silylated glucal (24) were obtained as crude syrups. 4,6-O-Benzylideneglucal 26 was unreactive under these conditions.

Cycloadditions proceeded regiospecifically, yielding a single isomer 5, 6, 7 and 30 as a result of addition to glycals 1, 2, 3 and 24, respectively, whereas in case of an addition to rhamnal 4 both isomeric products were obtained with substantial predominance of 8 (95%) over the alternative 31. Stereoselectivity of cycloaddition to 3-deoxyglycals 22, 23 and 25 was relatively low (cf. Experimental, Table 5), and therefore the respective mixtures of diastereoisomers 28, 32; 29, 33; 34, 35 were obtained. Owing to the instability of all β-lactams obtained, the mixtures of diastereoisomers could not be separated into pure components. The approximate ratios of isomeric β-lactams were determined from the ^{1}H NMR spectra of the crystalline materials isolated (cf. Experimental, Table 5). Cycloadducts 6 and 30 were characterized as crude products after careful evaporation of solvent.

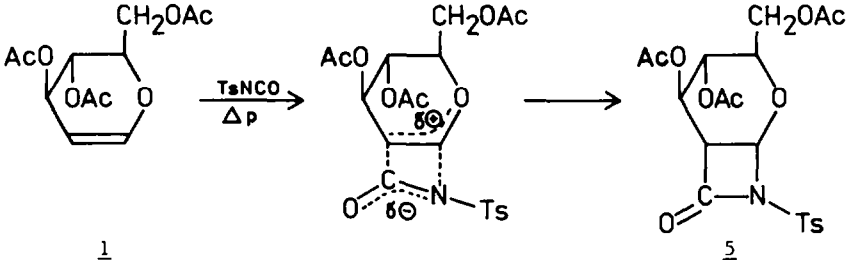
All post-reaction mixtures obtained at room temperature contained traces of starting materials (TLC). In case of cycloaddition to 3, the product 7 was contaminated also with a minute amount of more polar compound 37 which was isolated by chromatography from the mother liquor after separation of crystalline β-lactam, and it was characterized as 3-N-tosylcarbamoyl xylal. Raising of the temperature of high-pressure experiments to 50°C, followed by cooling of the reaction vessel to room temperature before decompression, increased the yield of cycloaddition. However, all reaction mixtures were contaminated with the respective α,β-unsaturated amides (5-10%); one of which (38) was isolated by chromatography and identified. Elevation of the temperature of cycloaddition to 3 caused a significant shift of the reaction towards amide 37.

Allal 27 did not react with the isocyanate at room temperature, whereas at 50°C amide 39 was obtained as the unique product.

The gross structure of products 5 - 8 and 28 - 39 was determined from the ^{1}H and ^{13}C NMR spectra (Tables 1 and 2). For assignment of the ^{13}C NMR signals to appropriate carbon atoms of β-lactams, we examined the respective data of starting glycals (Table 3). There is no, however, direct similarity between these two sets of spectral data. The upfield shift of C-3, C-4 and C-5 resonances can be explained by introduction of a four-membered ring into the molecule and by changes in the conformation of the pyranoid ring, which were also exhibited by the values of vicinal coupling constants (Table 1).

The [2+2]cycloaddition of tosyl isocyanate to glycals is probably a pseudo-concerted reaction[6] (Scheme 1).

Scheme 1



1 5

The presence of an α-substituent at the C-3 carbon atom greatly helps to specify the diastereofacedifferentiation of the double bond in glycals. The isocyanate enters preferentially *trans* with respect to the acetoxy group at C-3. This is well expressed by the high stereoselectivity of cycloaddition to glycals 1 - 4 and 24. The high stereoslectivity observed could, however, be the result of the lower stability of one diastereoisomer over the alternative one; in all reactions, the starting glycal was detected in the post-reaction mixture (TLC), although an excess of the isocyanate was used. 3-Deoxyglycals 22, 23 and 25 exhibited lower diastereofacedifferentiation, and thus afforded a mixture of products, with predominance of the adduct resulting from *trans* approach of the isocyanate with respect to the terminal oxymethyl group.

All β-lactams 5 - 8, 15, 28 - 35, treated with methanol at room temperature, undergo a rapid opening of the four-membered ring to give the respective glycosides 40 - 49. The opening of the β-lactam ring proceeded stereospecifically with inversion of the configuration at the C-1 carbon atom.

Table 1. ^{1}H NMR data for β-lactams 5 - 8 and 28 - 35

Comp.	H-1	H-2	H-3 H-3′	H-4	H-5	H-6 H-6′	J_{12}	J_{23}	$J_{23'}$	J_{34}	$J_{3'4}$	J_{45}	
5	5.88	3.55	5.27	4.91	3.67	4.01 4.20	6.2	3.1	-	5.6	-	7.7	J_{24}=1.3, J_{56}=4.4, $J_{56'}$=6.7, $J_{66'}$=14.5
6	6.03	3.40	a	a	a	a	5.3	5.3	-	a	-	a	
7	5.84	3.51	5.26	4.90	3.48 3.97	-	6.2	2.7	-	5.9	-	6.9 6.8	J_{24}=1.3
8	5.85	3.52	5.22	4.71	3.48	1.12	5.3	2.4	-	5.4	-	7.5	J_{24}=0.9, J_{56}=7.2
28	5.80	3.35	2.00 2.30	4.87	3.67	4.16	5.5	6.1	2.6	4.2	3.5	3.3	$\|J_{56}+J_{56'}\|$=8.3
29	5.77	3.31	a	a	3.73	3.97 4.05	5.4	4.1	8.5	a	a	b	J_{56}=4.5, $J_{56'}$=5.8
30	5.76	3.24	4.11	3.77	3.52	3.56 3.67	5.8	3.3	-	2.9	-	2.0	J_{24}=1.5, J_{56}=7.9, $J_{56'}$=6.0, $J_{66'}$=9.5
31	5.68	3.91	5.08	4.85	3.74	1.21	4.7	8.4	-	7.5	-	7.4	J_{56}=6.6
32	5.57	3.43	a	4.94	3.80	4.08 4.19	4.6	$\|J_{23}+J_{23'}\|$ =16.7		$\|J_{34}+J_{3'4}\|$ =9.4		4.0	J_{56}=5.3, $J_{56'}$=4.1, $J_{66'}$=12.1
33	5.69	3.40	a	a	a	3.83 3.88	5.6	2.0	6.8	a	a	a	J_{24}=1.0
34	5.77	3.32	2.05 2.37	a	a	3.61 4.00	5.4	11.1	7.1	4.8	12.5	a	J_{24}=1.0, $J_{33'}$=14.1, J_{56}=10.0, $J_{56'}$=5.3, $J_{66'}$=11.2
35	5.79	3.25	1.86	a	a	4.23	4.8	8.8	6.9	3.7	11.6	a	$J_{33'}$=11.6, J_{35}=2.2

[a] not resolved or too complex for analysis; [b] $|J_{45}+J_{4'5}|$=12.4

Table 2. ^{13}C NMR data for adducts 5 - 8, 28, 29, 33 - 35, 37 ($CDCl_3$) and 15, 18 (DMSO-d_6)

Comp.	5	6	7	8	15	18	28	29	33	34	35	37
C-1	80.42	80.29	79.91	80.99	89.48	165.53	80.24	81.19	80.31	80.31	79.78	160.62
C-2	51.78	49.79	51.36	52.47	46.53	108.00	45.63	45.97	48.81	45.22	48.80	103.84
C-3	66.86	65.48	66.42	66.77	23.79	20.65	23.41	21.43	a	23.68	a	64.48
C-4	66.65	62.86	65.37	72.04	18.44	18.60	66.50	16.82	a	73.21	73.60	64.42
C-5	69.49	68.72	60.72	67.40	57.94	66.50	71.89	67.43	66.59	64.11	a	61.38
C-6	62.71	61.58	-	18.22	-	-	64.26	65.91	65.81	68.58	a	-

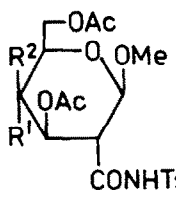
[a] not visible or overlaped by absorptions of a major isomer

Table 3. ^{13}C NMR data for glycals 1 - 4, 9, 22, 23, 25 - 27 ($CDCl_3$)

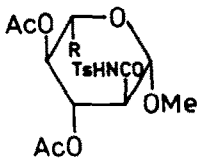
Comp.	1	2	3	4	9	22	23	25	26	27
C-1	145.71	145.46	148.04	146.00	144.50	142.71	143.38	143.14	145.42	147.35
C-2	99.07	98.92	97.42	98.85	100.60	97.75	100.52	98.66	100.79	98.43
C-3	67.48*	63.81*	67.22	68.33	23.20	25.68	24.27	26.37	68.90*	62.01
C-4	67.28*	63.95*	63.62*	72.55*	19.90	65.69	19.21	75.11	77.01	76.05
C-5	74.04	72.84	63.47*	71.88*	65.80	73.96	72.72	69.97*	68.31*	64.93
C-6	61.40	61.95	-	16.56	-	62.41	66.23	68.95*	68.90	68.60

* assignments may be reversed

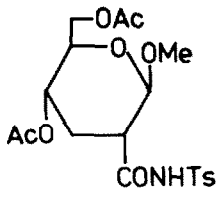
Chart 2



40: R^1=OAc, R^2=H
41: R^1=H, R^2=OAc



42: R=H
43: R=CH_3



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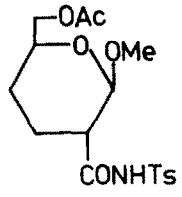

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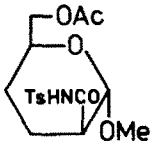

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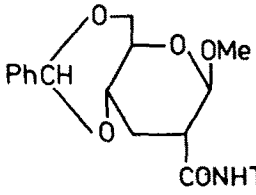

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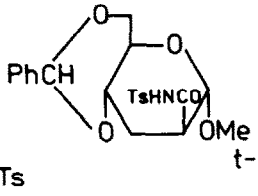

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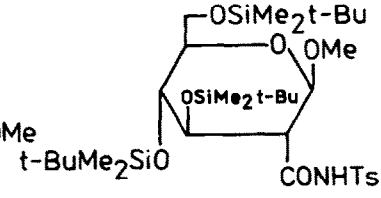

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The spectral data of the glycosides 40 - 49 (Table 4) help to prove the configuration of bicyclic β-lactams.

It is well known that high pressure accelerates the rate of reactions characterized by a negative activation volume, and greatly enhances the stereoselectivity, whereas it retards the retro-reaction. For (2+2)cycloaddition, the activation volume varies from -30 to -50 cm^3/mol, and this forecasts a significant acceleration of the reaction by high pressure.[7]

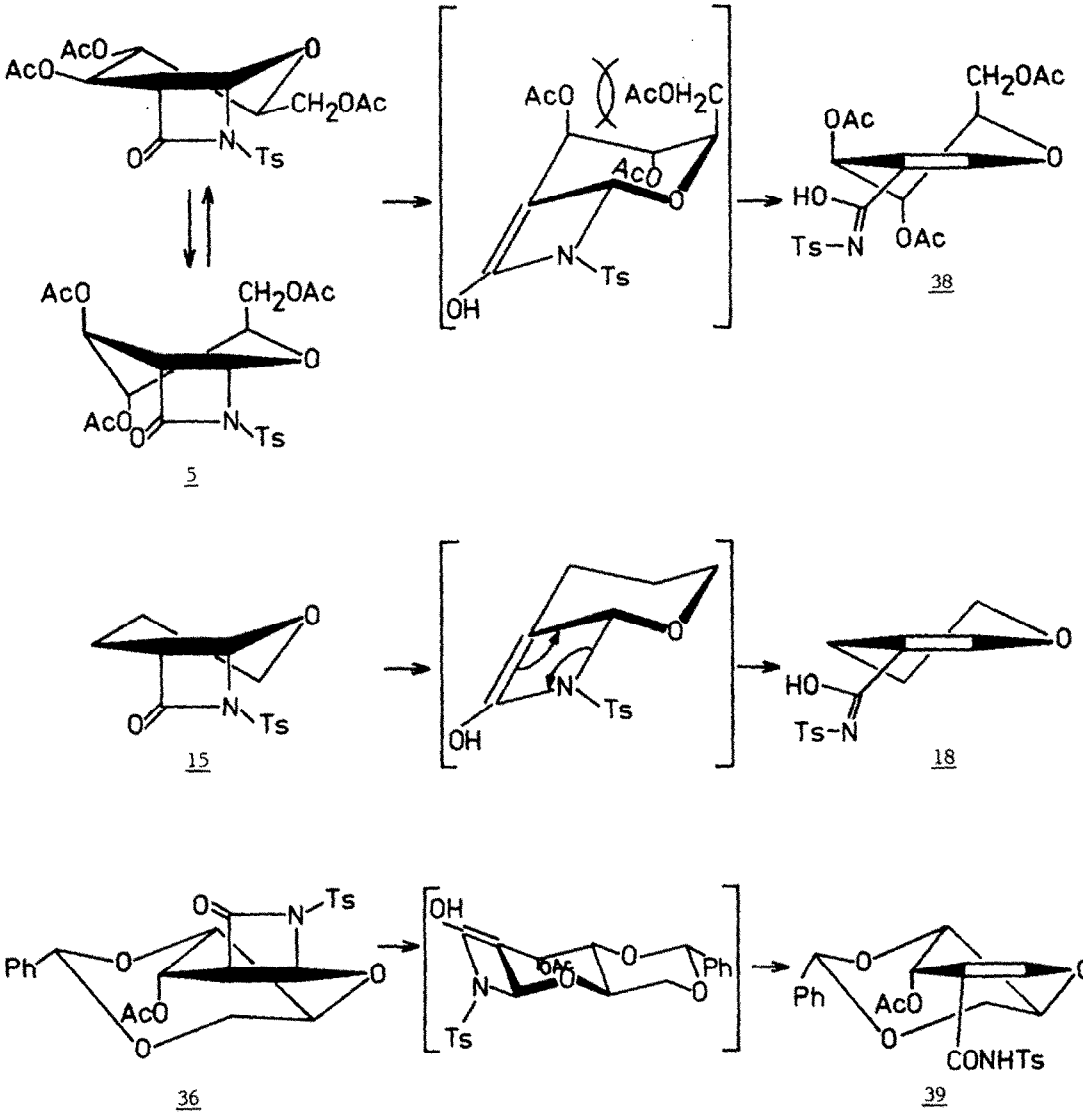
Table 4. ^{1}H NMR data for compounds 37 - 49

Comp.	H-1	H-2	H-3 H-3′	H-4	H-5	H-6 H-6′	J_{12}	J_{23}	$J_{23'}$	J_{34}	J_{45}	
37	7.97	-	5.51	5.08	4.49 4.20	-	-	-	-	a	a	$J_{55'}$=12.5
38	7.85	-	5.66	5.23	4.59	4.14 4.35	-	-	-	a	a	
39	7.71	-	5.69	3.89	4.36	3.84 4.54	-	-	-	3.4	10.6	J_{13}=0, J_{56}=10.6, $J_{56'}$=5.4, $J_{66'}$=10.7
40	4.51	2.80	5.47	4.99	3.74	4.17 4.37	8.3	10.7	-	9.1	9.8	
41	4.44	2.85	a	a	3.86	a	8.2	10.8	-	a	a	
42	4.12	2.70	5.43	4.97	a	-	7.6	10.0	-	9.5	5.3 9.0	
43	4.46	2.75	5.46	4.74	3.61	1.23	8.4	10.6	-	9.0	9.1	
44	4.38	2.52	1.72 2.32	4.71	3.62	4.15 4.23	8.4	13.0	4.3	11.1 5.1	10.0	$J_{33'}$=13.6, J_{56}=2.5, $J_{56'}$=5.3, $J_{66'}$=12.6
45	4.25	2.22	a	a	3.61	4.06 4.13	8.6	12.4	4.3	a	2.0 11.5	J_{56}=4.0, $J_{56'}$=6.5, $J_{66'}$=11.9
46	4.80	2.50	a	a	4.02	4.10 4.18	0	$\Sigma\|J\|$=10.9		a	3.4 11.5	
47	4.42	2.51	1.99 2.25	3.55	3.38	3.75 4.28	8.5	12.2	4.2	11.7 4.5	9.2	$J_{33'}$=13.0, J_{56}=10.4, $J_{56'}$=5.0, $J_{66'}$=10.8
48	4.85	2.82	2.15	3.69	3.83	3.74 4.22	0	5.0	3.0	9.9 6.2	10.1	J_{56}=10.1, $J_{56'}$=4.6, $J_{66'}$=10.5
49	4.72	2.45	3.84	4.51	∿ 3.8		8.0	1.0	-	3.5	0	

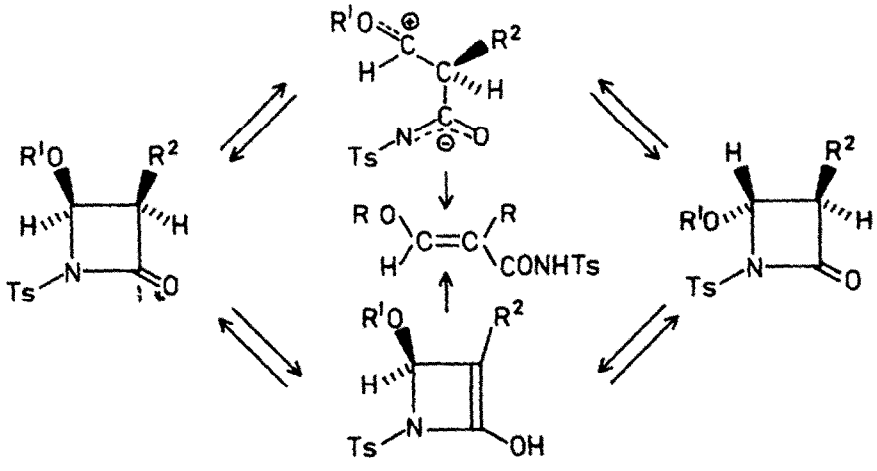
[a] not resolved or to complex for analysis

Upon heating or even after standing at room temperature, adducts 5 - 8, 28 - 30 and 34 underwent retro-addition to afford the starting glycals. This fact explains why β-lactams could not be obtained from glycals and isocyanates under thermal conditions. Moreover, this observation shows that the high-pressure technique not only accelerates the reaction rate but also allows to obtain compounds

Scheme 2



Scheme 3



thermodynamically forbidden at normal pressure. This phenomenon has earlier been observed by one of us for (4+2)cycloaddition.[8]

The rearrangement of the β-lactam ring to the α,β-unsaturated amide is a very characteristic process. Such a reaction has been recorded as a general behaviour of bicyclic β-lactams derived from dihydropyrans 9, 12 - 14,[2-4] whereas no retro-addition was observed. In case of β-lactams derived from glycals 1, 2, 4, 22 - 25, the rearrangement is possible only under high pressure. After decompression and temperature elevation the retro-process is favoured over the rearrangement, and this testifies to a lower energy barrier for the cycloaddition as compared with the rearrangement. The competition between retro-addition and rearrangement is closely related to the conformational properties of bicyclic β-lactams, and it deserves additional discussion.

It can be assumed that the pyranoid ring in adducts 34 and 35 exists in solution as a distorted $^4C_1$ chair form owing to the rigid 4,6-O-benzylidene blocking group. This is well supported by the values of coupling constants between the pyranoid ring protons. A distortion of the valence and dihedral angles is introduced in a part of the pyranoid ring, which belongs also to the four-membered β-lactam system. The conformational model drawn from adducts 34 and 35 is not, however, representative of other bicyclic β-lactams. Examination of the vicinal coupling constants between pyranoid ring protons (Table 1) testifies either to a time-average non-chair conformation of the molecule or to an equilibrium of two pseudo half-chair forms (Scheme 2). The ratio of conformers involved in the equilibrium depends on the substitution at the C-3 and C-4 carbon atoms. It can be assumed, however, that the geometry of the most stable conformation requires an equatorial or pseudo-equatorial position of the C-6 carbon atom, whereas the C-1 - N bond occupies a position favoured by the anomeric effect.

The mechanism of the *cis-trans* isomerisation and of the rearrangement of β-lactams derived from enol ethers and tosyl isocyanate to α,β-unsaturated amides has been studied in detail. Effenberger et al.[9,10] have postulated the dipolar form as an intermediate (Scheme 3); the same pathway was proposed for the rearrangement. The dipolar intermediate well explains the isomerisation of simple monocyclic β-lactams; however, it does not elucidate the properties of bicyclic β-lactams obtained from glycals or dihydropyrans. The rearrangement of the β-lactam ring is probably an electrocyclic process which follows enolization of the β-lactam ring (Schemes 2 and 3). The occurrence of sp^2 hybridization in the C-2 carbon atom changes the conformation of the molecule to a distorted chair form with an equatorially positioned nitrogen atom. Such a conformation is free from torsional strains, leaving only the valence angles distorted in the part of the four-membered ring. In case of bicyclic β-lactams having a relative *trans*-configuration at the C-1 and C-5 carbon atoms (5, 6, 8, 28 - 30, 34), enolization requires a shift of the C-6 carbon atom to the axial position and hence causes a 1,3-diaxial repulsion between the substituents at the C-3, C-4 and C-5 carbon atoms (Scheme 2). Such a conformation fails to be destabilized in case of the cycloadduct derived from xylal 7 (there is no 1,3-diaxial repulsion between the OAc and CH_2OAc group) and of those obtained from unsubstituted dihydropyran 15. Adducts with mutual *cis*-orientation of substituents at C-1 and C-5 can be easily transformed into an enolic form without inversion of the pyranoid ring.

Elevation of the temperature of high-pressure experiments before decompression shifts the reaction to the stage of unsaturated amides, because the retro-reaction is retarded. Allal 27 which reacts with tosyl isocyanate at 50°C undergoes cycloaddition *trans* to the axial acetoxyl at C-3 to afford 36, followed by a rapid rearrangement to open-chain amide 39. This result corresponds well with the model proposed above (Scheme 2). Also the shift of the high-pressure reaction from β-lactams to unsaturated amides suggests a concerted electrocyclic mechanism of rearrangement rather than one *via* the dipolar intermediate.

The difference in behaviour between β-lactams 5, 6, 8, 28 - 30, 34 with a methyl or oxyalkyl substituent attached to the pyranoid ring and those without it (7, 15), as well as stereospecificity of opening of the β-lactam ring with methanol strongly suggest an absence of the dipolar intermediate in both reactions. Such a mechanism involving the enol form as an intermediate can also be proposed for the *cis* ⇄ *trans* equilibrium in monocyclic β-lactams (Scheme 3).

Table 5. Analytical data for adducts 5 - 8, 28 - 35, 37 and 39[a]

Substrate	Temp. °C	Products[b]	Yield %	IR cm^{-1}	$(\alpha)_D$ c=1, $CHCl_3$	M.p. °C
1	RT	5	43	1800	+80.3°	102-104
1	50	5	59			
		38	~5	1600, 1695	c	c
2	RT	6	-	1810	c	syrup
3	RT	7	75	1805	-110.0°	89-90
3	50	37	25	1605, 1695	c	c
4	RT	8(95), 31(5)	77	1805	-110.0°	95-97
15	RT	28(75), 32(25)	65	1815	c	c
16	RT	29(65), 33(35)	81	1800	c	c
17	RT	30	-	1810	c	syrup
18	RT	34(50), 35(50)	71	1810	c	c
20	50	39	50	1605, 1695	+77.8°	98-101

[a] elemental analysis of compounds shown in this table are not consistent due to the instability of material obtained

[b] ratios of isomers given in brackets are taken from the ^1H NMR spectra

[c] crude product or a mixture of products

Table 6. Analytical data for compounds 40 - 49

Substrate	Product	$(\alpha)_D$ c=1, $CHCl_3$	IR cm^{-1}	M.p. °C	Molecular formula	Elemental analysis Calcd. C%	H%	N%	Found C%	H%	N%
5	40	+45.0°	3370, 1750	92-93	$C_{21}H_{27}O_{11}NS$	50.3	5.4	2.8	a	a	a
6	41	+16.6°	3360, 1750	61-65	$C_{21}H_{27}O_{11}NS$	50.3	5.4	2.8	49.7	5.5	2.8
7	42	-29.2°	3370, 1755	79-82	$C_{18}H_{23}O_9NS$	50.3	5.4	3.3	50.0	5.4	3.4
8	43	-60.6°	3380, 1755	58-60	$C_{19}H_{25}O_9NS$	51.5	5.7	3.2	51.4	5.8	3.2
28, 32	44	+5.6°	3240, 1740	49-54	$C_{19}H_{25}O_9NS$	51.5	5.7	3.2	a	a	a
29, 33	45, 46	-	3240, 1740	-	$C_{17}H_{23}O_7NS$	53.0	6.0	3.6	a	a	a
30	49	-7.2°	3240, 1730	93-98	$C_{33}H_{63}O_8NSSi_3$	55.2	8.8	1.9	55.0	9.1	2.0
31, 32	47	-10.5°	3240, 1725	167-169	$C_{22}H_{25}O_7NS$	59.0	5.6	3.1	59.1	5.7	3.3
	48	+42.4°	3250, 1725	219-221	$C_{22}H_{25}O_7NS$	59.0	5.6	3.1	58.7	5.7	3.5

[a] samples of 40, 44 and the mixture of 45 and 46 obtained from different experiments and which were identical (TLC, IR and ^1H NMR data) gave inconsistent elemental analyses

EXPERIMENTAL

Melting points are uncorrected. ^{1}H NMR spectra were recorded for $CDCl_3$ solutions with a Jeol JNM-4H-100, Bruker WH-270 or Bruker WM-500 spectrometer (δ scale, TMS=0 ppm). ^{13}C NMR spectra were obtained on a Varian CFT 20 spectrometer. Optical rotations were measured with a Perkin-Elmer 141 spectropolarimeter. IR spectra were recorded on a Beckman 4240 spectrophotometer. Gravity column chromatography was performed on Merck Kieselgel 60 (230-400 mesh). TLC was performed on Merck DC Alufolien Kieselgel 60F-254.

A mixture of diastereoisomers 29 and 33 were obtained according to the procedure described earlier.[2]

General method of the high-pressure cycloaddition. Reactions between glycals 1 - 4, 22, 24 - 27 and toluene-4-sulphonyl isocyanate were carried out for 18 - 20 h in absolute ethyl ether as solvent, at room or 50°C temperature under 10 - 11 kbar. The reaction mixture: 1 mmol of glycal, 1.5 mmol of the isocyanate and 2.5 ml of ethyl ether was placed in a Teflon ampoule which was inserted into the high-pressure vessel filled with hexane as a transmission medium. After decompression, the mixture was diluted with absolute ethyl ether (10 ml), dry pentane was added until the solution became cloudy, and then it was left at refrigerator overnight. The crystalline cycloadduct precipitated from the post-reaction mixture, was isolated by filtration and characterized as crude solid (Table 5). Ratios of diastereoisomers were determined from the ^{1}H NMR spectra.

General method of methanolysis of the bicyclic β-lactams. A bicyclic β-lactam (0.5 mmol) was treated with 5 ml of methanol and left at room temperature for 1 h. Subsequently the solvent was evaporated and the product was purified by chromatography to give the appropriate methyl glycoside in about 70% yield (Table 6). Diastereoisomeric glycosides 47 and 48 were chromatographically separated into pure components.

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REFERENCES

1. M. Chmielewski, Z. Kałuża, C. Bełżecki, P. Sałański and J. Jurczak, Tetrahedron Lett., 25, 4797 (1984).
2. E. Effenberger and R. Gleiter, Chem. Ber., 97, 1576 (1964).
3. A. G. M. Barrett, A. Fenwick and M. J. Batts, J. Chem. Soc., Chem. Commun., 299 (1983).
4. J. H. Chan and S. S. Hall, J. Org. Chem., 49, 195 (1984).
5. R. H. Hall, A. Jordaan and G. J. Laurens, J. Chem. Soc., Perkin I, 38 (1973); R. H. Hall, A.Jordaan and O. G. de Villiers, Ibid., 626 (1975).
6. E. J. Moriconi and W. C. Meyer, J. Org. Chem., 36, 2841 (1971).
7. T. Asano and W. J. leNoble, Chem. Rev., 78, 407 (1978).
8. J. Jurczak, T. Kozluk, S. Filipek and C. H. Eugster, Helv. Chim. Acta, 66, 222 (1983).
9. E. Effenberger, P. Fischer, G. Prossel and G. Kiefer, Chem. Ber., 104, 1987 (1971).
10. E. Effenberger, G. Prossel and P. Fischer, Chem. Ber., 104, 2002 (1971).