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HIGH- AND ATMOSPHERIC-PRESSURE CYCLOADDITION OF TRICHLOROACETYL ISOCYANATE TO 3,4-DI-O-ACETYL-L-RHAMNAL

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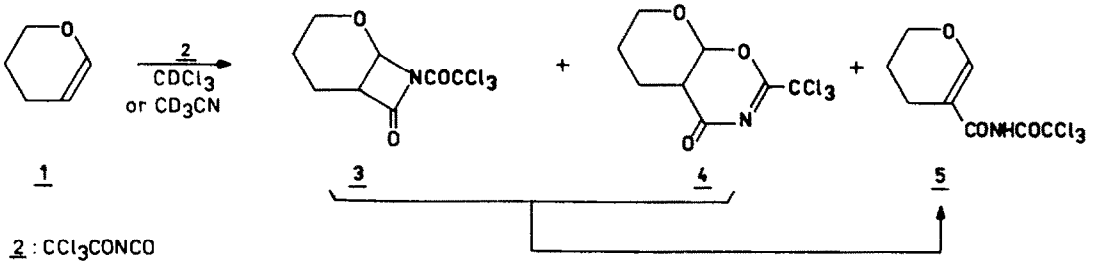
Abstract - High- and atmospheric-pressure cycloaddition of trichloroacetyl isocyanate (2) to 3,4-di-O-acetyl-L-rhamnal (11) leads to formation of four products: α-*gluco* (4+2)cycloadduct 12, two stereoisomeric α-*gluco* 13 and β-*manno* 14 (2+2)cycloadducts, and α,β-unsaturated amide 15. The isocyanate enters the rhamnal molecule preferentially *anti* with respect to the 3-O-acetyl substituent. It is found that under conditions of both - high and normal pressure (4+2)cycloaddition is preferred over (2+2)cycloaddition, more so under high pressure. Under normal pressure, better stereoselectivity in (2+2) cycloaddition is obtained. Elevation of temperature and prolongation of the reaction time promote rearrangement to α,β-unsaturated amide.

Transformations of the reaction products into N-unsubstituted: 1-O-trichloroacetyl compound 20, methyl glycosides 23 and 24, β-lactam 25, α,β-unsaturated amide 26, and into the 4-aza-2,10-dioxabicyclo(4.2.0)decan-5-one skeleton 16-19 are described.

Chitwood, Gott, and Martin[1] have found that dihydro-2H-pyran (1) treated with trichloroacetyl isocyanate (2) affords the amide 5, *via* intermediate formation of unstable β-lactam 3, and (4+2)adduct 4. They have observed that the reaction performed in acetonitrile proceeds ten times faster than that run in chloroform. Owing to their low stability, both by-products have only been detected in a n.m.r. test-tube[1] (Scheme 1).

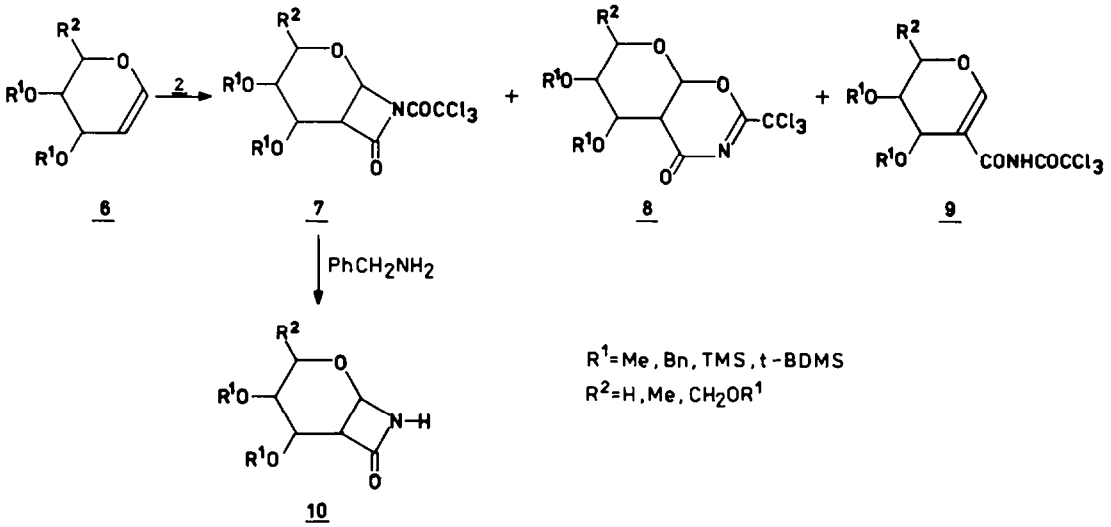
Scheme 1



Recently we have found that acetylated glycals treated with sulfonyl or acyl isocyanates in chloroform solution remains unreactive.[2] Prolongation of the reaction time has led to slow decomposition of the sugar substrate. Application of high pressure has been found to enable cycloaddition of sulfonyl[3] and acyl[4] isocyanates to acetylated glycals; cycloaddition of sulfonyl isocyanates proceeded with high stereoselectivity to afford the β-lactam ring *anti* with respect to the C-3 substituent.[3] On the other hand, trichloroacetyl isocyanate (2) has been observed to exhibit low chemo- and stereoselectivity, yielding three products: (4+2)cycloadduct and two β-lactams.[4]

Glycals with non-polar substituents at the hydroxyl groups have been found to react readily under atmospheric pressure with 2-3 molar equivalents of sulfonyl[5] or acyl[5,6] isocyanates; the rate of addition and the composition of the reaction mixture differed in dependence on the solvent and substrates used (Scheme 2). The pathway of cycloaddition of glycals 6 to trichloroacetyl isocyanate (2) has been found to be similar to that reported by Chitwood at al.[1] for unsubstituted dihydro-2H--pyran (Scheme 1). The former cycloaddition exhibits high stereoselectivity of β-lactam formation, in contrast to that found for acetylated glycals and for the same isocyanate under high pressure conditions.[4] Intermediate products 7 and 8 can be followed using the ^{1}H-n.m.r. technique. The progress of reactions leading from 6 to 9 can be stopped by addition of benzylamine to the reaction mixture.[5,6] This leads to N-deprotection of (2+2)adduct and to formation of stable bicyclic β-lactam 10 which can be easily isolated from the post-reaction mixture.[5,6]

Scheme 2



6 7 8 9 10

Cycloadducts produced under high pressure from acetylated glycals, usually crystallize during the experiment. This fact creates a unique possibility of investigating the properties of these unstable compounds being very sensitive to traces of protonic solvents, readily rearranging to α,β--unsaturated amides, and easily undergoing retro addition. We have earlier studied labile β-lactams obtained by addition of tosyl isocyanate to acetylated glycals.[3]

In this paper we selected 3,4-di-O-acetyl-1,5-anhydro-2,6-dideoxy-L-*arabino*-hex-1-enitol (di--O-acetyl-L-rhamnal; 11) as the model glycal for investigation of cycloaddition to trichloroacetyl isocyanate (2). We also studied the properties of unstable (4+2)cycloadduct which can be obtained using this method in a nearly pure form.

RESULTS AND DISCUSSION

Reactions between di-O-acetyl-L-rhamnal (11) and trichloroacetyl isocyanate (2) were conducted in abs. ethyl ether under 6, 10, and 15 kbar pressure, in abs. chloroform-d or abs. acetonitrile-d_3 under 6 kbar pressure, and in abs. acetonitrile-d_3 at normal pressure. Atmospheric pressure experiments were performed at 20°, 40°, and 60° C, whereas those at high pressure were carried out at room temperature. In all experiments, two molar equivalents of 2 were used. Experiments performed under normal pressure were carried out in n.m.r. test-tubes. The progress of all reactions was monitored by ^{1}H-n.m.r. spectra recorded in CD_3CN solutions. In all reactions four products were obtained: α-*gluco* (4+2)cycloadduct (12), two stereomeric α-*gluco* and β-*manno* 14 (2+2)cycloadducts, and α,β--unsaturated amide 15. The isocyanate enters the rhamnal molecule preferantially *anti* with respect to the 3-O-acetyl substituent.

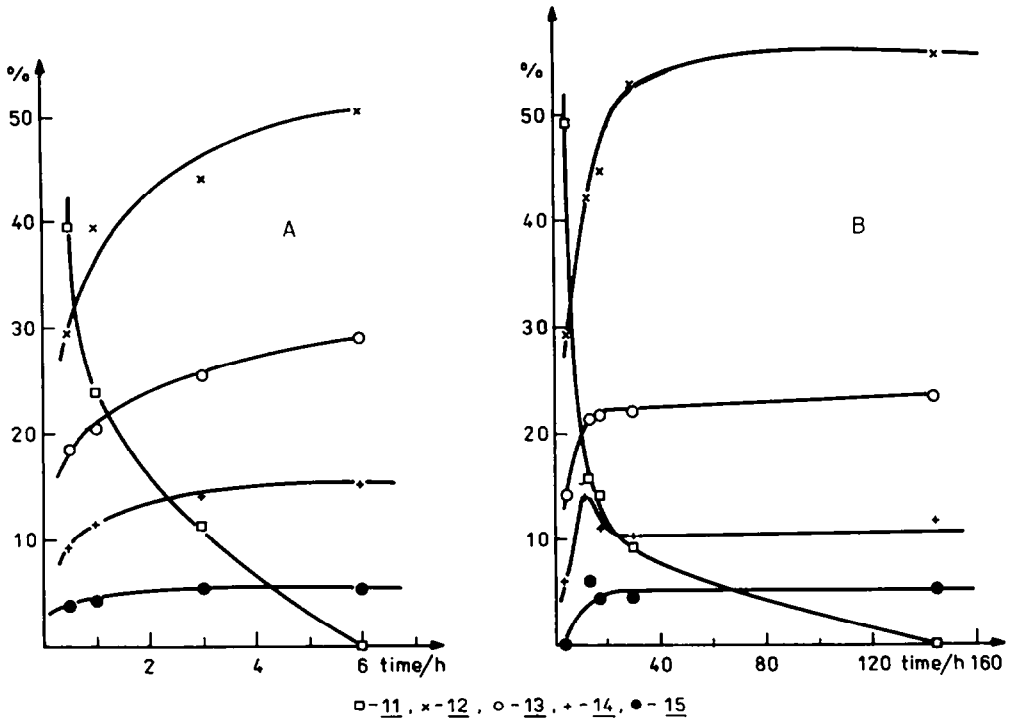


Fig. 1. Plots representing the time-dependence of the reaction mixture composition, for the addition of trichloroacetyl isocyanate (2) to 3,4-di-O-acetyl-L-rhamnal (11); room temperature, 6 kbar pressure; A in CD_3CN, B in $CDCl_3$.

Table 1. The pressure-dependence of the reaction mixture composition, for the addition of trichloroacetyl isocyanate (2) to 3,4-di-O-acetyl-L-rhamnal (11); ethyl ether, room temperature, 20° C.

ΔP/kbar	11	12	13	14	15
6	19.6	39.8	23.9	13.8	2.9
10	-	56.4	24.1	15.8	3.7
15	-	54.6	25.0	13.9	6.5

Table 2. The relationship between the reaction mixture composition and molar ratio of 3,4-di-O-acetyl-L-rhamnal (11) to trichloroacetyl isocyanate (2); CD_3CN, atmospheric pressure, 20° C.

11:2	time/h	11	12	13	14	15
1:2	24	52.5	20.7	18.3	8.5	-
	72	24.0	34.7	30.0	8.0	3.3
1:4	24	48.4	25.8	23.6	2.2	-
	72	19.4	42.7	28.2	6.5	3.2
1:6	24	45.7	27.1	24.3	2.9	-
	72	14.8	45.2	31.3	5.2	3.9
1:10	24	40.4	29.2	27.0	3.4	-
	72	14.3	41.8	31.8	7.7	4.4

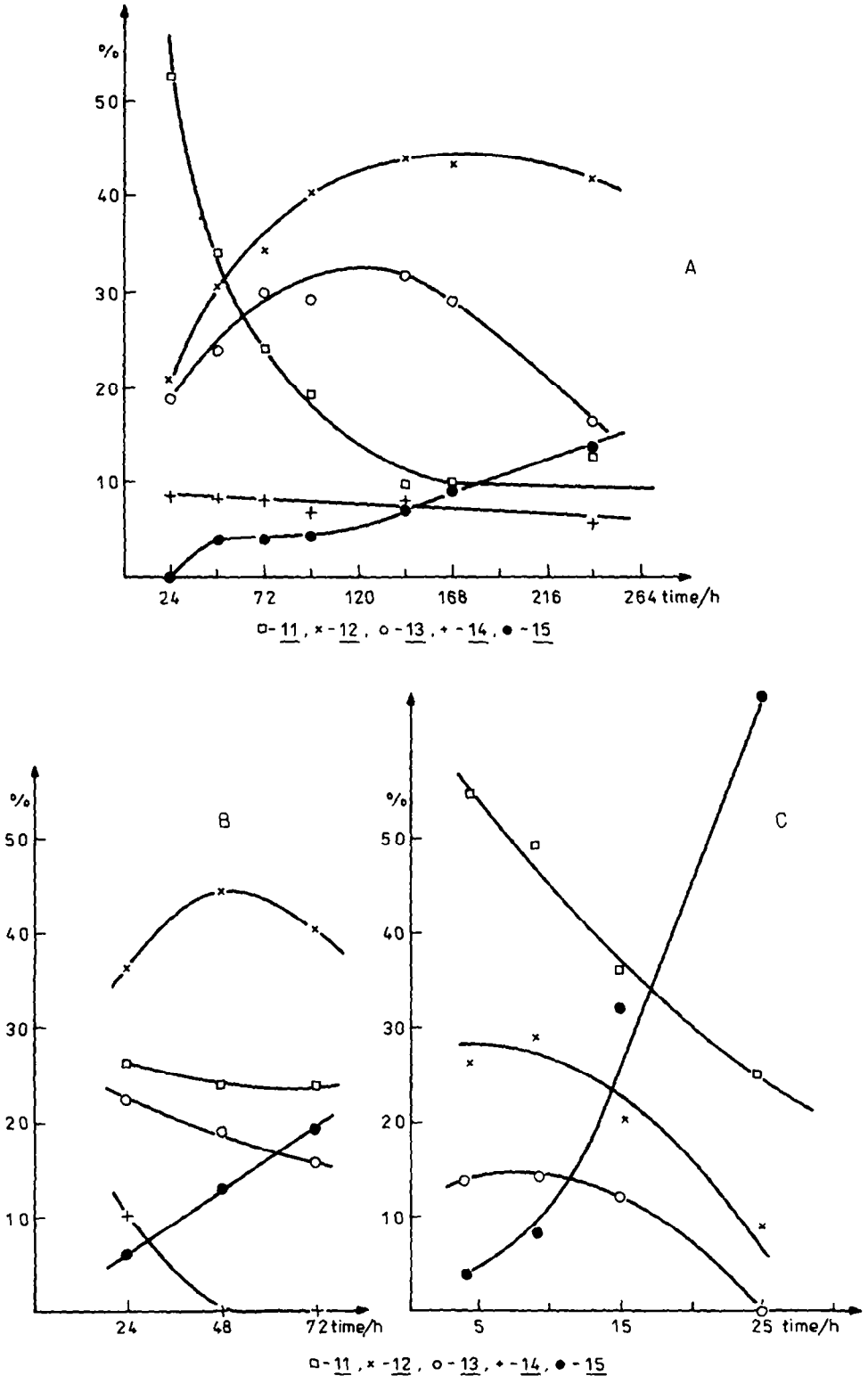


Fig. 2. Plots representing the time-dependence of the reaction mixture composition, for the addition of trichloroacetyl isocyanate (2) to 3,4-di-O-acetyl-L-rhamnal (11); CD_3CN, atmospheric pressure; A at 20°, B at 40°, and C at 60° C.

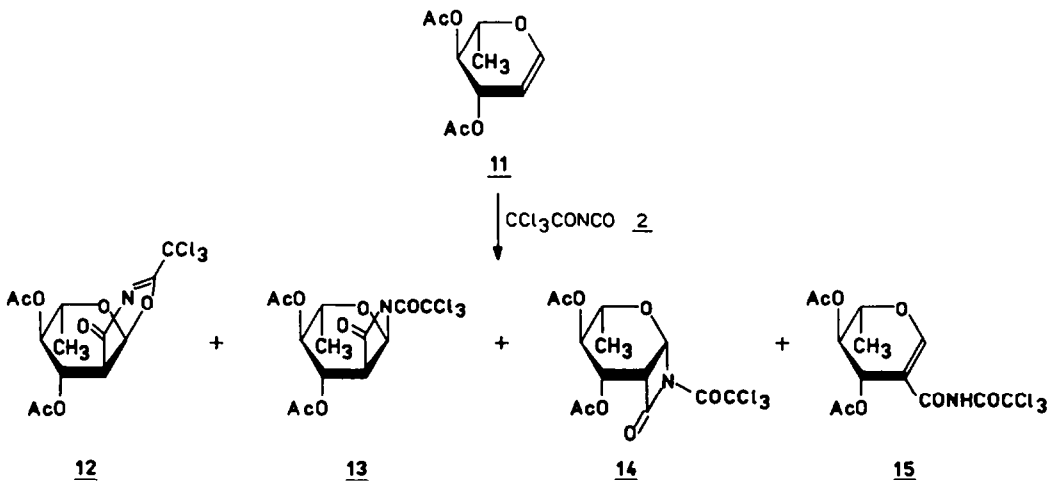
Cycloadducts 12-14 were characterized by chemical shift and coupling constants for protons H-1, whereas amide 15 was characterized by chemical shift of H-1 proton. Integration of the respective signals gave the composition of the reaction mixtures. Percentages of substrate 11 and of products 12-15, in dependence on solvent, pressure, temperature, and initial proportion of substrates are presented in Table 1, 2 and Fig. 1, 2.

The present results may be summarized as follows:

1. Under conditions of both - high and normal pressure (4+2)cycloaddition is favored over (2+2)cycloaddition, more so under high pressure (cf. Table 1 and Fig. 1 with Fig. 2).
2. Under high pressure, upon prolongation of reaction time, the initial proportion of products 12-15 remains unchanged (Fig. 1).
3. The stereoselectivity of (2+2)cycloaddition at atmospheric pressure is higher than that under high pressure. At 20° the ratio of α-*gluco* 13 to β-*manno* 14 amounts to 2:1 after 24 h, whereas after 4 days it reaches 4:1. On the other hand, under high pressure the proportion of respective β-lactams 13 and 14 never exceeds 2:1.
4. At 20°, under atmospheric pressure the proportion of 11 and of cycloadducts 12-14 after 6 days remains constant.
5. At 40° and 60° the content of 12 initially rises, and then decreases.
6. The content of α,β-unsaturated amide 15 increases with a rise of temperature and prolongation of the reaction time; at 60°, after 48 h the amide 15 becomes the only product.
7. The initial proportion of 11:2 displays a slight effect on the rate of cycloaddition, whereas it does not influence the chemo- and stereoselectivity (Table 2).

Our experiments performed under high and atmospheric pressure clearly point to the reversibility of cycloaddition of isocyanates to glycals. High pressure not only accelerates the reaction rate but also allows obtainment of compounds thermodynamically unstable at normal pressure. In the light of the literature data and of our findings, free energy of activation of cycloaddition, that of the reverse reaction, and that of the rearrangement to α,β-unsaturated amide do not differ considerably. Hence, slight modification of the glycal moiety, such as introduction of non-polar protection to the hydroxyl groups, or even a change in the solvent, can shift the reaction toward the desired cycloadduct, or subsequently toward the unsaturated amide. Polar solvents, such as acetonitrile, act in a dual manner, causing acceleration of the reaction rate and a shift of the equilibrium toward cycloadducts. Elevation of temperature of the reaction increases the rate of the rearrangement and that of the retro addition. At 40° and 60°, initially an excess of 2 causes a shift of the reaction toward cycloadducts. Subsequently the rate of the rearrangement and that of the retro reaction begin to play a decisive role. This is well visible upon comparison of the conversions of the substrate at 40° and 60°, which after 24 h are the same, although, there is a dramatic difference in the composition between both mixtures.

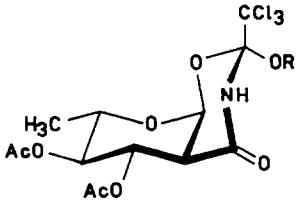
Scheme 3

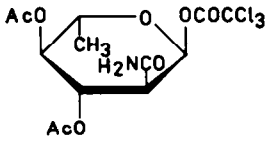


The rearrangement of β-*manno* adduct 14 is faster than that of 12 and 13. This can be assumed on the basis of the high selectivity of (2+2)cycloaddition at 40° and 60°; this fact is in good agreement with our earlier speculations concerning high-pressure (2+2)cycloaddition of tosyl isocyanate to acetylated glycals.[4]

The addition of 2 to di-O-acetyl-L-rhamnal (11) under 10 kbar pressure was used for preparation of (4+2)cycloadduct 12. The post-reaction mixture obtained after decompression was left standing overnight for crystallization. The crystals of 12 were separated in a good yield and in a nearly pure form. (4+2)Cycloadduct 12 was obtained stereospecifically, as a result of addition of 2 *anti* with respect of the C-3 acetoxy group. Formation of both stereomeric (4+2)cycloadducts was observed for 3-deoxy glycals only.[6] The stereospecificity of formation of 12 can be attributed to the kinetic control of addition by the C-3 substituent, but a shift of the equilibrium β(4+2)⇄ β(2+2)cycloadducts entirely toward β-lactam should also be taken into consideration. This equilibrium found by Martin at al.[1] is usually shifted toward (4+2)cycloadduct, although a higher stability of β-lactam has also been observed.[5,6]

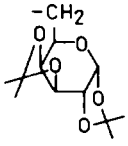
Scheme 4

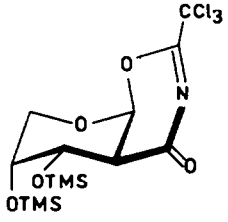




20

16 ; R=Me
17 ; R=Et
18 ; R=PhCH2





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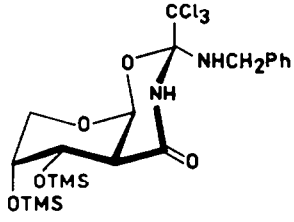

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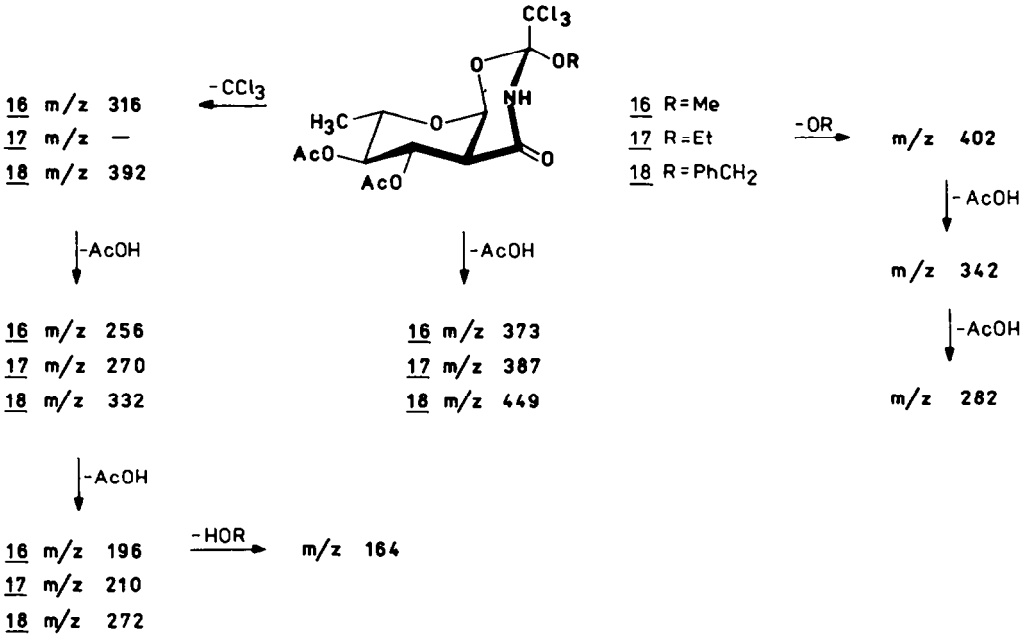
Compound 12 represents a reactive intermediate with the cyclic imidate structure. Such an unstable bicyclic system has been isolated in pure form, for the first time. On account of the role played in the synthesis of oligosaccharides by anomeric imidates derived from trichloroacetonitrile,[7] we resolved to investigate the chemistry of compound 12.

Compound 12 treated with an excess of alcohol (e.g. methanol, ethanol, or benzyl alcohol) gave bicyclic compounds 16, 17, and 18, respectively.[8] Sugars containing the free primary alcohol function, such as diisopropylidene galactose, are unreactive under these conditions. Application of 10 kbar pressure enables, however, formation of pseudo disaccharide 19. The nucleophile enters exclusively the imidate carbon atom, with formation of one diastereomer only. The bicyclic structure of compounds 16–19 was proved by ^{1}H-n.m.r. and MS spectral data. The same direction of attack is observed upon addition of water molecule; the initially formed bicyclic product undergoes immediate opening to give the 1-O-trichloroacetyl derivative 20.[8] Recently, we have found that benzylamine could also be added to the C=N double bond of the silylated β-*arabino* adduct 21, yielding unstable bicyclic compound 22.[6] The configuration of the quaternary carbon atom in 16–19, and in 22 was assigned on the assumption of axial attack of the approaching nucleophile.[9]

The mass spectra of compounds 16–19 clearly testify to their bicyclic structure; they do not show any peak which can be attributed to splitting off of the anomeric substituent (cf. ion 258 found for 20 and 23). The mass spectra of 16–19 do not point to the presence of molecular ions $M^{+\cdot}$; the major fragmentation pathways are shown in Scheme 5, and they were supported by the high-resolution

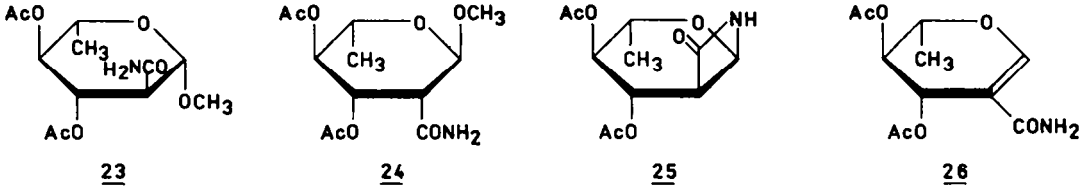
measurements. The sequence $M^+ \rightarrow 402 \rightarrow 342 \rightarrow 282$ was proved by linked scan measurement (parent and daughter ions).

Scheme 5



The post-reaction mixture, obtained under 10 kbar pressure in ethyl ether solution, after separation of imidate 12 was subjected to methanolysis. This led to a mixture of 23 and 24, with β-L-*gluco* and α-L-*manno* configuration, thus proving the configuration of the respective β-lactam precursors 13 and 14 (Scheme 6).

Scheme 6



Glycosides 23 and 24 were accompanied by compound 16 derived from imidate 12, and by traces of β-lactam 25 and amide 26.

The mixture 12-15 obtained under 10 kbar pressure in ethyl ether was passed through a Florisil column to remove the trichloroacetyl substituents. As a result, compound 20, β-lactam 25, and amide 26 were obtained. It is noteworthy that the low stability of β-*manno* adduct 14, manifesting itself by the absence of the respective N-unsubstituted β-lactam, is consistent with our earlier observations.

Studies on high- and atmospheric pressure cycloaddition of trichloroacetyl isocyanate to 3,4-di-O-acetyl-L-rhamnal facilitate understanding of chemo- and stereoselectivity in these reactions, and provide the basic informations necessary for further utilization of these reactions.

EXPERIMENTAL

Melting points are uncorrected. Optical rotations were measured with a Perkin-Elmer 141 spectropolarimeter. I.r. spectra were recorded with a Beckman 4240 spectrophotometer. Column chromatography was performed on Merck Kieselgel 60 (230-400 mesh). ^{1}H-n.m.r. spectra were recorded with a Varian EM 360 and a Bruker 300 MHz spectrometer. Mass spectra were recorded with a Finigan Mat 8200 mass spectrometer.

General method for carrying out high-pressure cycloaddition. Reactions between rhamnal 11 and trichloroacetyl isocyanate (2) were carried out in abs. ethyl ether (6, 10, and 15 kbar), chloroform (6 kbar), and acetonitrile-d_3 (6 kbar) at room temperature. The reaction mixture containing 2.5 mmol of 11, 5.0 mmol of 2, and 2.5 ml of solvent was placed in a Teflon ampoule which was then inserted into a high-pressure vessel filled with hexane as a transmission medium. After decompression the composition of the reaction mixture was determined by integration of the appropriate signals of H-1 proton in ^{1}H-n.m.r. spectra taken in CD_3CN (in case of the reactions performed in ethyl ether or chloroform, the solvent was replaced by CD_3CN; an appropriate experiment showed that low-temperature evaporation did not affect the composition). The results are recorded in Table 1 and Fig. 1.

Experiments performed in n.m.r. test-tubes. A solution of 11 (0.5 mmol) in CD_3CN (~0.5 ml) was placed in a n.m.r. test-tube, and trichloroacetyl isocyanate (1.0 mmol) was added; subsequently the tube was located in a thermostat at either 20°, or 40°, or else 60° C. The composition of the reaction mixtures was determined approximately by integration of the appropriate signals of H-1 proton and recorded in Fig. 2 and Table 2.

Cycloaddition of trichloroacetyl isocyanate (2) to 3,4-di-O-acetyl-1,5-anhydro-2,6-dideoxy-L-*arabino*-hex-1-enitol (11). *Procedure A.* Rhamnal 11 (1.1 g, 5.0 mmol) was dissolved in abs. ethyl ether (2 ml) and the solution was placed in a Teflon ampoule (4 ml). Subsequently isocyanate 2 (1.32 g, 0.83 mmol) was added, the ampoule was filled with abs. ethyl ether, closed with a Teflon stopper, inserted into a high-pressure vessel filled with hexane as a transmission medium, and 10 kbar pressure was applied for 20 h. After decompression the mixture was diluted with abs. ethyl ether (10 ml) and refrigerated overnight for crystallization. Crystals of (1S,6S,7S,8S,9S)-7,8-diacetoxy-4-aza-3-trichloromethyl-9-methyl-2,10-dioxabicyclo[4.2.0]dec-2-ene-5-one (12) 0.88 g (40.6%) were separated; mp. 92-97° C decomp.; $[\alpha]_D$ +9.8° (c 2, CH_2Cl_2); ^{1}H-n.m.r. ($CDCl_3$): 1.36 (d, 3H, CH_3), 2.07 (s, 6H, 2OAc), 3.13 (dd, 1H, J_{16}=3.8, J_{67}=11.2 Hz, H-6), 4.20 (dq, 1H, J_{89}=10.0 Hz, H-9), 4.97 (t, 1H, J_{78}=9.5 Hz, H-8), 5.25 (dd, 1H, H-7), 6.03 (d, 1H, H-1); ^{13}C-n.m.r. ($CDCl_3$): 17.19 (CH_3), 47.27 (C-6), 67.83, 70.32, 71.41 (C-7,8,9), 100.62 (C-1). The mother liquer was concentrated and treated with methanol (10 ml). Subsequently the mixture was evaporated and separated on a silica gel column to give the following three fractions:
(1S,3R,6S,7S,8S,9S)-7,8-Diacetoxy-4-aza-3-trichloromethyl-3-methoxy-9-methyl-2,10-dioxabicyclo[4.2.0]-decan-5-one (16), 0.26 g; m.p. 181-182° C; $[\alpha]_D$ -139.0° (c 2, CH_2Cl_2); ^{1}H-n.m.r. ($CDCl_3$): 1.28 (d, 3H, CH_3), 2.06 (2s, 6H, 2OAc), 2.85 (dd, 1H, J_{16}=3.3, J_{67}=10.7 Hz, H-6), 3.68 (s, 3H, OCH_3), 4.21 (dq, 1H, J_{89}=9.6 Hz, H-9), 4.88 (t, 1H, J_{78}=9.6 Hz, H-8), 5.62 (d, 1H, H-1), 5.76 (dd, 1H, H-7); ^{13}C-n.m.r. ($CDCl_3$): 17.30 (CH_3), 46.85 (C-6), 54.37 (OCH_3), 68.08, 68.83, 72.57 (C-7,8,9), 93.32 (C-1), 101.63 (CCl_3), 104.21 (C-3); MS m/z: M^+-Cl, 397.0339 (397.0336 for $C_{14}H_{17}NO_8Cl_2$), M^+-OCH_3-AcOH, 342.9728 (342.9703 for $C_{11}H_{11}NO_5Cl_3$).
3,4-Di-O-acetyl-2-carboxy-2,6-dideoxy-α-L-*gluco*-pyranosylaminolactam (25), 0.05 g; m.p. 123-125°; $[\alpha]_D$ -101.4° (c 1.5, CH_2Cl_2); ^{1}H-n.m.r. ($CDCl_3$): 1.25 (d, 3H, CH_3), 2.05, 2.07 (2s, 6H, 2OAc), 3.41 (m, 1H, H-2), 4.09 (dq, 1H, H-5), 4.81 (dd, 1H, J_{34}=6.3, J_{45}=8.8 Hz, H-4), 5.33 (dd, 1H, J_{23}=2.3 Hz, H-3), 5.52 (d, 1H, J_{12}=4.5 Hz, H-1); MS m/z: M^+-HNCO, 214.0841 (214.0841 for $C_{10}H_{14}O_5$), M^+-AcOH, 197.0682 (197.0682 for $C_9H_{11}NO_4$).
3,4-Di-O-acetyl-1,5-anhydro-2-carbamoyl-2,6-dideoxy-L-*arabino*-hex-1-enitol (26), 0.12 g; m.p. 151-152° C; $[\alpha]_D$ +96.6° (c 2, CH_2Cl_2); ^{1}H-n.m.r. ($CDCl_3$): 1.44 (d, 3H, CH_3), 2.08, 2.11 (2s, 6H, 2OAc), 4.47 (m, 1H, H-5), 4.99 (t, 1H, J_{34}=3.0, J_{45}=2.8 Hz, H-4), 5.64 (dd, 1H, J_{35}=1.6 Hz, H-3), 7.73 (s, 1H, H-1); MS m/z: M^+-AcOH-CH_2CO, 155.0570 (155.0588 for $C_7H_9NO_5$).
A mixture of 23 and 24, 0.27 g; crystallization from chloroform-hexane gave methyl 3,4-di-O-acetyl-2-carbamoyl-2,6-dideoxy-β-L-*gluco*-hexopyranoside (23), 0.14 g; m.p. 200-201° C; $[\alpha]_D$ -37.7° (c 1.2, CH_2Cl_2); ^{1}H-n.m.r. ($CDCl_3$): 1.26 (d, 3H, CH_3), 2.00, 2.05 (2s, 6H, 2OAc), 2.63 (dd, 1H, J_{12}=8.4, J_{23}=11.0 Hz, H-2), 3.54 (s, 3H, OCH_3), 3.63 (dq, 1H, H-5), 4.58 (d, 1H, H-1), 4.77 (t, 1H, J_{34}=9.3, J_{45}=9.5 Hz, H-4), 5.52 (dd, 1H, H-3); MS m/z: M^+-CH_3O, 258.0977 (258.0977 for $C_{11}H_{16}NO_6$). ^{1}H-n.m.r. data of methyl 3,4-di-O-acetyl-2-carbamoyl-2,6-dideoxy-α-L-*manno*-hexopyranoside (24) taken from the spectrum of a mixture of 23 and 24; ($CDCl_3$): 1.26 (d.3H, CH_3), 2.05, 2.08 (2s, 6H, 2OAc), 3.22 (dd, 1H, J_{12}=1.6, J_{23}=6.2 Hz, H-2), 3.42 (s, 3H, OCH_3), 3.92 (dq, 1H, J_{45}=9.8 Hz, H-5), 5.07 (d, 1H, H-1), 5.17 (t, 1H, J_{34}=9.3 Hz, H-4), 5.42 (dd, 1H, H-3).
Procedure B. A solution of compound 11 (0.32 g, 1.5 mmol) and 2 (0.22 ml, 1.7 mmol) in abs. ethyl ether (2 ml) was compressed as described above. After decompression the mixture was diluted with abs. ethyl ether (20 ml) and passed through a Florisil (10 g) column. The column was washed with ethyl ether (10 ml) and washings were combined with the eluate. Subsequently the column was washed with 10% methanol in chloroform (50 ml). Concentration of the ethereal solution afforded 3,4-di-O-acetyl-2-carbamoyl-2,6-dideoxy-1-trichloroacetyl-α-L-*gluco*-hexopyranose (20), 0.2 g (32%), m.p. 147-149° C; $[\alpha]_D$ -125.4° (c 1.1, CH_2Cl_2); ^{1}H-n.m.r. ($CDCl_3$): 1.27 (d, 3H, CH_3), 2.10 (s, 6H, 2OAc), 3.17 (dd, 1H, J_{12}=3.2, J_{23}=10.8 Hz, H-2), 4.10 (dq, 1H, J_{45}=9.8 Hz, H-5), 4.88 (t, 1H, J_{34}=9.8 Hz, H-4), 5.63 (dd, 1H, H-3), 6.52 (d, 1H, H-1); ^{13}C-n.m.r. ($CDCl_3$): 17.34 (C-6), 51.15 (C-2), 68.37, 69.00, 73.67 (C-3,4,5), 95.61 (C-1); MS m/z: M^+-CCl_3CO_2, 258.0970 (258.0978 for $C_{11}H_{16}NO_6$). The methanol solution was evaporated and the mixture was separated on a silica gel column to give 25 (0.046 g, 12%) and 26 (0.037 g, 9%).

(1S,3R,6S,7S,8S,9S)-7,8-Diacetoxy-4-aza-3-trichloromethyl-3-methoxy-9-methyl-2,10-dioxabicyclo-[4.2.0]decan-5-one (16). Compound 12 (0.04 g, 0.1 mmol) was dissolved in methanol (1 ml). After 30 min methanol was evaporated and the residue was recrystallized from a ethyl acetate - hexane mixture to afford 16 (0.036 g, 83%).

(1S,3R,6S,7S,8S,9S)-7,8-Diacetoxy-4-aza-3-trichloromethyl-3-ethoxy-9-methyl-2,10-dioxabicyclo-[4.2.0]decan-5-one (17). Compound 17 was obtained according to the procedure described above (80%); m.p. 182-185° C; $[\alpha]_D$ -150.0° (c 1.3, CH_2Cl_2); ^{1}H-n.m.r. ($CDCl_3$): 1.28 (d, 3H, CH_3), 1.29 (t, 3H, OCH_2CH_3), 2.06, 2.07 (2s, 6H, 2OAc), 2.84 (dd, 1H, J_{16}=3.3, J_{67}=10.8 Hz, H-6), 4.00 (m, 2H, OCH_2CH_3), 4.22 (dq, 1H, H-9), 4.88 (t, 1H, J_{78}=9.7, J_{89}=10.0 Hz, H-8), 5.59 (d, 1H, H-1), 5.75 (t, 1H, H-7); MS m/z: M^+-OEt, 401.9914 (401.9914 for $C_{13}H_{15}NO_7Cl_3$), M^+-Cl, 412.0566 (412.0566 for $C_{15}H_{20}NO_8Cl_2$).

(1S,3R,6S,7S,8S,9S)-7,8-Diacetoxy-4-aza-3-benzyloxy-3-trichloromethyl-9-methyl-2,10-dioxabicyclo[4.2.0]decan-5-one (18). Compound 18 was obtained according to the procedure described above (85%); m.p. 82-84° C; $[\alpha]_D$ -134.0° (c 1.2, CH_2Cl_2), ^{1}H-n.m.r. ($CDCl_3$): 1.28 (d, 3H, CH_3), 2.03 (s, 6H, 2OAc), 2.80 (dd, 1H, J_{16}=3.4, J_{67}=10.9 Hz, H-6), 4.21 (dq, 1H, H-9), 4.87 (t, 1H, J_{78}=9.9, J_{89}=9.7 Hz, H-8), 5.02 (s, 2H, CH_2Ph), 5.54 (d, 1H, H-1), 5.76 (dd, 1H, H-7), 7.3 (bs, 5H, Ph); MS m/z: M^+-OCH_2Ph, 401.9909 (401.9914 for $C_{13}H_{15}NO_7Cl_3$), M^+-CCl_3, 392.1348 (392.1345 for $C_{19}H_{22}NO_8$).

(1S,3R,6S,7S,8S,9S)-7,8-Diacetoxy-4-aza-3-trichloromethyl-3-[6′-(1′,2′:3′,4′-diizopropylidene--D-*galacto*-piranose)]-9-methyl-2,10-dioxabicyclo[4.2.0]decan-5-one (19). Compound 12 (0.12 g, 0.3 mmol) and diizopropylidene-D-*galacto*-piranose (0.08 g, 0.32 mmol) were dissolved in methylene chloride, and high pressure (10 kbar) was applied at room temp. for 20 h. After decompression the solvent was evaporated and the crude syrup was purified on a silica gel column to give 19, 0.1 g (50%); m.p. 96-98° C; $[\alpha]_D$ -130.9° (c 1.2, CH_2Cl_2); ^{1}H-n.m.r. ($CDCl_3$): 1.27 (t, 3H, CH_3), 2.84 (dd, 1H, J_{16}=3.2, J_{67}=10.4 Hz, H-6), 4.23 (dq, 1H, J_{89}=9.7 Hz, H-9), 4.89 (t, 1H, J_{78}=9.0 Hz, H-8), 5.78 (t, 1H, H-7), 5.83 (d, 1H, H-1), signals due to the galactose portion: 4.02 (m, 1H, H-5′), 4.12, 4.15 (m, 2H, CH_2), 4.25 (dd, 1H, $J_{3',4'}$=7.6, $J_{4',5'}$=1.6 Hz, H-4′), 4.32 (dd, 1H, $J_{1',2'}$=4.6, $J_{2',3'}$=2.2 Hz, H-2′), 4.65 (dd, 1H, H-3′), 5.57 (d, 1H, H-1′); Anal. calc. for $C_{25}H_{34}Cl_3NO_{13}$: C, 45.3; H, 5.2; N, 2.1. Found: C, 46.0; H, 5.7; N, 1.9.

4,5-Di-O-acetyl-2-carbamoyl-2,6-dideoxy-1-O-trichloroacetyl-α-L-*gluco*-hexopyranose (20). Compound 12 (0.13 g, 0.3 mmol) was dissolved in THF (1 ml) and water (0.05 g) was added. After 15 min. the solvent was evaporated. The crude syrup was treated with ethyl ether (2 ml) to give crystals of 20 (0.1 g, 81%).

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