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PAPER

Hydrogen-bond-rich ionic liquids as effective organocatalysts for Diels-Alder reaction

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The synthesis and characterisation of new hydrogen-bond-rich ionic liquids and studies of their catalytic performance in Diels-Alder reactions are described. D-Glucose and chloroalcohols were used as the raw materials and as sources of hydroxyl groups for the synthesis of ionic-liquid cations, whereas weakly coordinating bis(trifluoromethylsulfonyl)imide was used as the anion. The new ionic liquids were analysed by ^{1}H and ^{13}C NMR spectroscopy and by ESI-MS experiments, which confirmed their structures. In addition, the thermal data of the studied ionic liquids measured by differential scanning calorimetry and thermogravimetric analysis showed that these compounds tend to form a glass at temperatures in the range of -29 °C to -16 °C and are thermally stable from ambient temperature to at least 430 °C, most likely because of the presence of bis(trifluoromethylesulfonyl)imide anions. The performance of the ionic liquids in the model reaction of cyclopentadiene with diethyl maleate or methyl acrylate was investigated. The studied ionic liquids showed high activity, even when present in catalytic amounts (4 mol% with respect to the dienophile). An increased number of hydroxyl groups present in the ionic liquid structure resulted in higher reaction rates.

1. Introduction

Over the past 20 years, ionic liquids, supercritical fluids and water have become powerful alternatives to conventional organic solvents. Because of their properties, which include an undetectable vapour pressure, the ability to dissolve numerous organic and inorganic substances, high thermal stability, and a wide liquid phase range, ionic liquids have become one of the most promising new reaction media.[1]

The term "green solvents" has been used to describe ionic liquids because of their negligible vapour pressure. Significant efforts have been made to design "fully green", non-toxic and biodegradable ionic liquids using renewable compounds as the starting materials. The synthesis of ionic liquids from environmentally sustainable and renewable raw materials, *e.g.*, amino alcohols (choline[2] and ephedrine[3]), hydroxy acids (lactic and tartaric acids[4]), amino acids,[5] and terpenes,[6] is becoming more reasonable compared with the use of compounds derived from fossil feed stocks.

Sugars appear to be suitable precursors for ionic liquids because they are among the most abundant and relatively inexpensive naturally occurring substances available. Research involving sugars for the preparation of ionic liquids has been limited and has only recently come to the forefront.[7] The following ionic liquids with a sugar moiety as part of the cation have been reported: ionic liquids derived from methyl D-glucopyranose,[8] glucose-tagged triazolium ionic liquids,[9] ionic liquids obtained from isosorbide,[10] mono- and bis-ammonium ionic liquids from isomannide,[11] and ionic liquids with a pentofuranose unit.[12,13] In addition, certain sugar-derived quaternary ammonium salts containing iodides and bromides have also been described in the literature.[14]

Currently, only one example of tetraalkylammonium ionic liquids with a sugar moiety on the anion has been reported: ionic liquids from D-galacturonic and D-glucuronic acids.[15]

The presence of hydroxyl groups in the sugar-derived ionic liquid structures enables them to be highly coordinating solvents, and they can be used in stereoselective and metal catalysed reactions. However, the potential utility of these sugar-derived ionic liquids has been investigated for only a few reactions.[7] The utility of ionic liquids for asymmetric induction was investigated using ionic liquids based on isosorbide in aza-Diels–Alder cycloaddition reactions between chiral imines and dienes, and moderate yields and diastereoselectivities of up to 60% *d.e.* were achieved.[10] Chiral ionic liquids obtained from 2,3,5-tri-O-benzyl-D-ribose and D-xylose have been used as co-solvents for the addition of methylmagnesium chloride to various aromatic aldehydes. The resulting chiral alcohols were recovered in nearly quantitative yield, but as racemic mixtures.[12]

The number of published articles related to the application of sugar-based ionic liquids in Diels-Alder reactions is limited. However, numerous studies on Diels–Alder reactions in other ionic liquids have shown that both the solvent and the dienophile structure influence the reaction rate and selectivity.[16] The coordination of the ionic liquid cation to dienophile decreases the gap between diene HOMO and dienophile LUMO leading to an increased chemical reactivity.[17] The interactions between characteristic groups on the dienophile and ions from the ionic

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liquids have been described.[16] The selectivity of Diels–Alder reactions in ionic liquids appears to be dependent on the hydrogen-bond donor capacity of the ionic liquid; the ions can stabilise the transition state of the Diels–Alder reaction by forming hydrogen bonds, *e.g.*, with the carbonyl oxygen in the dienophile. Furthermore, ionic liquids possessing weakly coordinating bis(trifluoromethylsulfonyl)imide (bistriflamide, [Tf_2N]) anions are one of the most active ionic liquids for the Diels-Alder reaction.

Inspired by the literature, we decided to design new hydrogen-bond-rich ionic liquids based on D-glucopyranoside derivatives as the cation precursor and the bistriflamide anion. The potential of these compounds to act as organocatalysts in a Diels-Alder reaction was demonstrated. This study expands the chemistry of sugar-based ionic liquids, which is currently in its infancy.

2. Experimental section

2.1. Materials and instrumentation

D-Glucose, chloroalcohols (2-chloroethanol, 3-chloropropanol, and 3-chloro-1,2-propanediol), 1-methyl-3-butylimidazolium chloride, sulfamic acid, trialkylamines, lithium bistriflamide, *n*-decane, and the dienophiles (diethyl maleate and methyl acrylate) were commercial materials purchased from Sigma-Aldrich. Cyclopentadiene was obtained as a result of thermal cracking of dicyclopentadiene, which was purchased from Sigma-Aldrich. The ionic liquid XIII were synthesised according to established procedures.[18]

The structure and purity of all of the synthesised substances were confirmed by spectral analysis. ^{1}H NMR spectra were recorded at 400 MHz and ^{13}C NMR at 100 MHz (Varian Unity Inova plus, using TMS as an internal standard). High-resolution electrospray ionisation mass spectroscopy (ESI-MS) experiments were performed using a Waters Xevo G2 QTOF instrument equipped with an injection system (cone voltage 50 V; source 120 °C). GC analyses were performed using a Perkin Elmer Clarus 500 chromatograph equipped with a SPB^{TM}-5 column (30 m × 0.25 mm × 0.25 μm); *n*-decane was used as an internal standard. Thermogravimetric analysis was performed with a Mettler Toledo TGA/SDTA 851e/1100 analyser (temperature program 25–600 °C, 20 °C/min, N_2 60 ml/min). Differential scanning calorimetry was performed with a Mettler Toledo analyser (temperature program -65–250 °C, 20 °C/min, N_2 60 ml/min). Fourier-transform infrared absorption (FT-IR) spectra were recorded with a Fourier-transform infrared spectrometer (IC10, Mettler-Toledo) equipped with an ATR diamond probe and operated in transmission mode.

2.2. General methods

General method for the Fischer glycosylation: Into a 250 ml round-bottom flask equipped with condenser and magnetic stirrer, D-glucose (58.9 mmol) and chloroalcohol (223.8 mmol) were introduced. Sulfamic acid (14.2 mmol) was subsequently added at room temperature. The reaction was stirred at 80 °C for 10 h. After completion of the reaction, reaction mixture was concentrated. Next 100 ml of acetone was added. The solvent was decanted from the precipitate, and the precipitate was washed three times with 10 ml of acetone. The acetone extracts were collected, the solvent was removed under reduced pressure, and the crude product was dissolved in methanol, filtrated, concentrated under reduced pressure, and purified by column chromatography (methanol : chloroform (3:7)) to give chloroalkyl glycosides III a-c as creamy solids in yields of 50-78%, depending on the structure of the chloroalcohol.

2-chloroethyl D-glucopyranoside: α:β= 0.7:0.3; ^{1}H-NMR (400 MHz, CD_3OD): δ 4.84 (d, J = 3.8 Hz, 0.7 H, H-1α), 4.32 (d, J = 7.8 Hz, 0.3 H, H-1β), 4.07 (dt, J = 11.2, 6.0 Hz, 0.3H, OC*H*HCH$_2$Clβ), 3.94 (dt, J=11.2, 5.6 Hz, 0.7H, OC*H*HCH2Clα), 3.96-3.22 (m, 8 H, OCH$_2$CH$_2$Cl, H-3, H-4, H-5, H-6a,b), 3.39 (dd, J = 8.0, 3.8 Hz, 0.7 H, H-2α), 3.19 (dd, J = 8.8, 7.8 Hz, 0.3 H, H-2β); ^{13}C-NMR (100 MHz, CD_3OD): δ 104.52 (C-1β), 100.53 (C-1α), 77.96, 77.93, 74.94, 73.90 (2C), 73.44, 71.63, 71.50, 70.92, 69.71, 62.68, 62.56, 43.73, 43.59; ESI-MS: [M + Na]$^+$ calcd: 265.0455, found: 265.0437.

3-chloropropyl D-glucopyranoside: α:β= 0.7:0.3; ^{1}H-NMR (400 MHz, CD_3OD): δ 4.78 (d, J = 3.8 Hz, 0.7 H, H-1α), 4.26 (d, J = 7.8 Hz, 0.3 H, H-1β), 4.00 (dt, J=8.0, 6.0 Hz, 0.3 H, OC*H*HCH$_2$CH$_2$Clβ), 3.89 (ddd, J=11.0, 7.2, 5.2 Hz, 0.7 H, OC*H*HCH2Clα), 3.88-3.25 (m, 8 H, OCH$_2$CH$_2$CH$_2$Cl, H-3, H-4, H-5, H-6a,b), 3.39 (dd, J=9.6, 3.8 Hz, 0.7 H, H-2α), 3.17 (t, J= 7.8 Hz, 0.3 H, H-2β), 2.16-1.98 (m, 2 H, OCH$_2$C*H$_2$*CH$_2$Cl); ^{13}C-NMR (100 MHz, CD_3OD): δ 104.47 (C-1β), 100.22 (C-1α), 78.01, 77.85, 75.05, 73.69, 73.51, 71.71, 71.59, 67.46, 65.53 (2C), 62.72, 62.57, 43.73, 42.67, 34.09, 33.69; ESI-MS: [M + Na]$^+$ calcd: 279.0611, found: 279.0612.

3-chloro-2-hydroxypropyl D-glucopyranoside: α:β= 1:2; ^{1}H-NMR (400 MHz, CD_3OD) (selected data): δ 5.08 (d, J = 3.9 Hz, 0,15 H, H-1α), 5.05 (d, J = 3.9 Hz, 0.2 H, H-1α'), 4.50 (d, J = 7.8 Hz, 0,15 H, H-1β), 4.34 (d, J = 7.8 Hz, 0.5 H, H-1β'), 4.12-3.24 (m, 11H, OCH$_2$CH(OH)CH$_2$Cl, H-2, H-3, H-4, H-5, H-6a,b); ^{13}C-NMR (100 MHz, CD_3OD) (selected data): δ 104.76 (C-1β), 104.72 (C-1β'), 100.61 (C-1α), 100.36 (C-1α') 46.99, 46.92, 46.79, 46.70 (4 OCH$_2$CH$_2$*C*H$_2$Cl); ESI-MS: [M + Na]$^+$ calcd: 295.0561, found: 295.0547.

General method for the synthesis of the tetraalkylammonium chlorides: Into a two-necked 250 ml round-bottom flask equipped with condenser, magnetic stirrer and dropping funnel, an ethanolic solution of trialkylamine (190 mmol) and 30 ml of methanol were introduced. The flask was closed under an inert gas atmosphere. The contents of the flask were cooled to 0 °C in an ice bath, and the chloroalcohol or chloroalkyl glycoside (126.5 mmol) was added. The reaction was stirred at 65-68 °C for 10 h, and the solvent was subsequently evaporated. The product was washed five times with 50 ml of diethyl ether and seven times with 50 ml of acetone until the white solid precipitated. After drying under vacuum, the tetraalkylammonium chlorides were obtained as white solids in satisfactory yields (52-92%).

***N*-[2-(D-glucopyranosyl)ethyl]-*N,N,N*-trimethylammonium chloride (IVa):** ESI-MS [M$^+$] calcd: 266.1604, found: 266.1609.

***N*-[3-(D-glucopyranosyl)propyl]-*N,N,N*-trimethylammonium chloride (IVb):** ESI-MS [M$^+$] calcd: 280.1760, found: 280.1764.

***N*-[3-(D-glucopyranosyl)-2-hydroksypropyl]-*N,N,N*-trimethylammonium chloride (IVc):** ESI-MS [M$^+$] calcd: 296.1709 , found: 296.1708.

***N*-[(2,3-dihydroxy)prop-1-yl]-*N,N,N*-trimethylammonium chloride**: ESI-MS [M$^+$] calcd: 134.1181, found: 134.1174.

***N*-[(2,3-dihydroxy)prop-1-yl]-*N,N,N*-triethylammonium chlo-**

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ride: ESI-MS [M^+] calcd: 176.1651, found: 176.1650.

***N*-[(2,3-dihydroxy)prop-1-yl]-*N,N,N*-tributylammonium chloride:** ESI-MS [M+] calcd: 260.2590, found: 260.2589.

General method for the synthesis of the tetraalkylammonium bistriflamides (V-X): To a solution of tetraalkylammonium chloride (37.0 mmol) in 2 ml of distilled water lithium bistriflamide (42.7 mmol) in 2 ml of water was added. The reaction mixture was stirred at room temperature for 24 h and then extracted with dichloromethane or acetonitrile. The organic layer was dried over anhydrous $MgSO_4$. The solution was concentrated under reduced pressure to afford the bistriflamide salts in 70-95% yield.

***N*-[2-(D-glucopyranosyl)ethyl]-*N,N,N*-trimethylammonium bistriflamide (V)**: ESI-MS [M^+] calcd: 266.1604, found: 266.1610, [M^-] calcd: 279.9173, found: 279.9178.

***N*-[3-(D-glucopyranosyl)propyl]-*N,N,N*-trimethylammonium bistriflamide (VI)**: ESI-MS [M^+] calcd: 280.1760, found: 280.1765, [M^-] calcd: 279.9173, found: 279.9175.

***N*-[3-(D-glucopyranosyl)-2-hydroksypropyl]-*N,N,N*-trimethylammonium bistriflamide (VII)**: ESI-MS: [M^+] calcd: 296.1709 , found: 296.1708, [M^-] calcd: 279.9173, found: 279.9179.

***N*-[(2,3-dihydroxy)prop-1-yl]-*N,N,N*-trimethylammonium bistriflamide (VIII)**: ^{1}H-NMR (400 MHz, CD_3OD): 4.16 (m, 1H, CH-OH), 3.56-3.32 (m, 4H, CH_2), 3.24 (s, 9H, CH_3). ^{13}C-NMR (100 MHz, CD_3OD): 125.97, 122.74, 119.56, 116.37, 69.93, 67.97, 65.22, 54.98. ESI-MS [M^+] calcd: 134.1181, found: 134.1174, [M^-] calcd: 279.9173, found: 279.9178.

***N*-[(2,3-dihydroxy)prop-1-yl]-*N,N,N*-triethylammonium bistriflamide (IX)**: ^{1}H-NMR (400 MHz, CD_3OD): 4.08 (m, 1H, CH-OH), 3.60-3.31 (m, 10H, CH_2), 1.32 (t, 9H, CH_3). ^{13}C-NMR (100 MHz, CD_3OD): 125.49, 122.73, 119.45, 116.34, 67.27, 65.25, 60.66, 54.83, 7.69. ESI-MS [M^+] calcd: 176.1651, found: 176.1650, [M^-] calcd: 279.9173, found: 279.9178.

***N*-[(2,3-dihydroxy)prop-1-yl]-*N,N,N*-tributylammonium bistriflamide (X)**: ^{1}H-NMR (400 MHz, CD_3OD): 4.06 (m, 1H, CH-OH), 3.59-3.22 (m, 10H, CH_2), 1.82-1.56 (m, 6H, CH_2), 1.50-1.31 (m, 6H, CH_2), 1.01 (m, 9H, CH_3). ^{13}C-NMR (100 MHz, CD_3OD): 125.98, 122.80, 119.61, 116.42, 67.38, 65.25, 62.21, 60.48, 24.75, 20.71, 13.86. ESI-MS: [M^+] calcd: 260.2590, found: 260.2589, [M^-] calcd: 279.9173, found: 279.9179.

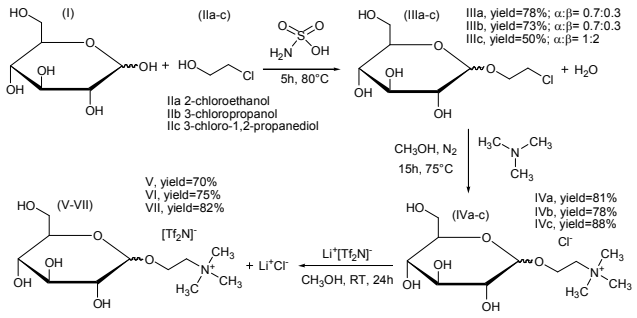
FT-IR spectra of all new ionic liquids are available in Supplementary Information section.

General method for the Diels–Alder reactions: The reaction was performed in 5 ml flasks equipped with a stirring bar and a balloon filled with nitrogen. The dienophile (1.0 mmol) and the ionic liquid (1.0 mmol) were introduced into the flask, followed by the addition of diene (1.5 mmol) at room temperature. The reaction mixture was subsequently stirred at room temperature for 5–120 min. The reaction yield and the *endo:exo* ratio were determined by GC analysis with precision ± 1%. After adequate period of time, the reaction was stopped by the addition of 5 ml of dichloromethane. Next, 200 µl of sample was taken, added to 1 ml of dichloromethane and analysed. Each point in figures 1-4 represents the result from independent reaction. In order to identify, the products were isolated from the reaction mixture by extraction with dichloromethane. Next, organic layer was concentrated in a vacuum and purified by column chromatography (hexane : ethyl acetate (5:1)) when necessary. All products were characterised by comparison of their NMR spectra with authentic samples.

3. Results and discussion

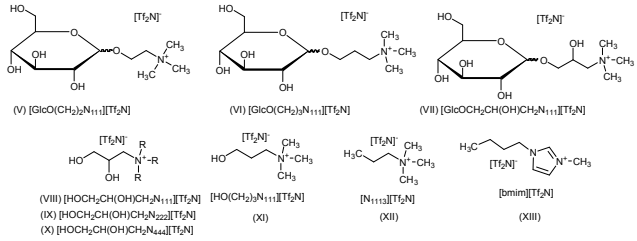
3.1. Synthesis of hydrogen-bond-rich ionic liquids

The goals of this study included the synthesis of ionic liquids possessing hydroxyl groups in their structure. To design the proper ionic liquids, we selected D-glucose as the raw material. We used the modified procedure described elsewhere (Scheme 1).[19]



Scheme 1 The synthesis of the ionic liquids using D-glucose as the raw material

Glycosylation of D-glucose (I) with the chloroalcohols: 2-chloroethanol, 3-chloropropanol, and 3-chloro-1,2-propanediol (II a-c) using sulfamic acid as the catalyst yielded the chloroalkyl glycosides (III a-c) in high yields (50-78%) as a mixture of glycosides with α:β ratio 0.7:0.3 in case of glucosides III a, III b and 1:2 in case of glucosides III c (trace amount of disaccharide and trisaccharide chloroalkyl derivatives were detected by MS analysis, probably as a result of 1,6-glycosidic bond formation in the reaction conditions). Next, quaternarisation with trimethylamine gave the ammonium chlorides (IV a-c), which have been previously described in the literature.[19,8] In this study, we went one step further by completing the process *via* metathesis of the chloride anion, which resulted in the bistriflamide ionic liquids (V-VII). In contrast to the chlorides, the new ionic liquids are liquids at room temperature.



Scheme 2 The ionic liquids used in this study

For purposes of comparison, we sought to prepare ionic liquids with a few hydroxyl groups incorporated into the alkyl group of the aglycone and therefore used chloroalcohols as the source of the hydroxyl groups.[20] Ionic liquids possessing two hydroxyl groups and different hydrophobicity properties, such as the trialkyl-2,3-dihydroxypropylammonium bistriflamides (alkyl = methyl, ethyl, butyl), were designed (VIII-X). The synthesis was

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based on the quaternarisation of trialkylamine with an adequate amount of chloroalcohol, followed by salt metathesis. In addition, ionic liquids with one hydroxyl group, *i.e.*, trimethyl-3-hydroxypropylammonium bistriflamide (XI), and without the ability to form hydrogen bonds, *i.e.*, trimethylpropylammonium bistriflamide (XII) and 1-butyl-3-methylimidazolium bistriflamide, were synthesised (XIII).

The new ionic liquids were soluble in water, slightly soluble in methanol and acetonitrile, and poorly soluble in ethyl acetate. The physicochemical properties of the obtained ionic liquids were determined. All of the D-glucose-based ionic liquids were mixtures of anomers with α:β ratio 0.7:0.3 (ionic liquid V, VI) and 1:2 (ionic liquid VII). The structures of the new ionic liquids were confirmed by high-resolution ESI-MS experiments. The peaks observed in the positive and negative ESI modes confirmed the presence of bistriflamide anions and an adequate cations in all of the samples. Additionally, FTIR spectra of ionic liquids are presented in the Supplementary Information.

The thermal data of the studied ionic liquids as measured by differential scanning calorimetry are summarised in Table 1. The ionic liquids were heated from -65 °C to 250 °C, held at 250 °C before being cooled to -65 °C, heated again, and finally cooled to -65 °C. All of the samples were liquids at temperatures well below room temperature, and no melting points were detected. These compounds tend to form glasses at temperatures in the range of -29 °C to -16 °C. The data obtained from thermogravimetric analysis of the ionic liquids are also shown in Table 1. According to the experimental data, the ionic liquids are thermally stable from ambient temperature to at least 430 °C for both the tetraalkylammonium ionic liquid with hydroxyl groups incorporated into the alkyl group of aglycone and the tetraalkylammonium ionic liquid with D-glucose attached to the alkyl chain. Moreover, the absence of a glycosyl unit or a hydroxyl group in the tetraalkylammonium ionic liquid does not decrease the thermal stability of the obtained ionic liquids. This high thermal stability is most likely due to the presence of the bistriflamide anion.

Table 1 Thermal properties of the ionic liquids

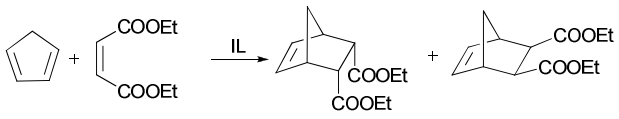
Ionic liquid	T_g [a] [°C]	$T_{50\%\ onset}$ [b] [°C]	T_{decomp} [c] [°C]
V [GlcO$(CH_2)_2N_{111}$][Tf_2N]	-30	433	454
VI [GlcO$(CH_2)_3N_{111}$][Tf_2N]	-20	435	456
VII [GlcO$CH_2CH(OH)CH_2N_{111}$][Tf_2N]	-14	446	460
VIII [$HOCH_2CH(OH)CH_2N_{111}$][Tf_2N]	-22	454	469
IX [$HOCH_2CH(OH)CH_2N_{222}$][Tf_2N]	-39	441	457
X [$HOCH_2CH(OH)CH_2N_{444}$][Tf_2N]	-45	417	431

[a] Glass transition temperature. [b] Decomposition of 50% of the sample. [c] Decomposition.

3.2. Application of the ionic liquids as organocatalysts in the Diels-Alder reaction

According to the literature, the presence of strongly interacting groups, such as hydroxyl, carboxyl, nitrile, or benzyl groups, in the ionic liquid cation structure increases the selectivity of the Diels-Alder reaction compared to that achieved with ionic liquids with neat alkyl chains. However, only one hydroxyl group was considered in the application of trimethylhydroxyethylammonium bistriflamide[21] or 1-hydroxyethyl-3-methylimidazolium bistriflamide.[22] Herein, we compare ionic liquids with different structures to investigate how the number of hydroxyl groups influences the reaction course.

The reaction of cyclopentadiene with diethyl maleate was used as a model reaction for the kinetic and stereochemical studies of a Diels-Alder reaction (Scheme 3).



Scheme 3 The model Diels-Alder reaction used in this study

In primary trials, the ratio of the ionic liquids (VI or VIII) to the dienophile was equimolar (Fig. 1). Consequently, in the presence of both of the ionic liquids, the complete conversion of diethyl maleate and a 99% yield of the product with a high ratio of the *endo:exo* isomers (13.1–13.5) was obtained immediately after 5-10 min. Similar results were obtained for other D-glucose ionic liquids (V and VII), which were not depicted in Figure 1 for clarity.

The metallic catalyst $Yb(OTf)_3$ in the ionic liquid 1-methyl-3-butylimidazolium bistriflamide [bmim][Tf_2N] was also very active. This catalyst is one the most active metallic catalysts used for Diels-Alder reactions.[23] The reaction was faster but resulted in a lower *endo:exo* ratio (9.2). High *endo:exo* ratios (13.2) were maintained for the reactions with one –OH group (ionic liquid XI) and without the –OH group (ionic liquid XII, with a ratio of 13.0, and ionic liquid XIII, with a ratio of 12.5). These reactions required longer reaction times, ranging from 1 h to several hours for completion.

The influence of the ionic liquids with hydroxyl groups on the reaction rate is evident, and a large reduction of the reaction time (from 1 h to 5 min) was achieved by shifting from one to several hydroxyl groups present in the structure of the D-glucose-based ionic liquids. D-glucose alone does not catalyse this reaction what confirms that catalytic activity is not only the result of the presence of hydroxyl groups in the catalyst structure.

The influence of the length of the alkyl chain in tetraalkylammonium bistriflamide with 2 hydroxyl groups is presented in Figure 2. The increase in the alkyl chain length resulted in longer reaction times and only slightly lower *endo:exo* ratios (up to 12.5 for ionic liquid X). The effect of the decreased *endo* selectivity of the product in the Diels-Alder reaction with increasing alkyl chain length of the cation has been described in the literature.[16]

The application of ionic liquids with different structures in the Diels-Alder reaction described in the literature is limited to the application of the ionic liquid as the solvent in equimolar or greater than equimolar amounts relative to the amount of dienophile.[16] In this study, the possibility of the effective application of catalytic amounts (up to 4 mol% with respect to the dienophile) of ionic liquids as organocatalysts was evaluated (Fig. 3).

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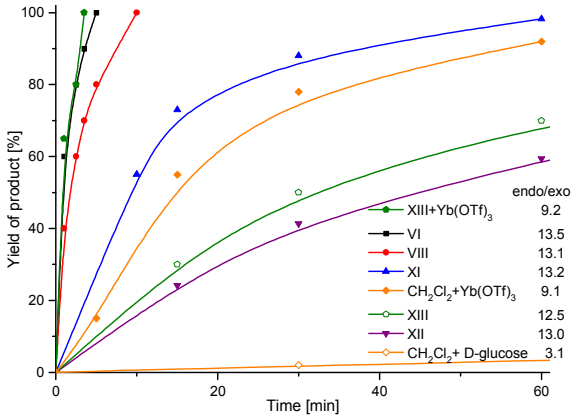


Fig. 1 The influence of the amount of hydroxyl groups present in the ionic liquid (1 mmol) structure on the reaction rate and the selectivity for the reaction of cyclopentadiene (1.5 mmol) with diethyl maleate (1 mmol).

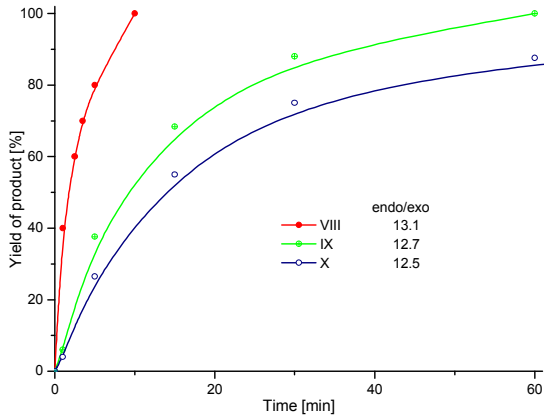


Fig. 2 The influence of the length of the alkyl chain in the structure of tetraalkylammonium ionic liquids (1 mmol) on the reaction rate and selectivity for the reaction of cyclopentadiene (1.5 mmol) with diethyl maleate (1 mmol).

All of the D-glucose-based ionic liquids and the ionic liquid with two hydroxyl groups (VIII) were active in the reaction, whereas the other ionic liquids possessing one -OH group (XI) or without an -OH group in their structure (XII and XIII) lost their activity, and longer reaction times were required to achieve full conversion of the dienophile. The metallic catalyst in dichloromethane was as active as the D-glucose based catalyst. In addition, the difference in the reaction rates among the D-glucose-based ionic liquids could be observed. The activity decreased in the order V > VI > VII. The longer alkyl chain linking the D-glucose unit with the tetramethylammonium cation resulted in longer reaction times to reach full conversion of the dienophile, with minor differences in selectivity.

The influence of selected ionic liquids on the reaction rate and the product distribution in the reaction of cyclopentadiene with methyl acrylate was also evaluated (Scheme 4). In the literature, the highest isomer *endo:exo* ratio (5.25-19) was achieved using chloroaluminate ionic liquids.[16] Many other non-metallic ionic liquids were tested and resulted in lower *endo:exo* ratios (4.8-6.7).

In this study, hydrogen-bond-rich (V, VIII, XI) and hydrogen-bond-poor (XII, XIII) ionic liquids were used in equimolar amounts relative to the amount of dienophile. The positive effect of the hydroxyl groups on the reaction rate and the selectivity is clearly visible in Figure 4. Using chiral column we also checked the possibility of the asymmetric induction in this reaction but unfortunately racemic forms of *endo* and *exo* products were detected. The best selectivity (7.1) was obtained with the D-glucose-based ionic liquid (V) and with the tetraalkylammonium ionic liquid (7.0) possessing two hydroxyl groups in its structure (VIII). After 2 h, full conversion of the dienophile was achieved. The reactions in which other ionic liquids were used as the reaction medium were slower, and a decrease in the selectivity was observed (4.2-5.5).

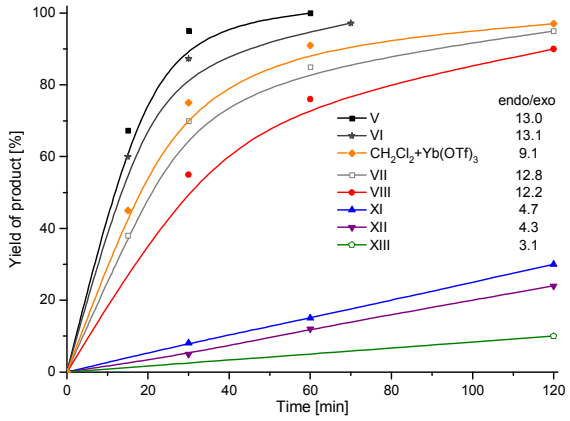
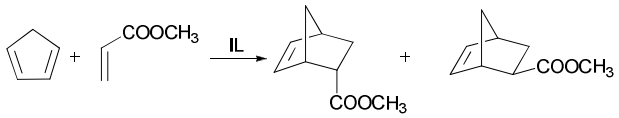


Fig. 3 The influence of catalytic amounts of the ionic liquids (0.04 mmol) on the rate and selectivity for the reaction of cyclopentadiene (1.5 mmol) with diethyl maleate (1 mmol).



Scheme 4 The reaction of cyclopentadiene with methyl acrylate.

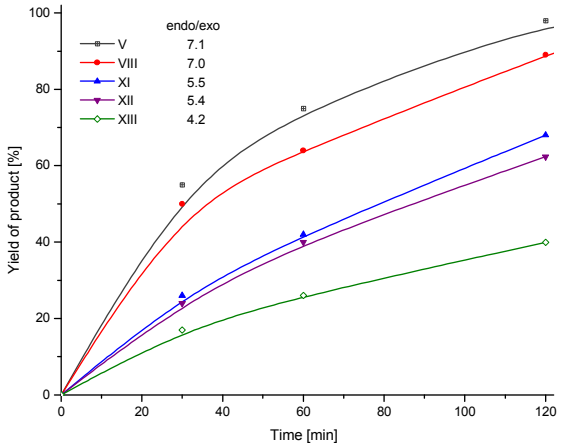


Fig. 4 The influence of the number of hydroxyl groups present in the ionic liquid (1 mmol) structure on the reaction rate and the selectivity for the reaction of cyclopentadiene (1.5 mmol) with methyl acrylate (1 mmol).

The cycloaddition of cyclopentadiene to diethyl maleate or methyl acrylate is one of the most studied models for the Diels–Alder reaction and for reactions using ionic liquids as the reaction medium.[16] In the literature, extensive studies using empirical

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parameters and theoretical calculations were performed to investigate the correlation of the *endo:exo* selectivities and kinetic constants to the solvent properties. Both the cation and the anion played important roles in the reaction mechanism. In summary, the factors that can influence the selectivity of the Diels-Alder reaction include the ability to form hydrogen bonds and the dipolarity/polarisability of the ionic liquid. In addition, the solvophobic effect can influence the selectivity of the reaction.

In this study, the presence of a carbonyl acceptor group in the structure of diethyl maleate or methyl acrylate enables hydrogen-bond interactions with the ionic liquid, thereby enhancing the *endo* selectivity. The course of the reaction of cyclopentadiene with methyl acrylate was monitored using FT-IR spectroscopy; the spectrum of the reaction mixture (cyclopentadiene with diethyl maleate in the presence of the D-glucose-based ionic liquid VI) was taken with the IR probe every 15 s. In Figure 5 spectrum of reaction mixture (after 10, 20, 30 and 60 min.) and for comparison spectrum of substrates was presented. In general, the entire reaction mixture spectrum is complicated (see the Supplementary Information). The appearance of a 3400-3600 [cm^{-1}] band during the reaction, which is characteristic of hydrogen bonds and the decline of signal from double bond from diethyl maleate were detected. However this is not a clear evidence for the presence of C=O…H bonds because the D-glucose-based ionic liquids themselves could also form HO…HO hydrogen-bonds (see the Supplementary Information).

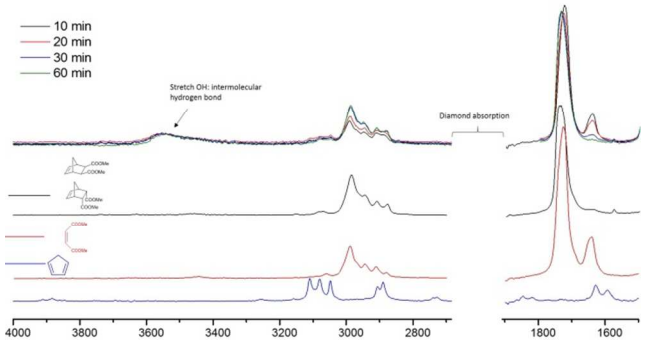
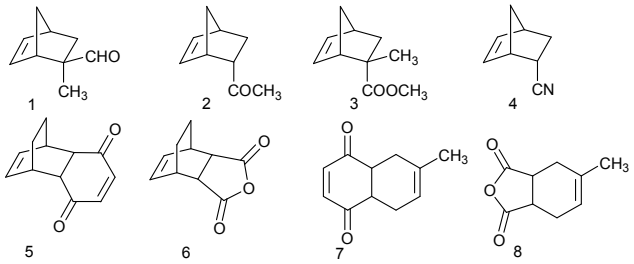


Fig. 5 FT-IR spectra of the reaction course of cyclopentadiene (5 mmol) with diethyl maleate (5 mmol) in the presence of the D-glucose-based ionic liquid VI in catalytic amounts (0.20 mmol).

Finally, the most active D-glucose-based ionic liquid V was examined in the Diels-Alder reaction of various dienes and dienophiles to determine its practical potentials. As can be seen from Table 2 and scheme 5 the cyclization processes proceeded very efficiently; in fact, products were readily obtained in high yields under mild conditions within short reaction times.

Table 2 D-glucose-based ionic liquid V (1 mmol) as catalyst in the Diels-Alder reaction of various dienes (1.5 mmol) and dienophiles (1 mmol)

Dienophile	Diene	Product	Time [h]	Yield [%]	*endo: exo*
cyclopentadiene	methacrolein	1	1	96	8.0 : 1
cyclopentadiene	methyl-vinyl ketone	2	10	85	8.2 : 1
cyclopentadiene	methyl methacrylate	3	1	92	1.9 : 1
cyclopentadiene	acrylonitrile	4	1	90	1.8 : 1
cyclohexadiene	1,4-benzoquinone	5	1	96	-
cyclohexadiene	maleic anhydride	6	1	95	-
isoprene	1,4-benzoquinone	7	1	98	-
isoprene	maleic anhydride	8	1	99	-



Scheme 5 Products of the reaction of cyclopentadiene and isoprene with various dienophiles.

Conclusions

The possibility of using a renewable and relatively inexpensive starting material, such as D-glucose, as the target ionic liquid cation precursor was investigated in this study. In addition, chloroalcohols served as a source of hydroxyl groups for the construction of the ionic liquid cation. The resulting ionic liquids were liquids at room temperature because of the presence of the weakly coordinating bistriflamide anion. The physicochemical properties of the studied ionic liquids were determined. The thermogravimetric analysis results revealed that the ionic liquids are thermally stable at temperatures up to 430 °C.

The resulting ionic liquids are able to create a large number of hydrogen bonds and were used in the Diels-Alder reaction of cyclopentadiene and diethyl maleate. The first approach used equimolar amounts of the ionic liquid with respect to the amount of dienophile, and showed high activity for the studied ionic liquids. The new D-glucose-based ionic liquids were as active as the metal catalyst with respect to the reaction rates but were significantly more active than the other ionic liquids tested. The *endo* selectivity was high in all cases (around 13). An increase in the length of the alkyl chain in the tetraalkylammonium ionic liquids caused a decrease in the reaction rate and a slight decrease in the *endo:exo* ratio. Similar results were obtained when methyl acrylate was used as the dienophile.

Encouraged by the successful outcome of the Diels-Alder reaction with hydrogen-bond-rich ionic liquids, we decided to use catalytic amounts (4 mol% with respect to the dienophile) of the ionic liquids, as organocatalysts. With this approach, only the D-glucose-based ionic liquids and the tetraalkylammonium ionic liquid with two –OH groups maintained their high activity, as indicated by the reaction rate and the *endo* selectivity.

The catalytic system proved to be active in the Diels-Alder reaction of various dienes and dienophiles carried out in the presence of the most active D-glucose-based ionic liquid.

In conclusion, this study showed that the D-glucose-based

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ionic liquids are efficient catalysts for Diels-Alder reactions.

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Notes and references

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