Concave Reagents. 31 [1])

A Merrifield Bound Concave Pyridine for the Selective Acylation of Polyols

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Abstract. The concave pyridine **2a** has been synthesized in 61% yield in the two macrocyclization steps. After deprotection to give **2b**, the concave pyridine has been attached to a Merrifield resin, and the resulting polymer **10** containing 0.3 mmol **2**/g has been used as a selective acylation catalyst for the addition of propane-1,2-diol (**11**) and the glucose derivative **14a** to diphenylketene (**12**) to form selectively 2-hydroxypropyl diphenylacetate (**13a**) (selectivity **13a**/**13b**: 11:1) and methyl 4,6-*0*-benzylidene-2-diphenylacetyl-α-*D*-glucopyranoside (**14b**), (selectivity **14b**/**13c**: 29:1), respectively. After successful applications in batch reactions, the selective addition of **11** to **12** has also been carried out in a flow reactor filled with the polymeric catalyst **10**.

The enhancement of selectivity is a major goal in the development of new reagents and catalysts, and continuously new answers are found for questions of chemo-, regio-, diastereo- and enantioselectivity. But in many cases, the price for increased selectivities is a costly synthesis of the reagent or catalyst.

While catalysts leave a reaction sequence unaltered reagents are consumed. However, many reagents can also be used over and over again, if a method has been established which "recharges" the reagent. For example a protonation or deprotonation can reestablish an acid or a base, respectively, or redox-active reagents can be "recharged" after the reaction by the use of an appropriate oxidizing or reducing process. Therefore, the following considerations are valid for both classes, for catalysts and for reagents which can be regenerated, although only one of the classes may be mentioned.

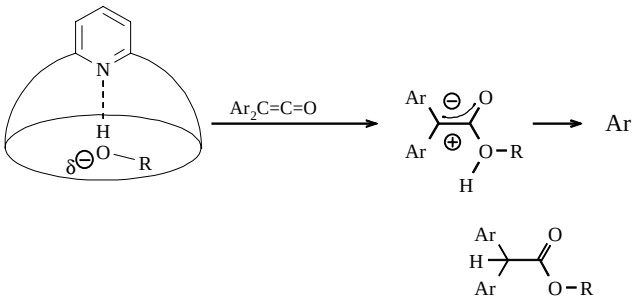
A multistep synthesis of a new catalyst (or reagent) will only pay off if it can be recovered and purified easily. These requirements are fulfilled by polymer bound catalysts.

Since the pioneering work of Merrifield [1], polymeric resins play an important role in organic synthesis [2]. Their use as a platform for the synthesis of larger molecules has enabled the chemist to construct automatic machines for the synthesis of oligopeptides or oligonucleotides [3]. In these reactions, the growing oligomer is covalently bound to the polymer, and the reactions are carried out by alternating turns of dipping the resin into the reagent solutions and washing. The same principle is used in combinatorial chemistry which uses several different reagents in parallel reactions to generate libraries of oligomers [4]. In the final reaction step of these reactions, the products must be cleaved off the polymer.

A second use of polymers in organic chemistry exchanges the positions of substrate and reagent: the reagent is bound to a polymer, the substrate is dissolved. After the reaction, product and reagent can again be easily separated by filtration, with the reagent remaining on the polymer. If the reagent is a catalyst or can easily be regenerated it can thus be used over and over again, and the synthetic effort in synthesizing the catalyst or reagent pays off. Therefore, many reagents and catalysts have been attached to polymers [5]. In addition with polymer bound catalysts, continuous flow set-ups can easily be realized, which will be shown here for a concave reagent.

Concave reagents [6] possess a lamp-shade like geometry with a reactive group (light bulb) on the *inside* of the molecule. As with enzymes where the high selectivity is largely caused by a concave environment, the concave geometry (lamp-shade) enhances the selectivity of the reactive center in a concave reagent.

With concave pyridines [7] a class of basic catalysts has been developed which can be used in selective acylations [8, 9] *e.g.* of polyols with diphenylketene [10] (see Scheme 1). In a two step reaction, the concave pyridine first forms a hydrogen bond to an alcohol thus increasing the nucleophilicity of its oxygen atom. In the second step this complex is attacked by a diarylketene, and a bond is formed between the sp-hybridized carbon atom



Scheme 1 By the formation of a hydrogen bond between an alcohol and a concave pyridine the nucleophilicity of the alcohol oxygen atom is increased facilitating the addition of the alkoxy group OR to a diarylketene. Protonation and deprotonation form the acylation product, a diaryl acetate, and regenerate the catalyst, the concave pyridine.

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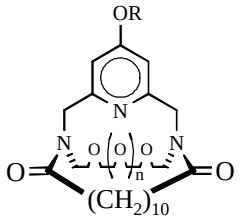
of the ketene and the alcohol oxygen atom. Protonation and deprotonation yield an ester and regenerate the catalyst.

In alcohol mixtures or when polyols are acylated, the selectivity of this reaction arises from the differences of the interactions of the macrocycle chains of the concave catalyst with the residues of the different alcohols and the arene rings of the ketenes. The catalysts, the ketenes and the alcohols have widely been varied [8, 9] and with catalysts like **2d**, high selectivities have been found, for instance for the preferred acylation of a primary hydroxyl group in the presence of a secondary one, or for the selective 2-*O*-acylation of 4,6-*O*-benzylidene protected α-methylglucoside **14a** [8] (see Scheme 4).



n = 0	**1**	
n = 1	**2a**	R = CH_2CH_2OBn
	2b	R = CH_2CH_2OH
	2c	R = CH_2CH_2ONa
	2d	R = Me

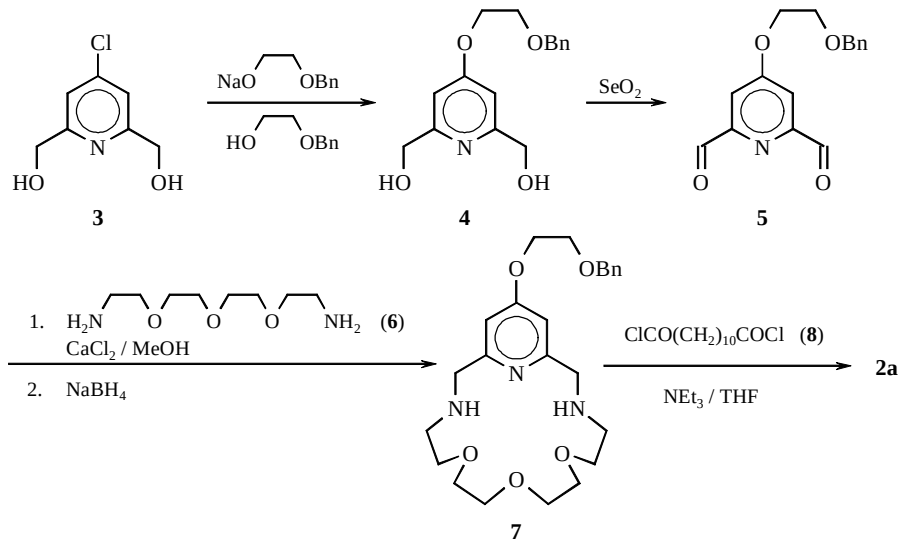
The synthesis of concave pyridines is well established [7–9] but nevertheless the multistep syntheses of the concave pyridines ask for a multiple use of these catalysts. Therefore, a concave pyridine **1** has already been attached to a Merrifield polymer resin [11]. But the selectivity of a concave pyridine **1** containing a dioxaoctane chain in the base catalyzed addition of alcohols to ketenes is small. Therefore, a larger concave pyridine **2** with a trioxaundecane chain has been modified in 4-position of the pyridine ring and has been attached to a chloromethyl substituted crosslinked polystyrene (Merrifield resin). Scheme 2 summarizes the synthesis of a concave pyridine **2** with a linker in 4-position.

Analogously to the synthesis of other 4-substituted concave pyridines [7], **2** was built up by a two step bis-macrocyclization starting from the pyridine-2,6-dicarbaldehyde **5** [11]. In general, 4-substituted dialdehydes are accessible in a few synthetic steps from chelidamic acid (4-hydroxypyridine-2,6-dicarboxylic acid) *via* the key compound 4-chloropyridine-2,6-bismethanol (**3**) [7b]. By nucleophilic aromatic substitution, a 2-benzyloxy-ethoxy substituent can be introduced. Oxidation with SeO_2 gives 4-(2-benzyloxyethoxy)-pyridine-2,6-dicarbaldehyde (**5**) [11].

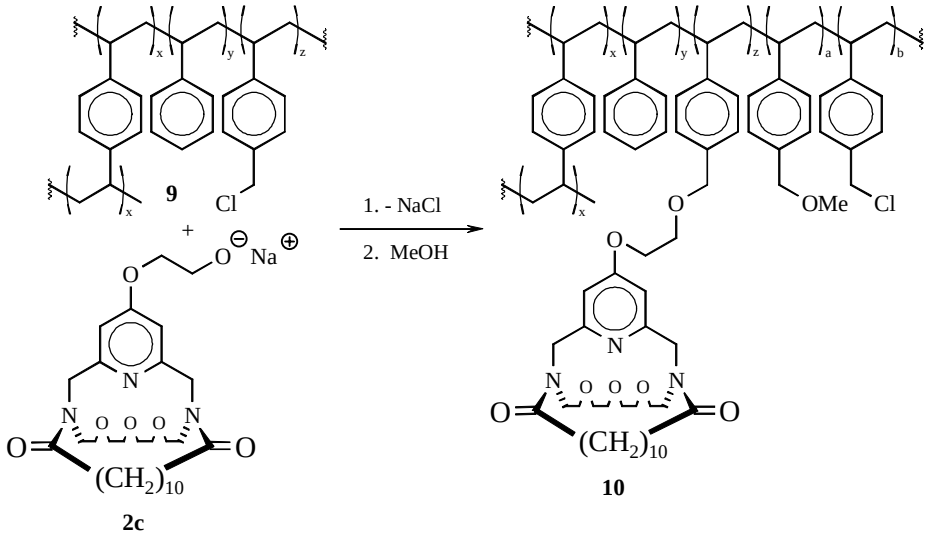
The first macrocyclization exploits the metal ion template effect [7, 12]: in the presence of Ca^{2+} ions a macrocyclic bis-Schiff base forms with the α,ω-diamine **6** in excellent yield as a Ca^{2+} complex. Without isolation this complex can be reduced by $NaBH_4$ to give the macrocyclic diamine **7** in almost quantitative yield.

The second macrocyclization is carried out obeying the high dilution principle [7, 13]. Solutions of the diamine **7** and dodecane diacid dichloride (**8**) were slowly and synchronically dropped into a solution of triethylamine in THF. The desired bimacrocyclic **2a** could be isolated in 61% yield.

In the last two reaction steps, first the protective benzyl group in **2a** was removed by catalytic hydrogenation (Pd/C, 91%). Then the OH-group of the 2-hydroxyethoxy spacer was deprotonated by sodium hydride in the presence of the Merrifield polymer (scheme 3) resulting in the fixation of **2** on the Merrifield polymer by nucleophilic substitution of chloride. Excess chloromethylene functions were quenched with methanol. Excess sodium hydride formed sodium methoxide which substituted the chloride. The resulting polymer **10** was analyzed by titrations, elemental analyses and (qualitatively) by NMR (CP-MAS technique).



Scheme 2 Synthesis of the benzyl protected concave pyridine **2a**.



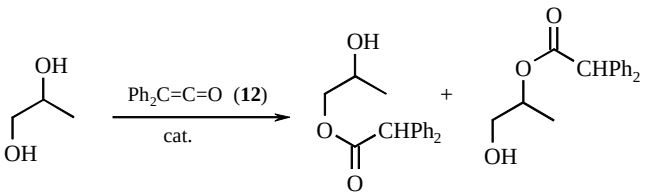
Scheme 3 Attachment of the concave pyridine **2c** (i.e. deprotonated **2b**) to a Merrifield polymer **9** to give the polymer bound catalyst **10**.

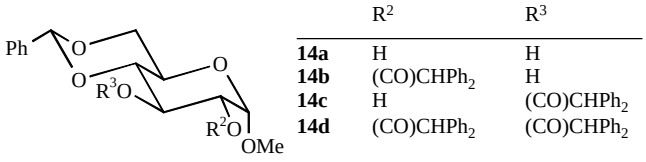
By titration with *p*-toluenesulfonic acid the content of basic centres (pyridines) in **10** was determined to be 0.28 mmol/g. The content of concave pyridines was also calculated from the nitrogen content of the elemental analyses varying from 0.28 to 0.34 mmol/g for various samples which were treated differently (directly after synthesis, recycled from titration experiments, recycled from acylation experiments). Remaining chlorine content may either arise from unreacted chloromethylene groups or from solvent inclusion (dichloromethane).

The catalytic activity and the selectivity of the polymer bound concave pyridine **10** was tested in acylations of propane-1,2-diol (**11**) and the glucoside **14a** with diphenylketene (**12**), which were carried out as batch reactions. By the fixation to the Merrifield polymer, the selectivity of the bimacrocyclic concave pyridine **2** was not altered as table 1 shows.

With insoluble catalysts, reactions can be carried out continuously when the catalysts are placed in a flow reactor. To check this option, a stainless steel column for HPLC chromatography was filled with polymer **10**. The column was conditioned with a 50 mM solution of propane-1,2-diol (**11**) in dichloromethane.

Then acylations of propane-1,2-diol (**11**) with diphenylketene (**12**) were carried out by injecting aliquots of a 57 mM solution of **12** in dichloromethane. The mass balance was > 97%, the yield of **13a** and **13b** was > 92% with a selectivity **13a**/**13b** of 10.8. The same selectivity





	R^2	R^3
14a	H	H
14b	$(CO)CHPh_2$	H
14c	H	$(CO)CHPh_2$
14d	$(CO)CHPh_2$	$(CO)CHPh_2$

Scheme 4 The base-catalyzed addition of the diols **11** and **14a** to diphenylketene gives the products **13a**–**b** and **14b**–**d**, respectively

Table 1 Selectivities of the acylations of propane-1,2-diol (**11**) and glycoside **14a** by diphenylketene (**12**) in the presence of different pyridine catalysts.

catalyst	**13a**/**13b** [a]	**14a** [b]	**14b** [b]	**14c** [b]	**14d** [b]
pyridine	6.3	26	50	12	12
2,6-dimethylpyridine	6.9				
2d	11.2 [c]	21 [d]	76 [d]	3 [d]	0 [d]
10 (batch)	10.6	11	86	3	0
10 (column)	10.8				

[a]) 50 mM catalyst, 50 mM **11**, 4 mM **12** [8]. Selectivities determined by GC. [b]) 20 mM catalyst, 200 mM **14a**, 200 mM **12** [8]. Selectivities determined by 200 MHz ^{1}H NMR. [c]) In the direct comparison experiment 11.2 was found. Other sets of experiments resulted in selectivities up to 13 [8]. For general procedures and acylation procedures see [8] and ref. cited. [d]) In other experiments, **14b** was found as the only product, *e.g.* when the reaction was carried out to 85% conversion (15% remaining **14a**) [16].

was found with an analogous run with a 5.7 mM solution of diphenylketene in dichloromethane, proving that the selectivities found in batch reactions are reproducible in a continuous process under pressure.

The described experiments now open the door to a large scale application of concave reagents, awarding the multistep synthesis of the concave reagents with easy recovery or continuous flow reactions combined with improved selectivities in comparison to 'cheap' catalysts as pyridine.

We thank Dr. G. Peters for the solid state NMR experiments.

Experimental

For general procedures and acylation procedures see [8] and ref. cited.

19-(2-Benzyloxyethoxy)-6,9,12-trioxa-3,15,21-triazabicyclo-[15.3.1]-heneicosa-1(21),17,19-triene (**7**)

13.05 g (67.9 mmol) of 1,11-diamino-3,6,9-trioxaundecane [7a] (**6**) was added to a solution of 19.37 g (67.9 mmol) of 4-(2-benzyloxyethoxy)-pyridine-2,6-dicarbaldehyde [11] (**5**) and 7.53 g (67.9 mmol) of dry $CaCl_2$ in 1.8 l of dry methanol. Under N_2, the solution was heated to reflux until the reaction was completed [ca. 5–6 h, TLC control: R_f (**5**) = 0.76, R_f (**7** · $CaCl_2$) = 0]. At 0 °C, 12.86 g (340 mmol) of $NaBH_4$ was added. After no more hydrogen was produced the mixture was stirred for 15 h at room temp. After addition of ca. 500 ml of water and 1 h of stirring the mixture was extracted with six portions of 100 – 200 ml of dichloromethane. The combined organic layer was dried with $MgSO_4$. After evaporation of the solvent, 30.35 g (quant.) of a brown, clear oil remained. – IR (KBr): $\tilde{\nu}$/cm^{-1} = 3500–3100 (N–H), 1595, 1565 (arom.). – ^{1}H NMR (250 MHz, $CDCl_3$): δ/ppm = 2.84 (m_c, 4H, NC$\underline{H}_2$CH$_2$O), 3.65 (m_c, 8H, OC$\underline{H}_2$C$\underline{H}_2$O), 3.72 (t, 4H, ^3J = 7 Hz, OC$\underline{H}_2$CH$_2$N), 3.81 (s, 4H, Py–CH$_2$N), 3.82 (m_c, 2H, CH$_2$–OBn), 4.18 (m_c, 2H, CH$_2$–OPy), 4.62 (s, 2H, CH$_2$–Ph), 6.62 (s, 2H, Py–H), 7.30–7.38 (m, 5H, C_6H_5). – MS (70 eV): *m/z*(%): 445 (M^+, 4), 298 (15), 257 (12), 91 (100).

29-(2-Benzyloxyethoxy)-17,20,23-trioxa-1,14,33-triazatricyclo [12.11.7.1^{27,31}]-tritriaconta-27(33),28,30-triene-2,13-dione (**2a**)

15.12 g (33.9 mmol) of the diamine **7** in 500 ml of dry THF and 9.07 g (33.9 mmol) of the diacid dichloride [14] **8** in 500 ml of dry THF were filled into two identical dropping funnels. Synchronically, and over 8 h, these two solutions were slowly added to a solution of 20.60 g (203.6 mmol) of dry NEt_3 in 2.5 l of dry THF, which was stirred at 1200 rpm under N_2. After additional stirring for 1 h the solution was filtered to remove triethylammonium hydrochloride. THF was evaporated, the residue was dissolved in ca. 250 ml of dichloromethane and washed twice with 100 ml of 2N NaOH. The layers separated badly, the water layer was washed five times with 100 ml of a chloroform/dichloromethane mixture. The combined organic layer was dried with $MgSO_4$, and the solvents were evaporated. 27.5 g of a red brown crude oil remained which was purified by chromatography [1.6 kg of silica gel, dichloromethane/ethanol (15:1), R_f (**2a**) = 0.5–0.6, R_f (impurities) = 0, 0.2–0.3] yielding 13.35 g (61%) of a slightly yellow oil. – IR (film): $\tilde{\nu}$/cm^{-1} = 1640 (C=O), 1595, 1570 (arom.). – ^{1}H NMR (300 MHz, $CDCl_3$): δ/ppm = 0.90–1.30 (3 m, 12H, $(CH_2)_6$), 1.24, 1.64 (2 m_c, 4H, C$\underline{H}_2$-(CH$_2$–CO)), 2.10–2.35, 2.50 (m, m_c, 4H, N–CH$_2$-polyether), 2.96–4.00 (m, 16H, CH$_2$–CO–N, polyether, CH$_2$–OBn), 4.14 (m_c, 2H, CH$_2$–O–Py), 4.62 (s, 2H, CH$_2$–Ph), 4.63, 4.68 (2d, J = 12.9 Hz and J = 8.9 Hz, ca. 0.5H), 4.72 (d, J = 4.3 Hz, 2.4H), 4.86 (d, ^2J = 17 Hz, 0.22H), 5.18 (d, ^2J = 15.3 Hz, 0.23H), 5.40 (d, ^2J = 13.0 Hz, 0.09H), 6.51 (d, ^4J = 2.0 Hz, 0.26H, *EZ*-Py–H), 6.58 (s, 1.37H, *ZZ*-Py-H), 6.70 (d, ^4J = 2.1 Hz, 0.26H, *EZ*-Py–H), 6.99 (s, 0.11H, *EE*-Py-H), 7.37 (m_c, 5H, C_6H_5). – MS (70 eV): *m/z*(%): 639 (M^+, 32), 257 (14), 91 (100). – HR-MS: calcd.: 639.3884, found: 639.3898.

$C_{36}H_{53}N_3O_7$	Calcd.:	C 67.58	H 8.34	N 6.56
(638.83)	Found:	C 67.60	H 8.28	N 6.31.

29-(2-Hydroxyethoxy)-17,20,23-trioxa-1,14,33-triazatricyclo[12.11.7.1^{27,31}]-tritriaconta-27(33),28,30-triene-2,13-dione (**2b**)

A suspension of ca. 0.8 g of Pd/C (10%) in 800 ml of ethyl acetate was saturated with H_2, and 13.30 g (20.79 mmol) of the concave pyridine **2a** was added. Further hydrogen was bubbled in, and the mixture was warmed to 50 °C while stirring until TLC control showed almost complete conversion but yet only slight amounts of by-products. TLC-conditions: dichloromethane/ethanol (15:1), R_f (**2b**): 0.2–0.25, R_f (**2a**): 0.5–0.6, R_f (by-products): 0–0.05. The reaction time depended on the quality of the catalyst: 5–30 h. The less reactive the catalyst, the better was the yield of **2b**: 68–91%. When the reaction slowed down (TLC), further catalyst was added. Prior to the addition of portions of new catalyst hydrogen was substituted by nitrogen, and the hydrogen flow was only turned on again *after* the addition of Pd/C. The total amount of Pd/C was 1.5–2 g.

The catalyst was filtered off, and the solution was concentrated to dryness. **2b** was purified by chromatography [1.2 kg of silica gel, 2–3 l of dichloromethane/ethanol (15:1) for the elution of **2a**, ca. 4 l of dichloromethane/ethanol (10:1) for **2b**] yielding 0.47 g (4%) of **2a** and 10.38 g (91%) of white crystalline **2b**, *m.p.* 105.5–110.5 °C. – IR (KBr): $\tilde{\nu}$/cm^{-1} = 3600–3100 (O–H), 1630 (C=O), 1595, 1570 (arom.). – ^{1}H NMR (300 MHz, $CDCl_3$): δ/ppm = 0.91–1.37 (m, 12H, $(CH_2)_6$), 1.37–1.87 (2 m, 4H, C$\underline{H}_2$CH$_2$–CO), 2.07–2.40 (2 m, 4H, N–CH$_2$-Polyether), 2.52, 3.06 (2 m_c, 0.7H), 3.20–4.02 (m, 22H, CH$_2$–CO–N, OH, polyether), 3.99 (m_c, 2H, C$\underline{H}_2$–OH), 4.11 (m_c, 2H, CH$_2$–OPy), 4.27 (m_c, 0.4H), 4.66 (d, ^2J = 21 Hz, 0.41H), 4.74 (s, 2.85H), 4.89 (d, ^2J = 17 Hz, 0.27H), 5.18 (d, ^2J = 15 Hz, 0.28H), 5.40 (d, ^2J = 15 Hz, 0.13H), 6.50 (d, ^4J = 2.2 Hz, 0.27H, *EZ*-Py–H), 6.59 (s, 1.35H, *ZZ*-Py–H), 6.71 (d, ^4J = 2.2 Hz, 0.27H, *EZ*-Py–H), 7.00 (s, 0.12H, *EE*-Py–H). – ^{13}C NMR (50 MHz, $CDCl_3$): δ/ppm = 24.38, 24.90, 25.57 (CH$_2$); 26.97, 27.49–28.47 (CH$_2$), 32.09, 32.18, 33.89, 45.07, 47.06; 47.94 (CH$_2$OH), 50.18, 53.42, 54.93; 55.48 (CH$_2$-Opy); 60.63; 68.62, 69.32, 69.42, 70.02, 70.62, 70.74, 70.89, 70.97, 71.08, 72.30 (Py–CH$_2$); 104.81 (4.7 %, *ZZ*-Py–C-3,5); 105.51, 106.10 (1.1 and 1.0%, *EZ*- and *ZE*-Py–C-3,5), 109.42 (0.3%, *EE*-Py–C-3,5); 158.17, 158.25

(Py–C-4), 159.99 (Py–C-2,6); 166.37, 166.55 (Py–C-2,6); 173.05, 173.41 (C=O); 174.61, 174.63 (Py–C-2,6). – ^{13}C CP-MAS-NMR (5 kHz): δ/ppm = 22 ($\Delta\nu_{1/2}$ = 210 Hz, CH_2), 29 ($\Delta\nu_{1/2}$ = 285 Hz, CH_2), 47, 51, 57, 61 (CH_2), 71 ($\Delta\nu_{1/2}$ = 240 Hz, CH_2CO, $ArCH_2N$, CH_2O), 101 ($\Delta\nu_{1/2}$ = 265 Hz, Py–C-3,5), 108 ($\Delta\nu_{1/2}$ = 265 Hz, Py–C-3,5), 159 ($\Delta\nu_{1/2}$ = 360 Hz, Py–C-4, Py–C-2,6), 167 ($\Delta\nu_{1/2}$ = 160 Hz, Py–C-2,6), 175 ($\Delta\nu_{1/2}$ = 230 Hz, C=O, Py–C-2,6). – MS (70 eV): *m/z*(%): 549 (M^+, 100), 519 (37), 460 (33), 444 (24), 431 (36), 236 (21), 209 (20), 208 (21), 207 (25), 193 (25), 123 (22), 122 (21). – MS (CI, isobutane): *m/z*(%): 550 (M^+ + 1, 100). – HR-MS: calcd.: 549.3414, found: 549.3401.

$C_{29}H_{47}N_3O_7$	Calcd.:	C 63.36	H 8.61	N 7.64
(549.71)	Found:	C 63.40	H 8.44	N 7.50.

Polymer bound Concave Pyridine **10**

To allow swelling 8.00 g of Merrifield polymer **9** containing 31.1 mmol Cl/g was added to 300 ml of dry THF under N_2. After 73 h a solution of 2.92 g (5.31 mmol) of the concave pyridine **2b** in 50 ml of dry THF was added. Against a N_2 flow, 1.3 g (54 mmol) NaH was added in portions, and the mixture was then heated to reflux. The progress of the reaction was controlled: 1 ml aliquots of the reaction mixture were quenched with little water and were extracted with dichloromethane [TLC: silica gel, dichloromethane/ethanol (15 : 1): R_f (**2b**) = 0.2–0.3]. After 87 h, **2b** was not detected anymore. 70 ml of dry methanol was added, and the mixture was heated to reflux for 26 h. The mixture was filtered, and the yellow residue was washed several times with distilled water resulting in a discoloration. For purification and drying a five step washing-filtering sequence was used three times using ≥ 100 ml of the following solvents each time:
1. dry methanol, 2. dry dichloromethane, 3. distilled water, 4. dry THF, 5. dry dichloromethane. After the third cycle the polymer was dried for 24 h at 0.01–0.05 Torr, giving 9.26 g of a slightly beige powder. Elemental analysis (carried out five times): C 79.58 ± 0.28, H 7.59 ± 0.04, N 1.32 ± 0.08, Cl 2.04 ± 0.05, other: 9.72 ± 0.07, *i.e.* 0.3141 ± 0.0190 mmol **2**/g, 0.5754 mmol Cl/g, ca. 2.36 mmol OMe/g. – IR (KBr): $\tilde{\nu}$/cm^{-1} = 2819 (OCH_3), 1647 (C=O), 1598 (arom.), 1096 (C–O–C), 816 (arom.). – ^{13}C CP-MAS-NMR (Bruker AM 400, 7 mm BB-probe, rotation: 5 kHz): δ/ppm = 28 ($\Delta\nu_{1/2}$ = 470 Hz, CH_2), 40 ($\Delta\nu_{1/2}$ = 345 Hz, $ArCHCH_2$), 46 ($\Delta\nu_{1/2}$ = 390 Hz, $ArCHCH_2$, $ArCH_2Cl$), 58 ($\Delta\nu_{1/2}$ = 390 Hz, OCH_3), 71 ($\Delta\nu_{1/2}$ = 390 Hz, CH_2O), 74 ($ArCH_2OCH_3$, $ArCH_2O$-Py), 128 ($\Delta\nu_{1/2}$ = 470 Hz, Ar–C-2,3,5,6), 136 ($\Delta\nu_{1/2}$ = 260 Hz, Ar–C-1), 145 ($\Delta\nu_{1/2}$ = 470 Hz, Ar–C-4), 164, 173 (Py–C); the Py–C-signals had extremely low intensities, and were only observed after recalculation [15]. The Py–C-3,5 signals at ca. 105–110 ppm were not observed.

Titration (carried out twice): 5.000 ml (481 µmol) of a 96.2 mM solution of *p*-TsOH in ethanol was treated with 237.0 (207.6) mg of **10** in 5 ml of dry EtOH. After 1 h the mixture was filtered, and the polymer was washed with 35 ml of dry ethanol. Ethanol solutions were combined, and dry ethanol was added to 50.00 ml. 10 ml aliquots were mixed with 20 ml of water, and the *p*-TsOH contents were determined by titration with 0.01N NaOH. *p*-TsOH in ethanol: 0.4125 (0.4235) mmol. Basic centres (concave pyridine) on polymer **10**: 0.289 (0.277) mmol of **2**/g.

Deprotonation and repeated elemental analysis: The protonated polymer fractions, resulting from 237.0 and 207.6 mg of unprotonated **10**, were combined and washed ten times with ca. 5 ml of 0.1N NaOH in ethanol/water (1:1). Before filtration, the mixture was allowed to stand for 5 min. Following this procedure, **10** was then washed ten times with 10 ml of dry ethanol, ten times with 10 ml of ethanol/dichloromethane (dry, 1:1) and 20 times with 10 ml of dry dichloromethane. After drying *in vacuo* (0.05–0.10 Torr) 423.4 mg (95%) remained. Elemental analyses (carried out three times): C 78.98 ± 0.09, H 7.54 ± 0.03, N 1.22 ± 0.03, Cl not determined, *i.e.* 0.291 ± 0.007 mmol of **2**/g.

Recycling from catalysis experiments: The polymer **10** was isolated by filtration, washed thoroughly with dichloromethane and dried *in vacuo* (0.05–0.1 Torr). Elemental analyses (carried out three times): C 78.71 ± 0.42, H 7.57 ± 0.01, N 1.42 ± 0.02, Cl not determined, *i.e.* 0.338 ± 0.05 mmol of **2**/g.

Base-catalyzed Addition of Propane-1,2-diol (**11**) *to Diphenylketene* (**12**), *Batch Reaction: Synthesis of 2-Hydroxypropyl Diphenylacetate* (**13a**) *and 2-Hydroxy-1-methylethyl Diphenylacetate* (**13b**)

167.4 mg of the polymer **10** was dried *in vacuo*. Under nitrogen, 900 µl of a 55.6 mM solution of propane-1,2-diol (**11**) in dichloromethane was added and the mixture was stirred for ca. 45 min. Then, 100 µl of a 45 mM solution of diphenylketene (**12**) in dichloromethane was added and the mixture was stirred for ca. 18 h. After filtration and washing of the polymer **10** with dichloromethane, the combined organic layer was concentrated to dryness. To allow GC analysis this residue was silylated by adding 1.0 ml of dry pyridine, 0.2 ml of 1,1,1,3,3,3-hexamethyldisilazane and 0.1 ml of freshly distilled chlorotrimethylsilane and heating to 70–80 °C for ca. 5 min. Then the turbide mixture was filtered through Al_2O_3, which was washed with dry dichloromethane. After concentration to 1–1.5 ml, the mixture was analyzed by GC (SE 30, 25 m, split injector, starting temp 130 °C for 5 min, heating with 5 °C/min until 220 °C were reached, then further heating to 250 °C with 20 °C/min, r_t (**13b**): 25.6 min, r_t (**13a**): 26.1 min). Analytical data for 2-hydroxypropyl diphenylacetate (**13a**) and 2-hydroxy-1-methylethyl diphenylacetate (**13b**): [9a].

Base-catalyzed Addition of Methyl 4,6-O-Benzylidene-a-D-glucopyranoside (**14a**) *to Diphenylketene* (**12**), *Batch Reaction: Synthesis of 4,6-O-Benzylidene-a-D-glucopyranosides* **14b**–**d**

335 mg of the polymer **10** and 281.3 mg (1.000 mmol) of methyl 4,6-*O*-benzylidene-α-*D*-glucopyranoside were dried *in vacuo*. Under nitrogen, 5 ml of dichloromethane was added first followed by 180 µl (200 mg, 1.00 mmol) of diphenylketene after 30 min. The mixture was stirred for 285 h. After filtration and washing of the polymer with 0.5 ml of dichloromethane, the combined organic layer was concentrated to dryness and the residue was analyzed by ^{1}H NMR. Analytical data for methyl 4,6-*O*-benzylidene-2-diphenylacetyl-α-*D*-glucopyranoside (**14b**), methyl 4,6-*O*-benzylidene-3-diphenylacetyl-α-*D*-glucopyranoside (**14c**) and methyl 4,6-*O*-benzylidene-2,3-bis(diphenylacetyl)-α-*D*-glucopyranoside (**14d**): [8a].

Base-Catalyzed Addition of Propane-1,2-diol (**11**) *to Diphenylketene* (**12**), *Continous Flow Reaction*

A stainless steel column for HPLC chromatography (volume 3.14 ml) was filled with 1.42 g (0.43 mmol) of polymer **10**. The column was conditioned with a 50 mM solution of propane-1,2-diol (**11**) in dichloromethane (5 h, 0.1 ml/min, 70 bar). Then acylations of propane-1,2-diol (**11**) with diphenylketene (**12**) were carried out by injecting 1000 µl of a 57.2 mM solution of **12** in dichloromethane in 20 µl shots. The mass balance was >97%, the yield of **13a** and **13b** was >92% with a selectivity **13a**/**13b** of 10.8 (for analysis: see above). The same selectivity was found with an analogous run with 1000 µl of a 5.7 mM solution of diphenylketene in dichloromethane.

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