N-Acylpyridinium Trifluoromethanesulfonates and Tetrafluoroborates: Shuttle Reagents for the Acylation of Enantiopure Secondary Alcohols

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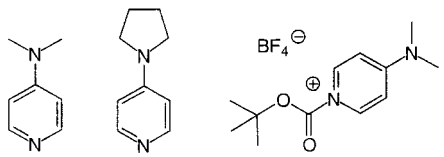
Dedicated to Professor Alan R. Katritzky on the occasion of his 70th birthday

Abstract: Several enantiopure alcohols are esterified with *N*-acyl-4-benzylpyridinium trifluoromethanesulfonates **7b,d,f** or tetrafluoroborates **7a,c,e.** These reagents, which can be generated in situ, or isolated as stable salts, are synthesized from readily available 4-alkylpyridines **3**, acyl chlorides **4** and strong protic acids **6**. The acyl moiety is transferred under neutral conditions and in high yields. The heterocyclic component **3a** can be re-isolated almost quantitatively. The acetate, benzoate and pivaloate groups were selected with regard to their application as frequently used protecting groups for hydroxy compounds. As shown by paramagnetic shift experiments with a chiral europium(III) complex, these acylations proceed without detectable racemization or epimerization.

Key words: shuttle reagents, esterification, *N*-acyl-4-benzylpyridinium trifluoromethanesulfonates or tetrafluoroborates, enantiopure secondary alcohols

Although the formation of carboxylic esters is one of the best studied organic reactions,[1, 2] there still is the need for versatile methods which allow the efficient transformation of sensitive hydroxy compounds into carboxylic esters. This is the *conditio sine qua non* in the case of such chiral alcohols which reveal a significant tendency to undergo racemization in the presence of minor amounts of acids or bases (both Brønstedt and Lewis). In such cases, the acylating reagent must be activated under very mild conditions, in particular, the formation of protic acids HX or basic species during the reaction course must be suppressed.

Steglich and co-workers showed[3] that 4-aminopyridines **1**, especially 4-(dimethylamino)pyridine (**1a**) and 4-pyrrolidinopyridine (**1b**), greatly assist the acylation of sterically hindered alcohols using carboxylic acid anhydrides or the free acid in combination with DCC, respectively.

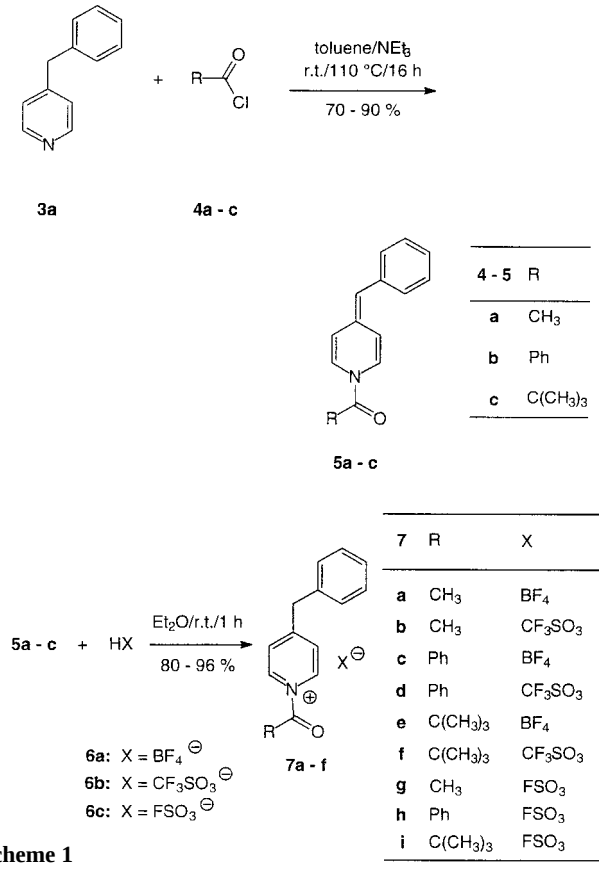


1a **1b** **2**

The strong catalytic activity of **1** is due to the intermediate formation of *N*-acylpyridinium salts which are thought to be highly activated carbonyl groups. The structures of these cations were supported by NMR spectroscopy[4] and the synthesis of a stable *N-tert*-butoxycarbonyl derivative **2**,[5] and that of the latter was confirmed by X-ray analysis.[6]

Rao and Roth[7] successfully applied the carbodiimide acylation method to hydroxy-, dihydroxy-, and mercaptocarboxylic acids. No racemization was observed when ethyl lactate (*S*)-(–)-**8a** was esterified with simple, and more complex, pharmacologically important acids. However, these authors derived the optical purity of the products by comparison with specific rotation values reported in the literature, and diastereomeric esters formed from racemic acids and (*S*)-(–)-**8a** were analyzed indirectly with NMR spectroscopy. It was impossible to decide whether the reaction proceeded under complete inversion or retention of configuration. Detailed information about the stereochemistry is available for the well-established Mitsunobu reaction[8, 9] and by a method developed by Burkhard and Effenberger.[10] In both cases enantiomeric esters are produced with complete inversion of configuration. A very unreliable stereochemical course occurs for secondary chiral alcohols [for instance (*S*)-(–)-**8a**] if they are treated with a mixture consisting of alkaline metal carboxylates, PPh_3 and CCl_4.[11] We report a new method for esterification in which we have thoroughly investigated both the chemical and optical purity of the resulting products.

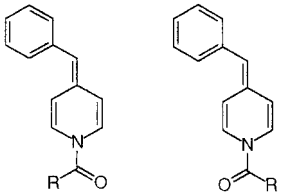
Previously, a method to isolate stable, but still reactive, pyridinium salts **7** in preparative yields, not using 4-aminopyridines **1** but 4-alkylpyridines **3** as starting materials,[12] has been developed by our group (Scheme 1).



Scheme 1

4-Benzylpyridine (**3a**) is the most convenient compound for the formation of 1-acyl-4-alkylidene-1,4-dihydropyridines **5a–c** which are obtained by the sequential treatment of **3a** with acyl chlorides **4a–c** and triethylamine.[13] Electron-withdrawing groups at the exocyclic carbon stabilize the dihydropyridines **5**, whereas alkyl substituents activate **5** and deactivate the corresponding pyridinium salts **7**.

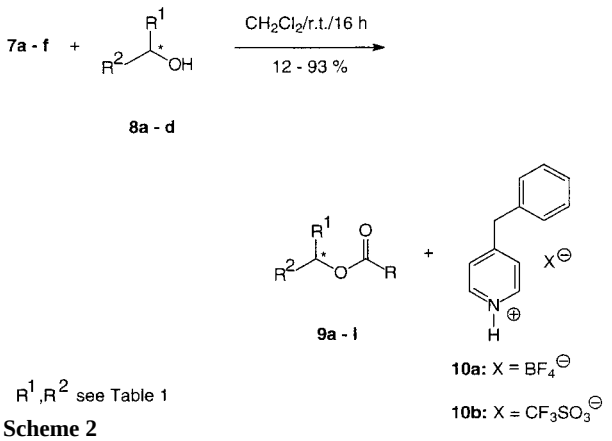
The dihydropyridines **5a–c** reveal a dynamic behavior in solution, which was not previously described in the literature.[12] Due to the partial double bond character of the C–N bond and according to their NMR spectra, **5a,b** exist at room temperature as two rotamer pairs, which we assign *cisoid* and *transoid* structures.



transoid - **5a-c** *cisoid* - **5a-c**

The precursors **5a–c** are suitable for storage under inert conditions, but slowly decompose when exposed to moisture. They may be regarded as the deactivated forms of the title compounds **7a–f** from which the latter are obtained by reaction with strong protic acids **6a–c**. The properties of **7a–f** are controlled by the nature of the counterion X^-. In general, we prefer non-nucleophilic anions (BF_4^-, $CF_3SO_3^-$, FSO_3^-). In such cases the synthesis of **7** from **5** is quantitative. Since all salts **7** are very moisture sensitive, they should be prepared just before use and strictly have to be kept under an inert nitrogen or argon atmosphere. Thus, the reactivity of the oily pyridinium salts **7g–i** resulting from protonation of **5a–c** with fluorosulfonic acid (**6c**) was not investigated further because it is easier and more effective for our purpose to handle solid compounds.

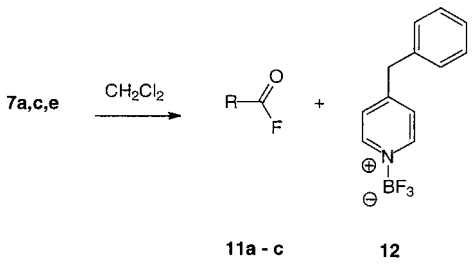
The dihydropyridines **5a–c** react readily with various nucleophiles, whereas little is known about the synthetic potential of the pyridinium salts **7a–f**, besides their reactivity towards aldehydes and ketones.[14] We therefore investigated a simple, but important, reaction; the preparation of chiral esters **9a–l** performed with a variety of optically pure alcohols **8a–d** (Scheme 2). These substrates **8a–d** are



Scheme 2

taken from the chiral pool and some of them are structural subunits of natural products.[15, 16] They and their esters have frequently been used as chiral auxiliaries in organic synthesis,[17–21] for the study of enantioselective chemical processes[22–26] and for investigating the capacity of microorganisms and enzymes.[27–31] Generally, **8a–d** have been esterified with acyl halides or anhydrides in the presence of nitrogen heterocycles, dominantly pyridine (known as the Einhorn reaction[32]) or DMAP (**1a**).

The experimental results of the reaction according to Scheme 2 are summarized in Table 1. Analytical data of new compounds **9c,f,l** and insufficiently described esters **9i,k** are given in Table 2. Table 1 clearly shows that best results are achieved using the trifluoromethanesulfonates **7b,d,f.** The yields obtained from the reaction with tetrafluoroborates **7a,c,e** are poor; the crude mixture consisted of unreacted alcohols and the corresponding carboxylic acid produced from a partial hydrolysis of the group-transfer reagents **7a,c,e.** However, there are NMR spectroscopic indications that the non-nucleophilic BF_4^- ion is not as stable as expected but reacts with the acyl moiety producing acyl fluorides (Scheme 3).

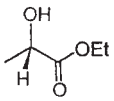
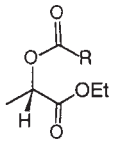
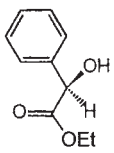
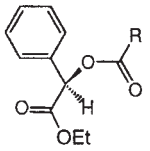
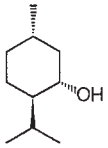
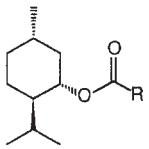
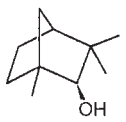
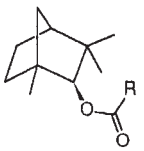


Scheme 3

In view of the simplicity of the experimental procedure the use of the trifluoromethanesulfonates **7b,d,f** is an excellent preparative method for the esterification of alcohols compared with other methods using heterocycles as auxiliaries or catalysts. There is no need for an external proton acceptor, since **3a**, which is split off in the course of the reaction, plays this role. The separation of the pyridinium salts **10a,b** is quantitative due to their insolubility in diethyl ether or benzene. No purification with diluted mineral acids or sodium carbonate solution is necessary. Furthermore, it is possible to regenerate the pyridine source **3a** by aqueous neutralization in 80–90% yield, and in the case of more expensive pyridine derivatives this would be very useful.

The salts **7a–f** were isolated in bulk, analyzed prior to use and dissolved in CH_2Cl_2 for further reactions (Method A). This is advantageous compared with the properties of the analogous *N*-acylpyridinium halides derived from **1a** and **1b**[33] or from pyridine.[34] Salts with chlorides or bromides as anions are not suitable for preparative acylation due to their poor solubility in aprotic solvents and because they exist in equilibrium with the corresponding acyl halide and *N*-heterocycle.

Table 1. Chiral Esters **9a–l** Prepared

Alcohol	Pyridinium Salt		Product	Yield (%)	Method	$[\alpha]_{589}^{22}$ (c = 1, CH_2Cl_2)[a]
 (*S*)-(-)-**8a**	**7a**	R = Me: (*S*)-(–)-**9a**		36	**A, B**	–[b]
	7b			91	**A, B**	–51.0[c]
	7c	R = Ph: (*S*)-(+)-**9b**		23	**A, B**	–
	7d			92	**A, B**	+10.0[d]
	7f	R = $C(CH_3)_3$: (*S*)-(–)-**9c**		88	**A, B**	–31.0
 (*R*)-(-)-**8b**	**7a**	R = Me: (*R*)-(–)-**9d**		16	**A, B**	–
	7b			86	**A, B**	–110.5[e]
	7c	R = Ph: (*R*)-(–)-**9e**		50	**A, B**	–
	7d			72	**A, B**	–104.0[f]
	7f	R = $C(CH_3)_3$: (*R*)-(–)-**9f**		83	**A, B**	–89.0[g]
 (1*S*,2*R*,5*S*)-(+)-**8c**	**7a**	R = Me: (2*R*)-(+)-**9g**		41	**A, B**	–
	7b			91	**A, B**	+79.5[h]
	7c	R = Ph: (2*R*)-(+)-**9h**		20	**A**	–
	7d			72	**A**	+84.5[i]
	7f	R = $C(CH_3)_3$: (2*R*)-(+)-**9i**		65	**A**	+73.0[j]
 (1*R*)-*endo*-(+)-**8d**	**7a**	R = Me: (1*R*)-(+)-**9j**		43	**A, B**	–
	7b			64	**A**	+53.5[k]
	7c	R = Ph: (1*R*)-(+)-**9k**		26	**A, B**	–
	7d			78	**A**	+28.5[l]
	7f	R = $C(CH_3)_3$: (1*R*)-(+)-**9l**		82	**A**	+34.5[m]

[a] All given values are the average from 3–5 measurements: c = 1, CH_2Cl_2, T = 22°C, D = 589 nm.
[b] Crude reaction mixture, rotation values not determined.
[c] $[\alpha]_D^T$ –52.3 (neat), ref[24] $[\alpha]_D^{25}$ –50.3 (c = 0.99, $CHCl_3$), $[\alpha]_D^{25}$ –53.26 (neat).
[d] $[\alpha]_D^T$ +25.2 (neat), ref[16] $[\alpha]_D$ +13.6 (c = 3.48, $CHCl_3$), ref[38] $[\alpha]_D^{20}$ +25.6 (neat).
[e] $[\alpha]_D^T$ –132.8 (neat), ref[21] $[\alpha]_{578}^{20}$ –126 (neat).
[f] $[\alpha]_D^T$ –162.4 (neat), ref[16] $[\alpha]_D$ +103.2 (c = 5.12, $CHCl_3$): for enantiomer, ref[21] $[\alpha]_{578}^{20}$ –142.2 (neat).
[g] $[\alpha]_D^T$ –105.2 (neat).
[h] $[\alpha]_D^T$ +70.0 (neat), ref[42] $[\alpha]_D^{14}$ –73.92 (neat): for enantiomer, ref[43] $[\alpha]_D^{20}$ –77.6 (MeOH): for enantiomer.
[i] Solid, ref[44] $[\alpha]_D$ +89.5 (c = 10, EtOH).
[j] $[\alpha]_D^T$ +60.2 (neat), ref[45] $[\alpha]_D^{20}$ –76.4 (c = 1.85, EtOH): for enantiomer.
[k] $[\alpha]_D^T$ +53.0 (neat), ref[46] $[\alpha]_D$ –58.9 (c = 1, $CHCl_3$): for enantiomer, ref[30] $[\alpha]_D^{20}$ +69.5 (neat).
[l] $[\alpha]_D^T$ +25.2 (neat), ref[47] $[\alpha]_D$ +10.53 (neat).
[m] $[\alpha]_D^T$ +37.2 (neat).

Furthermore, it is possible to generate the group-transfer reagents **7a–f** in situ, by dissolving the precursors **5a–c** in CH_2Cl_2 and adding equimolar amounts of acids **6a** or **b** (Method B). An excess of acid suppresses the esterification completely and, therefore, has to be strictly avoided. This can be done easily, because the course of the protonation can be monitored by means of the color of the solution. The first drop of **6a,b** turns the yellow or orange solution of the dihydropyridines **5a–c** brown, and an excess of acid produces a yellow color again. This last change must be avoided.

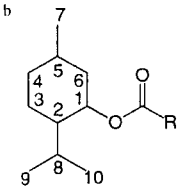
The optical purity of all products **9a–l** was determined with chiral lanthanide induced shift (LIS) experiments.[35–40] This method is "absolute" in the sense that it is capable of providing a direct measure of the optical purity without recourse to a standard whose optical purity is already known. Among many others, a well-described and commercially available chiral lanthanide shift reagent (LSR) is tris[3-(trifluoromethylhydroxymethylene)-*d*-camphorato]europium(III).[41] A LIS experiment with racemic (±)-**9e** using a fourfold excess of this LSR led to a small, but clearly observable, pseudocontact shift difference $\Delta\Delta\delta$ = 0.02 which was never detected for the enantiopure carboxylic esters **9a–l** under identical or similar conditions[41] (limit of detection ~2%). Since the absolute configuration of the enantiopure alcohols **8a–d** and most of the products **9** is known (by comparing the sign of optical rotation with literature values), we draw the conclusion that the described acylation reaction proceeds with complete retention of configuration. We, therefore, assign each product **9** an ee value of ≥96%. A comparison with the DMAP/anhydride method reveals that this well-defined stereochemical course is not self-evident (Table 3).

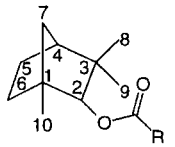
Although chemical yields are similar to our method and the synthesis of **9i** proceeds without racemization, stereochemically labile mandelic acid derivative **8b** is partially inverted when it is esterified with DMAP/anhydride under typical conditions which are taken from the original liter-

Table 2. Analytical Data for Carboxylic Esters **9c, f, i, k, l**[a,9]

Compound	^{1}H NMR (400 MHz, $CDCl_3$) δ [b,c]	^{13}C NMR (100 MHz, $CDCl_3$) δ [b,c]	bp (°C/ mbar)
9c	1.19 [s, 9H, C(C**H**$_3$)$_3$], 1.23 (t, 3H, C**H**$_3$CH$_2$), 1.44 (d, 3H, C**H**$_3$CH-O), 4.17 (m, 2H, CH$_3$C**H**$_2$), 4.99 (q, 1H, CH$_3$C**H**-O)	14.0 (**C**H$_3$CH$_2$), 16.7 (**C**H$_3$CH-O), 26.9 [C(**C**H$_3$)$_3$], 38.5 [**C**(CH$_3$)$_3$], 61.1 (CH$_3$**C**H$_2$), 68.4 (CH$_3$**C**H-O), 170.9 (**C**OOEt), 177.8 [**C**OOC(CH$_3$)$_3$]	183–185/1013
9f	1.16 (t, 3H, C**H**$_3$CH$_2$), 1.24 [s, 9H, C(C**H**$_3$)$_3$], 4.14 (m, 2H, CH$_3$C**H**$_2$), 5.85 (s, 1H, Ph-C**H**-O), 7.40 (m, 5H, Ph**H**)	13.9 (**C**H$_3$CH$_2$), 27.0 [C(**C**H$_3$)$_3$], 61.5 (CH$_3$**C**H$_2$), 74.3 (Ph-**C**H-O), 127.3, 128.6, 128.9, 134.2 (**Ph**-COO), 168.8 (**C**OOEt), 177.7 [(CH$_3$)$_3$**C**COO]	110–112/0.20[d]
9i	0.72 (d, 3H, C(9)H$_3$), 0.86 (d, 3H, C(10)H$_3$), 0.87 (d, 3H, C(7)H$_3$), 0.87 (m, 1H, C(4)H), 0.91 (m, 1H, C(6)H), 1.01 (m, 1H, C(3)H), 1.16 [s, 9H, C(C**H**$_3$)$_3$], 1.38 (m, 1H, C(2)H), 1.46 (m, 1H, C(5)H), 1.63 (m, 1H, C(3)H), 1.67 (m, 1H, C(4)H), 1.86 (m, 1H, C(8)H), 2.15 (m, 1H, C(6)H), 4.60 (td, 1H, C(1)H)	16.1 (C(10)), 20.8 (C(9)), 22.0 (C(7)), 23.3 (C(3)), 26.1 (C(8)), 27.2 [C(**C**H$_3$)$_3$], 31.3 (C(5)), 34.3 (C(4)), 38.8 [**C**(CH$_3$)$_3$], 40.7 (C(6)), 47.1 (C(2)), 73.8 (C(1)), 178.1 (**C**O)	107/9.0[e]
9k	0.83 (s, 3H, C(9)H$_3$), 1.10 (s, 3H, C(10)H$_3$), 1.17 (s, 3H, C(8)H$_3$), 1.18 (m, 1H, C(5)H), 1.24 (m, 1H, C(7)H), 1.50 (m, 1H, C(6)H), 1.64 (m, 1H, C(7)H), 1.75 (m, 1H, C(4)H), 1.76 (m, 1H, C(6)H), 1.93 (m, 1H, C(5)H), 4.60 (m, 1H, C(2)H), 7.43 (m, 2H, *m,m′*-PhH), 7.54 (m, 1H, *p*-PhH), 8.45 (m, 2H, *o,o′*-PhH)	19.4 (C(10)), 20.3 (C(9)), 25.9 (C(5)), 26.9 (C(6)), 29.7 (C(8)), 39.8 (C(3)), 41.4 (C(7)), 48.4 (C(4)), 48.6 (C(1)), 86.6 (C(2)), 128.3 (*m,m′*-PhC), 129.5 (*p*-PhC), 130.7 (*i*-PhC), 132.7 (*o,o′*-PhC)	94/0.064[f]
9l	0.73 (s, 3H, C(9)H$_3$), 0.99 (s, 3H, C(10)H$_3$), 1.07 (s, 3H, C(8)H$_3$), 1.07 (m, 1H, C(5)H), 1.19 [s, 9H, C(C**H**$_3$)$_3$], 1.14 (m, 1H, C(7)H), 1.42 (m, 1H, C(6)H), 1.55 (m, 1H, C(7)H), 1.67 (m, 1H, C(6)H), 1.68 (m, 1H, C(4)H), 1.73 (m, 1H, C(5)H), 4.27 (m, 1H, C(2)H)	19.3 (C(10)), 20.1 (C(9)), 25.8 (C(5)), 26.7 (C(6)), 27.3 [C(**C**H$_3$)$_3$], 29.6 (C(8)), 39.1 (C(3)), 39.4 [**C**(CH$_3$)$_3$], 41.2 (C(7)), 48.3 (C(4)), 48.4 (C(1)), 85.7 (C(2)), 178.7 (**C**O)	68/0.27

[a] Elemental analysis C ± 0.28, H ± 0.29 except **9c** H ± 0.46.

[b] 

[c] 

[d] Solidifies after redistillation, mp 46–48°C

[e] ref [43] bp 67°C/1.3 mbar.

[f] ref [47] bp 183–188°C/2.6 mbar.[9] Analytical data for all other compounds **9a, b, d, e, g, h, j** are in accordance to those given in the literature.

Table 3. Esters Prepared with DMAP/Anhydride

Compound	Yield[a)] (%)	$[\alpha]_{589}^{22}$ (c = 1, CH_2Cl_2)	ee (%)
9d	84	–85.5	54
9e	69	0	0
9f	80	–81.0	82
9i	70	+73.0	≥96[b]

[a] Isolated and purified substances, identical analytical data.

[b] de.

ature.[3] Complete racemization occurred in the course of the formation of compound **9e** with DMAP/anhydride. This might be the result of the workup procedure, since it is necessary to hydrolyze excessive benzoic acid anhydride and to remove the resulting acid under strong basic conditions (2 N NaOH).

All reactions were carried out under purified N_2 atmosphere by applying a positive pressure of the protecting gas, followed by non-inert workup. Standard syringe techniques were used to transfer solvents and to add liquid reagents. Glassware was flame-dried and flushed with N_2 before use. The reagents **3a**, **4a–c, 8a–d** were of commercial quality (Aldrich) and freshly distilled or recrystallized. All alcohols **8a–d** were 99% optical pure. The acids **6a,b** were taken from original containers (Fluka). Et_2O, toluene, and benzene were distilled from sodium benzophenone ketyl; CH_2Cl_2 was purified by column chromatography (alumina). Mps were taken using a copper block apparatus (Linström) and are uncorrected. Microanalyses were obtained with a LECO CHNS-932 element analyzer. Optical rotations were measured with an Eloptron Polarotronic E polarimeter (λ = 589 nm). IR spectra were recorded using a Nicolet Impact 400 spectrophotometer and wavelength (ν) are reported in cm^{-1}. ^{13}C and ^{1}H NMR spectra were determined on a Bruker DRX400 instrument operating at 100 and 400 MHz. Chemical shifts are given in ppm downfield from TMS or using the solvent signal of $CDCl_3$ (δ_H = 7.24, δ_C = 77.0) as an internal standard. The degree of substitution of C-atoms was determined with the aid of DEPT-90 and DEPT-135 spectra. All ^{1}H and ^{13}C resonances of alicyclic compounds **9g–l** were assigned using 2D NMR techniques (COSY, NOESY, HMBC, HMQC, Bruker standard pulse programs, Bruker software XwinNMR).

1-Acyl-4-alkylidene-1,4-dihydropyridines 5a–c; General Procedure:

This procedure was described in the literature,[12] but we modified the synthesis slightly and added a new derivative **5c.** A new interpretation of the ^{1}H NMR and additional ^{13}C NMR data are given:

To a stirred solution of 4-benzylpyridine (**3a**) (40.0 mL, 0.25 mol) in toluene (600 mL) the acyl halide **4a–c** (0.20 mol) was added with a syringe. The resulting yellow or orange suspension was stirred vigorously for 30 min followed by dropwise addition of NEt_3 (70 mL, 0.50 mol). The mixture was heated under reflux for 30 min and allowed to stand overnight at r.t. The precipitated $HNEt_3Cl$ was filtered off and the solvent was evaporated under reduced pressure to give the crude product which was recrystallized.

1-Acetyl-4-benzylidene-1,4-dihydropyridine (**5a**):

From acetyl chloride (**4a**) (14.2 mL); recrystallized from acetone; yield: 35.6 g (84%); yellow crystals; mp 81–82 °C [ref[12] mp 78–79 °C (Et_2O)].

^{1}H NMR (400 MHz, $CDCl_3$, 227 K): δ = *transoid*-**5a**: 2.28 (s, 3H, CH_3), 6.43 (d, 1H, H(5)), 6.54 (d, 1H, H(3)), 6.71 (d, 1H, H(6)), 7.36 (d, 1H, H(2)); *cisoid*-**5a**: 2.28 (s, 3H, CH_3), 5.85 (d, 1H, H(3)), 5.95 (d, 1H, H(5)), 6.65 (d, 1H, H(2)), 7.31 (d, 1H, H(6)); other resonances: 5.86 (s, 1H, H(α)), 5.88 (s, 1H, H(α)), 7.10–7.38 (m, 10H, PhH).

^{13}C NMR (100.6 MHz, $CDCl_3$, 227 K): δ = *transoid*-**5a**: 21.98 (CH_3), 110.13 (C(5)), 110.92 (C(3)), 124.11 (C(2)), 126.11 (C(6)); *cisoid*-**5a**: 21.98 (CH_3), 116.99 (C(3)), 117.86 (C(5)), 122.17 (C(6)), 124.16 (C(2)); other resonances: 116.24 (C(α)), 116.37 (C(α)), 126.08, 127.80, 128.62, 129.16, 137.72, 137.83, 166.22 (CO).

1-Benzoyl-4-benzylidene-1,4-dihydropyridine (**5b**):

From benzoyl chloride (**4b**) (23.2 mL); recrystallized from Et_2O; yield: 47.8 g (88%); orange crystals; mp 90–92 °C [ref[12] mp 9l–92 °C (acetone)].

^{1}H NMR (400 MHz, $CDCl_3$, 295 K): δ = 5.92 (s, 1H, H(α)), 5.94 (d, 1H, H(5)), 6.95 (d, 1H, H(3)), 7.10 (br, 2H, H(2,6)), 7.17 (m, 1H, Ph-*p*-H), 7.31–7.34 (m, 4H, Ph-*o*,*o*′, *m*,*m*′-H), 7.47–7.69 (m, 5H, BzH).

^{13}C NMR (100.6 MHz, $CDCl_3$, 295 K): δ = *cisoid*-**5b**: 110.55 (br, C(3,5)), 126.57 (br, C(2,6)); *transoid*-**5b**: 117.43 (br, C(3,5)), 124.45 (br, C(2,6)); other resonances: 116.60 (C(α)), 126.01, 127.82, 128.41, 128.50, 128.73, 129.37, 131.46, 132.96, 137.80, 166.60 (CO).

4-Benzylidene-1-pivaloyl-1,4-dihydropyridine (**5c**):

From pivaloyl chloride (**4c**) (24.6 mL); the reaction was complete after 7 h of heating, giving an orange oil after evaporation of toluene; crystallized from acetone; yield: 36.1 g (71%); yellowish powder; mp 56–58 °C.

$C_{17}H_{19}NO$	calcd	C	80.60	H	7.56	N	5.52
(253.3)	found		81.09		7.60		5.61

IR (KBr pellet): ν(C=O) = 1657 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$, 295 K): δ = 1.36 [s, 9H, C(CH_3)], 5.86 (s, 1H, H(α)), 5.90 (d, 1H, H(5)), 6.47 (m, 1H, H(3)), 7.22 (m, 1H, H(6)), 7.27 (m, 1H, H(2)), 7.12–7.33 (m, 5H, PhH).

^{13}C NMR (100.6 MHz, $CDCl_3$, 295 K): δ = 28.17 [C(CH_3)$_3$], 39.69 [C(CH_3)$_3$], 109.65 (C(5)), 115.50 (C(α)), 116.45 (C(3)), 124.62 (C(6)), 125.76 (Ph-*p*-C), 126.60 (C(2)), 127.24, 128.35 (Ph-*o*,*o*′,*m*,*m*′-C), 129.22 (C(4)), 138.0 (Ph-*i*-C), 173.42 (CO).

1-Acyl-4-alkylpyridinium Salts 7a–f; General Procedure:

The dihydropyridines **5a–c** (20.0 mmol) were dissolved in Et_2O (300 mL) and an 1.1 fold excess of acid **6a,b** (22.0 mmol) was subsequently added. The resulting suspension was stirred for 20 min at r.t. and the precipitated pyridinium salts **7a–f** were filtered off, washed with Et_2O and dried in vacuo.

Yields and analytical data of compounds **7a,c** are in accordance with those given in the literature.[12]

1-Acetyl-4-benzylpyridinium Trifluoromethanesulfonate (**7b**):

From dihydropyridine **5a** (4.3 g); trifluoromethanesulfonic acid (**6b**) (1.95 mL); yield: 6.90 g (96%); slightly yellowish powder.

^{1}H NMR (400 MHz, CD_3OCD_3): δ = 3.19 (s, 3H, CH_3), 4.70 (s, 2H, CH_2), 7.33 (m, 1H, Ph-*p*-H), 7.36–7.42 (m, 4H, Ph-*o*,*o*′,*m*,*m*′-H), 8.23 (d, 2H, Py-3,5-H), 9.55 (d, 2H, Py-2,6-H).

^{13}C NMR (100.6 MHz, CD_3OCD_3): δ = 21.26 (CH_3), 41.38 (CH_2), 127.44 (Py-3,5-C), 127.55 (Ph-*p*-C), 129.14, 129.46 (Ph-*o*,*o*′,*m*,*m*′-C), 136.80 (Ph-*i*-C), 140.38 (Py-2,6-C), 168.15 (Py-4-C), 168.82 (CO).

1-Benzoyl-4-benzylpyridinium Trifluoromethanesulfonate **(7d)**:

From dihydropyridine **5b** (5.50 g); trifluoromethanesulfonic acid (**6b**) (1.95 mL); yield: 7.96 g (94%); colorless powder.

^{1}H NMR (400 MHz, CD_3OCD_3): δ = 4.59 (s, 2H, CH_2), 7.34 (m, 1H, Ph[a]-p-H), 7.39–7.47 (m, 4H, Ph-*o*,*o*′,*m*,*m*′-H), 7.73 (m, Bz[b]-*m*,*m*′-H), 7.93 (m, 1H, Bz-*p*-H), 8.03 (m, 2H, Bz-*o*,*o* ′-H), 8.30 (dd, 2H, Py-3,5-H), 9.38 (dd, 2H, Py-2,6-H).

^{13}C NMR (100.6 MHz, CD_3OCD_3): δ = 41.54 (CH_2), 127.19 (Bz-*i*-C), 127.47 (Py-3,5-C), 127.64 (Ph-*p*-C), 129.17, 129.49 (Ph-*o*,*o*′,*m*,*m*′-C), 129.61 (Bz-*m*,*m*′-C), 132.29 (Bz-*o*,*o*′-C), 136.18 (Bz-*p*-C), 136.69 (Ph-*i*-C), 142.50 (Py-2,6-C), 167.23 (Py-4-C), 168.69 (CO).

[a] Ph = $PhCH_2$-moiety. [b] Bz = PhCO-moiety.

4-Benzyl-1-pivaloylpyridinium Tetrafluoroborate (**7e**):

From dihydropyridine **5c** (5.1 g); 54% tetrafluoroboric acid in Et_2O (**6a**) (3.0 mL); yield: 7.61 g (92%); yellowish oil which does not solidify.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.46 [s, 9H, C(CH_3)$_3$], 4.32 (s, 2H, CH_2), 7.20–7.32 (m, 5H, PhH), 7.95 (dd, 2H, Py-3,5-H), 8.94 (dd, 2H, Py-2,6-H).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 27.45 [C(CH_3)$_3$], 41.96 (CH_2), 43.39 [C(CH_3)$_3$], 127.82 (Ph-*p*-C), 127.96 (Py-3,5-C), 129.39, 129.50 (Ph-*o*,*o*′,*m*,*m*′-C), 135.32 (Ph-*i*-C), 140.44 (Py-2,6-C), 166.54 (Py-4-C), 176.79 (CO).

4-Benzyl-1-pivaloylpyridinium Trifluoromethanesulfonate (**7f**):

From dihydropyridine **5c** (5.1 g) in benzene/Et_2O mixture (1:1, 160 mL); trifluoromethanesulfonic acid (**6b**) (1.95 mL); yield: 6.9 g (79%); may be oily but solidifies upon standing and cooling, colorless solid.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.49 [s, 9H, C(CH_3)$_3$], 4.32 (s, 2H, CH_2), 7.16–7.37 (m, 5H, PhH), 7.91 (dd, 2H, Py-3,5-H), 8.87 (dd, 2H, Py-2,6-H).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 27.62 [C(CH_3)$_3$], 42.10 (CH_2), 43.33 [C(CH_3)$_3$], 127.53 (Py-3,5-C), 128.02 (Ph-*p*-C), 129.44, 129.56 (Ph-*o*,*o*′,*m*,*m*′-C), 135.13 (Ph-*i*-C), 140.76 (Py-2,6-C), 167.87 (Py-4-C), 175.87 (CO).

Esterification of Secondary Alcohols 8a–d; General Procedure:

Method A: The acylpyridinium salts **7a–f** (10.0 mmol) were weighed into a 500-mL flask and CH_2Cl_2 (300 mL) was added. In some cases a suspension resulted, but immediately became clear after addition of the alcohol (10.0 mmol). The mixture was stirred for 16 h at r.t. and the solvent was removed using a rotary evaporator. The residue was dissolved in Et_2O (20 mL) and the insoluble oily components were separated with a separating funnel. The solvent was evaporated and the crude product was distilled in vacuo.

Method B: In a 250-mL flask the dihydropyridines **5a–c** (10.0 mmol) were dissolved in CH_2Cl_2 (200 mL). To the solution an equimolar amount of acid (10.0 mmol; **6a**: 1.4 mL, **6b**: 0.9 mL) was added. After 10 min, the alcohol (10.0 mmol) was added and the mixture was allowed to stand overnight (16 h). The workup procedure as described above afforded the product.

Regeneration of 3a:
The insoluble residue (10 g) (from Method A or B), which consisted of nearly pure 4-benzylpyridinium salt **10a,b**, was dissolved in CH_2Cl_2 (200 mL), treated with sat. aq $NaHCO_3$ (200 mL), washed with water (2 × 100 mL) and dried (Na_2SO_4). The solvent was removed with a rotary evaporator and the residue was distilled in vacuo. Average yield: 85%.

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