8×Me); MS (CI) m/z 592 ($M + NH_4^+$). Anal. Calcd for $C_{27}H_{42}O_{13}$: C, 56.44; H, 7.37. Found: C, 56.67; H, 7.48.

(Methyl 2,3,6-tri-*O*-benzyl-α-D-glucopyranosid-4-yl) 2-Deoxy-3,4:6,7-di-*O*-isopropylidene-5-*O*-[(trimethylsilyl)-ethoxymethyl]-D-*manno*-heptonate (41). It was prepared from **14** and **40**, as previously described for the synthesis of **22**. Column chromatography (hexane–ethyl acetate (5:1)) afforded **41** (60%) as a colorless syrup: $[\alpha]_D$ +16.5° (c 0.9, chloroform); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.39–7.26 (m, 15 H, 3Ph), 5.15 (dd, $J_{4'/3'}$ = 9.5 Hz, $J_{4'/5'}$ = 10 Hz, 1 H, H-4'), 4.91 (d, J_{gem} = 12 Hz, 1 H, CH_2Ph), 4.89 (d, J_{gem} = 11.5 Hz, 1 H, CH_2Ph), 4.82 (d, J_{gem} = 12 Hz, 1 H, CH_2Ph), 4.77 (2s, 2 H, OCH_2O), 4.74 (d, J_{gem} = 11.5 Hz, 1 H, CH_2Ph), 4.66 (d, J_{gem} = 12 Hz, 1 H, CH_2Ph), 4.64 (d, $J_{1'/2'}$ = 4 Hz, 1 H, H-1'), 4.59 (ddd, $J_{3/4}$ = 5.5 Hz, $J_{2a/3}$ = 3.5 Hz, $J_{2b/3}$ = 10.5 Hz, 1 H, H-3), 4.58 (d, J_{gem} = 12 Hz, 1 H, CH_2Ph), 4.48 (d, J_{gem} = 12 Hz, 1 H, CH_2Ph), 4.15 (dd, $J_{7a/7b}$ = 8 Hz, $J_{6/7a}$ = 6.5 Hz, 1 H, H-7a), 4.13 (dd, $J_{4/5}$ = 8 Hz, 1 H, H-4), 4.01 (ddd, $J_{6/7b}$ = 8 Hz, $J_{5/6}$ = 6.5 Hz, 1 H, H-6), 3.98 (dd, $J_{2'/3'}$ = 9.5 Hz, 1 H, H-3'), 3.93 (dd, 1 H, H-7b), 3.82 (ddd, $J_{5'/6'a}$ = 7.5 Hz, $J_{5'/6'b}$ = 5.5 Hz, 1 H, H-5'), 3.72–3.59 (m, 5 H, $OCH_2CH_2SiMe_3$, H-5,2',6'a), 3.51 (dd, $J_{6'a/6'b}$ = 11 Hz, 1 H, H-6'b), 3.44 (s, 3 H, OMe), 2.53 (dd, $J_{2a/2b}$ = 14 Hz, 1 H, H-2a), 2.45 (dd, 1 H, H-2b), 1.40, 1.36, 1.35, 1.28 (4s, 12 H, 4×Me), 1.07–0.86 (m, J_{OCH} = 10 Hz, $J_{OCH'}$ = 6.5 Hz, J_{gem} = 13 Hz, 2 H, CH_2SiMe_3), 0.06 (s, 9 H, $SiMe_3$); MS (CI) m/z 884 ($M + NH_4^+$). Anal. Calcd for $C_{47}H_{66}O_{13}Si$: C, 65.10; H, 7.67. Found: C, 65.21; H, 7.60.

(Methyl 2,3,6-tri-*O*-benzyl-α-D-glucopyranosid-4-yl) 2-Deoxy-3,4:6,7-di-*O*-isopropylidene-5-*O*-pivaloyl-D-*manno*-heptonate (42). It was prepared from **15** and **40**, as previously described for the synthesis of **22**. Column chromatography (hexane–ethyl acetate (3:1)) afforded **42** (65%) as a colorless syrup: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.40–7.30 (m, 15 H, 3Ph), 5.16 (dd, $J_{3'/4'}$ = 9.5 Hz, $J_{4'/5'}$ = 10 Hz, 1 H, H-4'), 5.04 (dd, $J_{5/6}$ = 6.5 Hz, $J_{4/5}$ = 3 Hz, 1 H, H-5), 4.93 (d, J_{gem} = 11 Hz, 1 H, CH_2Ph), 4.84 (d, J_{gem} = 12 Hz, 1 H, CH_2Ph), 4.74 (d, J_{gem} = 11 Hz, 1 H, CH_2Ph), 4.68 (d, J_{gem} = 12 Hz, 1 H, CH_2Ph), 4.66 (d, $J_{1'/2'}$ = 4 Hz, 1 H, H-1'), 4.58 (m, 1 H, H-3), 4.55 (d, J_{gem} = 11.5 Hz, 1 H, CH_2Ph), 4.50 (d, J_{gem} = 11.5 Hz, 1 H, CH_2Ph), 4.31 (dd, $J_{3/4}$ = 6.5 Hz, 1 H, H-4), 4.17 (ddd, $J_{6/7b}$ = 7 Hz, $J_{6/7a}$ = 6 Hz, 1 H, H-6), 4.00 (dd, $J_{7a/7b}$ = 8.5 Hz, 1 H, H-7a), 3.95 (dd, $J_{2'/3'}$ = 9.5 Hz, 1 H, H-3'), 3.86 (m, 2 H, H-7b,5'), 3.64 (dd, 1 H, H-2'), 3.59 (dd, $J_{5'/6'a}$ = 2.5 Hz, $J_{6'a/6'b}$ = 11 Hz, 1 H, H-6'a), 3.51 (dd, $J_{5'/6'b}$ = 5 Hz, 1 H, H-6'b), 3.45 (s, 3 H, OMe), 2.32 (m, 2 H, H-2a,2b), 1.48, 1.40, 1.38, 1.30 (4s, 12 H, 4×Me), 1.23 (s, 9 H, *t*-Bu); MS (CI) m/z 839 ($M + NH_4^+$).

Registry No. **1**, 40036-82-6; **2**, 137945-76-7; **3**, 131444-81-0; **4**, 131444-82-1; **5**, 130481-65-1; **6**, 131444-80-9; **7**, 137945-77-8; **8**, 114729-42-9; **9**, 111833-99-9; **10**, 137945-78-9; **11**, 131444-70-7; **12**, 137945-79-0; **13**, 137945-80-3; **14**, 137945-81-4; **15**, 131444-71-8; **16**, 137945-82-5; **17**, 137945-83-6; **18**, 137945-84-7; **19**, 137945-85-8; **20**, 137945-86-9; **21**, 53008-65-4; **22**, 137945-87-0; **23**, 131456-52-5; **24**, 137964-64-8; **25**, 131444-84-3; **26**, 131465-47-9; **27**, 131444-86-5; **28**, 131444-88-7; **29**, 137945-88-1; **30**, 131444-89-8; **31**, 131444-90-1; **32**, 582-52-5; **33**, 131444-83-2; **34**, 131444-85-4; **35**, 131465-48-0; **36**, 131444-87-6; **37**, 131465-49-1; **38**, 137945-89-2; **39**, 131465-50-4; **40**, 19488-48-3; **41**, 137945-90-5; **42**, 137945-91-6.

Reaction of *N*-Vinylpyrazolium and *N*-Vinylindazolium Salts with Cyanide Ion: Formation of 1,2-Dihydropyrimidines, 3,4-Dihydroquinazolines, and Quinolines

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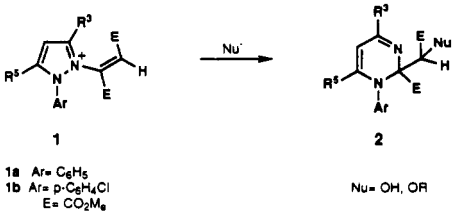
The reaction of 1-aryl-2-vinylpyrazolium tetrafluoroborates with potassium cyanide affords 2-hydroxy-1,2-dihydropyrimidines **3**, which exist as open-chain tautomers **4**, both in the solid state and in solution. The X-ray structure of the *p*-chlorophenyl derivative **4b** has been determined ($ClC_{14}N_2O_3H_{15}$, $P2_1/c$, a = 11.433 (3) Å, b = 16.086 (4) Å, c = 7.813 (4) Å, β = 94.22 (5)°, V = 1433.0 (9), Z = 4, R = 0.06 for 1334 observed reflections). Protonation of these vinylogous amidines **4** results in their cyclization and dehydration to pyrimidinium salts **6**. In the case of 1-vinyl-2-methylindazolium tetrafluoroborate **8**, the reaction with cyanide ion leads to a mixture of 3,4-dihydroquinazoline **12** and 2-(methoxycarbonyl)-3-cyanoquinoline (**13**). The mechanism proposed for this rearrangement is supported by the isolation of the open-chain intermediate in the case of 1-vinyl-2-phenylindazolium salt.

Introduction

Rearrangement of pyrazoles to pyrimidines is rather infrequent and usually takes place under strong conditions: use of sodium amide and high temperatures,[1] insertion of chlorocarbenes,[2] and flash vacuum pyrolysis.[3] We have reported such a rearrangement under very mild conditions, pH ca. 9 and room temperature.[4] The reaction takes place

Scheme I



when *N*-vinylpyrazolium salts **1** are treated with aqueous sodium carbonate or an alcohol. It proceeds through a

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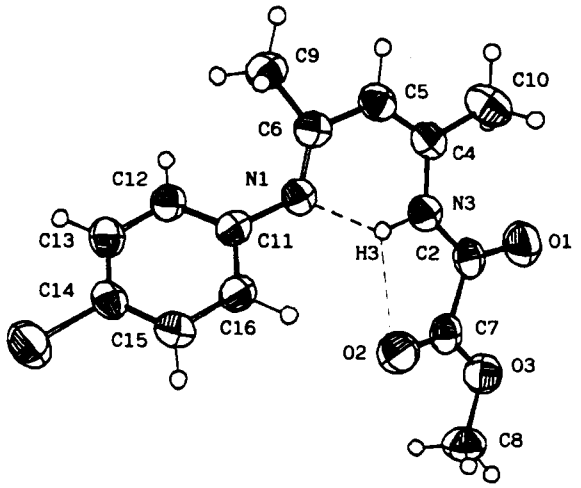


Figure 1. An ORTEP[19] view of molecule **4b** showing the atomic numbering used in the present crystallographic work.

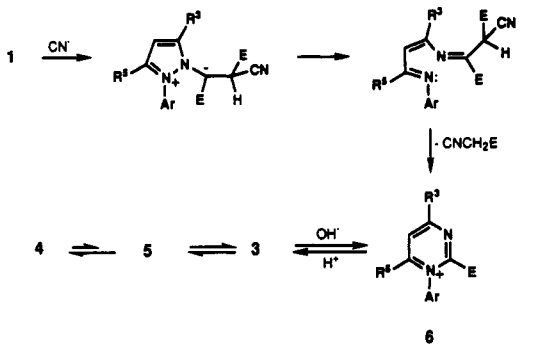
nucleophilic attack at the exocyclic double bond, followed by a ring expansion of the intermediate betaine, with final formation of 1,2-dihydropyrimidines **2** (Scheme I).

In order to determine if other nucleophiles undergo the same rearrangement, we selected a carbon nucleophile, the cyanide ion. In this paper, we report the results obtained when two vinylpyrazolium salts, **1a** and **1b**, and three vinylindazolium salts, **7**, **8**, and **19**, are made to react with potassium cyanide.

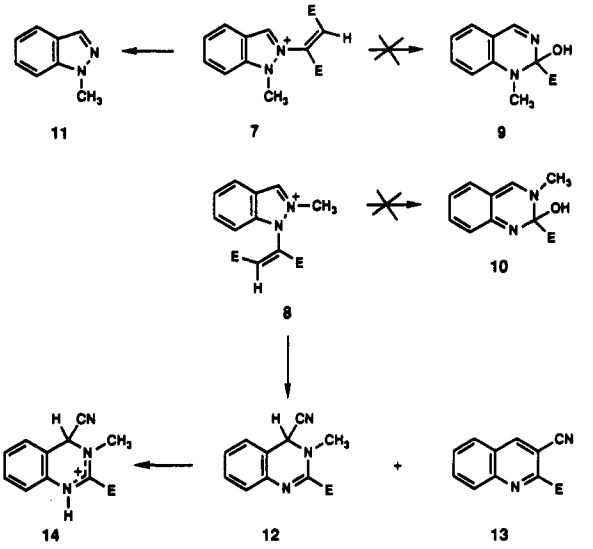
Results and Discussion

Reaction of 1-Aryl-2-vinyl-3,5-dimethylpyrazolium Salts with Potassium Cyanide. When pyrazolium salts **1a** (Ar = C_6H_5) and **1b** (Ar = C_6H_4Cl-4) react with potassium cyanide in water, the corresponding 1,2-dihydropyrimidine **2** (Nu = CN) is not formed. Instead, the reaction affords another dihydropyrimidine **3**, which formally corresponds to the attack of OH^- to a 1,4,6-trisubstituted pyrimidium cation. Concerning the position of the attack, literature results pointed to either an attack at position 2 or at position 6.[5-7] Taking into account that these hydroxydihydropyrimidines exist probably as open-chain tautomers and that there are 40 of such compounds (owing to prototropy and *E*/*Z* isomerism), the determination of the structure of **4** is a difficult task. It was decided therefore to determine its structure in the solid state by X-ray crystallography. Compound **4a** proved unsuitable since it decomposes on standing, but, after many attempts, suitable crystals of the *p*-chloro derivative **4b** were obtained. The structure (see supplementary material and Figure 1) corresponds to an attack at position 2, followed by a ring opening, and N1 to N3 prototropy, the double bonds maintaining the original stereochemistry (both are *Z*). There is an intramolecular asymmetrically bifurcated hydrogen bond between N3-H, N1, and O2 which fixes the geometry.

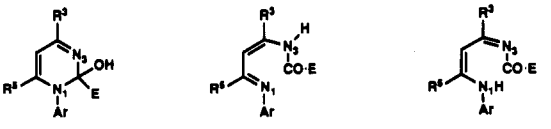
Scheme II



Scheme III



To determine if the structure in solution remains the same, i.e., N3-H/*ZZ*, the UV, IR, and ^1H NMR spectra were not very useful [λ_{max}(ethanol) = 309 nm, ν_{max}(KBr) = 1720 and 1640 cm^{-1}]. On the contrary, ^{13}C NMR (see supplementary material) showed that the structures in solution and in solid state are identical. The chemical shifts in the solid state (CP/MAS technique) and in solution are very similar; in particular, should a rapid prototropy between N3-H and N1-H (structure **4**) occur, a quasi equivalence of the signals of carbons C4 and C6 would be observed, which is clearly not the case.



Concerning the mechanism 1 + CN^- → **4**, a reasonable assumption is represented in Scheme II.

This mechanism is supported by the good leaving ability of methyl cyanacetate. A similar ring-open intermediate has been postulated in the ring transformation of triazolium 1-methanides into 1,2,4-triazines.[8]

If the reaction is carried out with potassium cyanide in methanol, dihydropyrimidine **2** (Nu = OCH_3) is obtained.

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Scheme IV

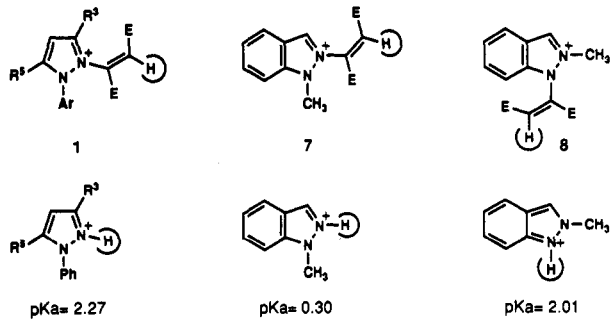


Table I. ^{1}H NMR Spectra of Compounds 12, 13, and 14 ($DCCl_3$)

compd	NCH_3	OCH_3	H_4	Ar
12	3.16	3.90	5.53	6.9–7.4
13		4.10	8.63	7.6–8.4
14	3.55	3.92	6.07	7.0–7.6

Compound **4** is in equilibrium with the ring-tautomer **3**, which explains its behavior as a typical pseudobase.[9] In acid medium (UV and NMR experiments) the compound is transformed into the pyrimidinium salt **6** (see supplementary material). The same behavior is observed for quinazolinium pseudobases when their ^{1}H NMR spectra are recorded in trifluoroacetic acid.[6a] Neutralization of a solution of salt **6** regenerates compound **4**.

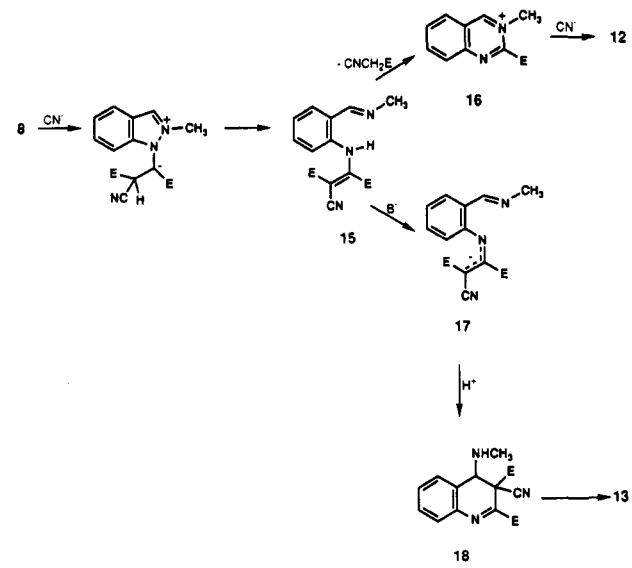
Reaction of *N*-Vinylindazolium Salts with Potassium Cyanide. If vinylindazolium salts **7** and **8** would react like vinylpyrazolium salts **1**, then structures **9** and **10**, or, more probably the corresponding open-chain tautomers, would be expected (Scheme III).

Actually, only 1-methylindazole **11** was isolated from **7**. Thus, instead of a nucleophilic attack on the exocyclic double bond, the base (CN^- or OH^-) abstracts the terminal hydrogen with elimination of **11** and, probably, formation of E—C≡C—E, i.e., the olefinic analogue of a β-elimination. The reason why for **1** (Scheme II) and **8** (see later on) the cyanide acts as a nucleophile whereas for **7** it acts like a base is probably related to the more acidic character of the terminal hydrogen in the case of 2-vinylindazolium salt **7**. Considering these cations as vinylogues of the protonated compounds, it is normal to assume a relationship between the pK_a's of azoles[10] and the acidity of the corresponding terminal hydrogens (Scheme IV).

It is clear that 1-methylindazole **11** is the less basic compound; hence, the terminal hydrogen of compound **7** should be the most acidic.

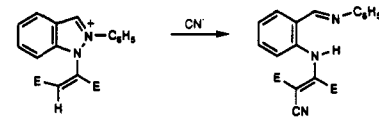
In the case of 1-vinylindazolium derivative **8**, the expected compound **10** was not formed. Instead a mixture of **12** (43%) and **13** (62%) was isolated (NMR data on Tables I and II). Compound **12** corresponds to an attack by CN^- instead of OH^- on the intermediate quinazolinium ion **16**, which can be related to differences in hardness between positions 2 of pyrimidium cation (between two nitrogen atoms) and position 4 of quinzolinium cation (α to the phenyl ring). Another difference between both series is that protonation of **3** leads to **6** with loss of a water molecule (Scheme II) whereas protonation of **12** leads to an amidinium salt **14**. A probable mechanism for the formation of quinoline **13** is reported in Scheme V, which

Scheme V



should proceed through the anion **17** and the dihydroquinoline **18**.

If instead of the *N*-methyl derivative **8**, the corresponding *N*-phenylindazolium salt **19** is used, the open-chain compound **20** corresponding to intermediate **15** (Scheme V) is isolated, supporting the above-mentioned mechanism.



All the proposed structures were consistent with spectroscopic data (IR, MS, and ^{1}H and ^{13}C NMR).

Conclusion

These results show the complexity of the rearrangements involving vinylazolium salts, which depending on the azole (pyrazole, 1*H*-indazole, and 2*H*-indazole) and on the base (aqueous sodium carbonate, methanol, and cyanide) can lead to dihydropyrimidines, enaminoimines, dihydroquinazolines, and quinolines. Thanks to the determination of the X-ray structure of compound **4b** and to the use mainly of ^{13}C NMR all the compounds have been identified, providing a reasonable basis for the proposed mechanisms.

Experimental Section

General Procedure. Melting points were taken on a Büchi 510 apparatus and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded at 300 and 75 MHz on a Varian VXR-300S system. ^{1}H and ^{13}C chemical shifts were measured relative to internal Me_4Si. Solid-state ^{13}C NMR spectra were recorded at 75 MHz using a Jacobsen solid Probe and adamantane as external reference. UV and infrared spectra were recorded on PE-Lambda 3 and PE-781 spectrometers, respectively. Mass spectra were recorded using a VG-12-250 mass spectrometer. Elemental analysis were determined at the Centro Nacional de Química Orgánica (CSIC).

The *N*-vinylazolium tetrafluoroborates were synthesized according to literature procedure.[11] **1a** was described in a previous paper.[11]

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Table II. ^{13}C NMR Spectra of Compounds 12, 13, and 14 ($DCCl_3$)[a]

compd	C2	C3	C4	C4a	C5	C6	C7	C8	C8a	CO	CN	OCH_3	NCH_3
12	147.4		53.2	115.9*	127.5	126.3#	130.6	125.5#	139.2	161.8	115.4*	52.0	38.1
13	147.1#	106.6	44.5	126.6	130.4*	127.7	130.1*	133.3	146.6#	163.5	115.9	53.4	
14	148.4		55.5	113.5*	120.1	126.6#	129.0#	131.8	130.2	155.8	113.0*	52.5	40.5

[a] Values with *, # can be interchanged.

1b: reaction time 4 h; white solid; yield 62%; mp 168–170 °C (ethanol–ethyl acetate); IR (KBr) ν 1740 and 1730 (CO), 1660 and 1060 (B–F) cm^{-1}; ^1H NMR (DMSO-d_6) δ 2.38 (s, 3 H, $CH_3$5), 2.45 (s, 3 H, $CH_3$3), 3.78 (s, 3 H, OCH_3), 3.80 (s, 3 H, OCH_3), 7.08 (s, 1 H, H4), 7.55 (s, 1 H, Hexo), 7.47 and 7.77 (m, 4 H, Ar). Anal. Calcd for $C_{17}H_{18}N_2O_4ClBF_4$: C, 46.77; H, 4.16; N, 6.42. Found: C, 46.72; H, 4.30; N, 6.45.

7: reaction time 6 h; unstable solid; yield 57%; mp 40–44 °C; IR (film) ν 1740 (CO) and 1150–900 (B-F) cm^{-1}; ^1H NMR (DMSO-d_6) δ 3.65 (s, 3 H, OCH_3), 3.88 (s, 3 H, OCH_3), 4.23 (s, 3 H, NCH_3), 6.9–8.4 (m, 4 H, Ar), 7.77 (s, 1 H, Hexo), 9.38 (s, 1 H, H3); ^{13}C NMR (DMSO-d_6) δ 36.9 (CH_3N), 53.3 (CH_3O), 54.6 (CH_3O), 111.6 (C7), 119.2 (C3a), 119.4 (C4), 123.7 (C5), 126.1 ($NCCO_2CH_3$), 130.3 (C6), 135.1 ($CHCO_2CH_3$), 136.0 (C3), 140.6 (C7a), 160.3 (CO), 161.7 (CO).

8: reaction time 19 h; white solid; yield 63%; mp 117–118 °C (ethanol–ethyl acetate); IR (KBr) ν 1750 and 1725 (CO) and 1140–940 (BF) cm^{-1}; ^1H NMR δ (DMSO-d_6) 3.60 (s, 3 H, OCH_3), 3.87 (s, 3 H, OCH_3), 4.33 (s, 3 H, NCH_3), 7.2–8.5 (m, 4 H, Ar), 7.82 (s, 1 H, Hexo), 9.50 (s, 1 H, H3); ^{13}C NMR δ (DMSO-d_6) 38.2 (CH_3N), 53.1 (CH_3O), 54.8 (CH_3O), 111.2 (C7), 119.3 (C3a), 123.7 (C4), 126.6 (C5), 128.4 ($NCCO_2CH_3$), 134.6 (C6), 137.1 ($CHCO_2CH_3$), 138.9 (C3), 140.8 (C7a), 160.7 (CO), 161.7 (CO). Anal. Calcd for $C_{14}H_{15}N_2O_4BF_4$: C, 46.44; H, 4.18; N, 7.74. Found: C, 46.73; H, 4.57; N, 7.72.

19: reaction time 2 h; white solid; yield 27%; mp 158–160 °C (ethanol–ethyl acetate); IR (KBr) ν 1720 (CO) and 1130–900 (BF) cm^{-1}; ^1H NMR (DMSO-d_6) δ 3.67 (s, 6 H, OCH_3), 7.4–8.4 (m, 9 H, Ar), 7.73 (s, 1 H, Hexo), 9.83 (s, 1 H, H3); ^{13}C NMR (DMSO-d_6) δ 53.4 (CH_3O), 54.3 (CH_3O), 111.8 (C7), 120.1 (C3a), 124.4 (C4), 126.8 (CoPh), 129.6 (C5 and $NCCO_2CH_3$), 130.6 (CmPh), 132.0 (CpPh), 133.1 (CiPh), 136.2, 136.5 and 139.2 (C6, C3, $CHCO_2CH_3$), 142.0 (C7a), 160.5 (CO), 162.1 (CO). Anal. Calcd for $C_{19}H_{17}O_4N_2BF_4$: C, 53.80; H, 4.04; N, 6.60. Found: C, 53.80; H, 3.98; N, 6.40.

^{13}C NMR of **7**, **8**, and **19** were assigned by comparison with the corresponding methoiodides[12] and with pyrazolium salts.[13]

General Procedure for Reaction of Vinylazolium Tetrafluoroborates with Potassium Cyanide. To a solution of 1.4 mmol of azolium salt in 200 mL of water was added a solution of 1.87 mmol of potassium cyanide in 12 mL of water dropwise at room temperature with magnetic stirring; the reaction mixture was treated as indicated in each case.

Reaction of 1a and 1b. The reaction mixture was stirred until the precipitation was complete. The solid was filtered off, throughly washed with water, and recrystallized from ethanol.

4a: yellow needles; yield 40%; mp 113–114 °C; mass spectrum Th 268 (28) M^+, 202 (26), 201 (100), 200 (17), 199 (13), 159 (22), 118 (9), 77 (24), 28 (13). Anal. Calcd for $C_{14}H_{16}N_2O_3$: C, 64.61; H, 6.15; N, 10.76. Found: C, 64.45; H, 6.30; N, 11.04.

4b: yellow needles; yield 38%; mp 144 °C dec. Anal. Calcd for $C_{14}H_{15}N_2O_3Cl$: C, 57.04; H, 5.09; N, 9.50. Found: C, 56.91; H, 5.24; N, 9.62.

Reaction of 8. The reaction mixture was extracted with dichloromethane, dried over $MgSO_4$, and evaporated. The oily residue was treated with ethanol and cooled. The precipitate was filtered off and recrystallized from ethanol yielding pure **13**: white solid; yield 62%; mp 160–162 °C; mass spectrum Th 212 (15) M^+, 182 (12), 154 (100), 153 (48), 127 (13), 126 (21) 100 (9); IR (KBr) ν 2220 (CN), 1725 (CO) cm^{-1}. Anal. Calcd for $C_{12}H_8N_2O_2$: C, 67.92; H, 3.80; N, 13.20. Found: C, 68.23; H, 4.26; N, 13.66.

The ethanolic solution was evaporated and the residue was purified by chromatography (Merck silica gel 230–400 mesh). Elution with hexane/ethyl acetate (1/1) affords pure **12**: yellow oil; yield 43%; IR (film) ν 2230 (CN), 1740 (CO) cm^{-1}.

Reaction of 19. The reaction mixture was stirred until the precipitation was complete. The solid was filtered off, thoroughly washed with water, and recrystallized from ethanol affording **20** as an unstable yellow solid: yield 60%; mp 56–58 °C; IR (KBr) ν 3300–3400 (NH), 2205 (CN), 1730, 1700, 1605 cm^{-1}; ^1H NMR ($DCCl_3$) δ 3.85 (s, 3 H, CH_3O), 3.86 (s, 3 H, CH_3O) 7.0–7.7 (m, 9 H, Ar), 8.59 (s, 1 H, CHN); ^{13}C NMR ($DCCl_3$) δ 52.2 (CH_3O), 53.5 (CH_3O), 112.0 and 118.4 (CN and $NCCCO_2CH_3$), 121.1 (CoPh), 129.1 (CmPh), 120.5, 125.8, 126.9, 131.1 and 133.6 (CHAr), 137.9 (CiNH), 129.2 (CiCN), 147.9 (CiPh), 155.8 ($NHCCO_2CH_3$), 158.7 (C=N), 162.5 (CO), 165.6 (CO).[14]

Crystal Structure of Compound 4b. A summary of the fundamental crystal data is given in Table III. A yellow crystal of prismatic shape was coated with resin epoxy and mounted in a κ diffractometer. The cell dimensions were refined by least-squares fitting the values of 25 reflections. The intensities were corrected for Lorentz and polarization effects. Scattering factors for neutral atoms and anomalous dispersion corrections for Cl atom were taken from the *International Tables for X-Ray Crystallography*.[15] The structure was solved by Multan[16] and Fourier methods. An empirical absorption correction was applied at the end of the isotropic refinement.[17] A difference synthesis showed H3 at the highest peak of the map. Final refinement was

Table III. Crystal and Refinement Data

formula	$ClC_{14}N_2O_3H_{15}$
M_r	194.7
crystal system	monoclinic
space group	$P2_1/c$
a, Å	11.433 (3)
b, Å	16.086 (4)
c, Å	7.813 (4)
β, (°)	94.22 (5)
V, Å^3	1433.0 (9)
Z	4
F(000)	616
ρ(calcd), g cm^{-3}	1.37
temp, °C	22
μ, cm^{-1}	2.71
cryst dimens, mm	0.06 × 0.12 × 0.04
diffractometer	Enraf-Nonius CAD4
radiation	graphite-monochromated Mo Kα (λ = 0.710 69 Å)
scan technique	$\Omega/2\theta$
θ	$1 < \theta < 25$
data collected	(−13,0,0) to (13,19,9)
rflns collected	2829
unique data	2522
unique data (I) $\geq 2\sigma$ (I)	1334
R(int), %	1.0
std rflns	3/96 rflns
R_F, %	6.0
Rw_F, %	5.8
average shift/error	0.01

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undertaken with fixed isotropic factors and coordinates for H atoms, except for H3 whose coordinates were refined. Most of the calculations were carried out with the X-ray 80 system.[18]

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Supplementary Material Available: Tables of bond lengths (Å) and angles (deg) and hydrogen bond distances (Å) and angles (deg) of compound **4b**, NMR data of compounds **4a**, **4b**, and **6a**, final atomic parameters, bond distances, and angles (13 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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Stereoselective Synthesis of β-Lactams by Condensation of Titanium Enolates of 2-Pyridyl Thioesters with Imines

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A mild and versatile one-pot synthesis of β-lactams has been performed by condensation of the easily generated titantium enolates of 2-pyridyl thioesters with imines employing chiral reaction partners. Both imines obtained from enantiomerically pure alkoxy aldehydes and the enolate derived from 3-hydroxybutyrate showed high diastereofacial preferences, efficiently transferring the stereochemical information to the stereocenters of the azetidinone ring. Advanced precursors of (+)-PS-5, (+)-PS-6, thienamycin, and 1β-methylthienamycin were prepared to illustrate the potential of this method. A ^1H-NMR study of the enolization process and a tentative rationalization of the stereochemical results are presented.

The well-recognized importance of β-lactams as antibiotics stimulated the pharmaceutical industry to develop new derivatives of this class of compounds possessing broader activity and enhanced resistance to biological degradation.[1] As a consequence, there is growing interest in improved synthetic methods that allow the assembly of a 2-azetidinone ring in a mild and selective fashion. In relation to this, we recently reported[2] a synthesis of β-lactams by the high yielding, one-pot condensation of imines with titanium enolates of 2-pyridyl thioesters.[3,4] The method is very mild and simple, not requiring strong bases or sophisticated reagents, and appears perfectly suitable to be extended to the preparation of nonracemic derivatives. We report here that our procedure can be successfully applied to the synthesis of optically active β-lactams using chiral imines or chiral enolate precursors.

Chart I

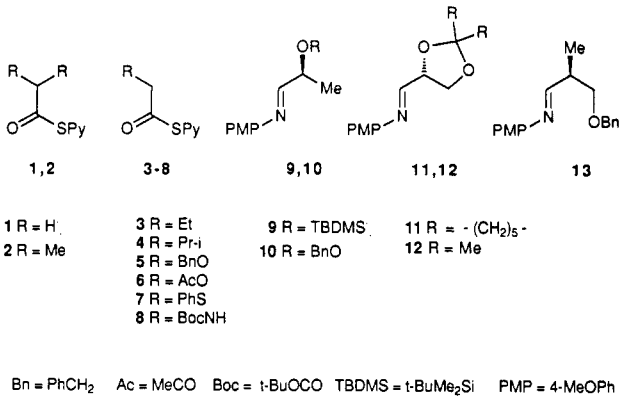

Table I. Synthesis of β-Lactams 14–20 from Thioesters 1 and 2 and Imines 9, 10, 11, and 13

thioester	imine[a]	product	yield[b] (%)	dr[c] s:a
1	9	14	42	>98:2
2	9	15	66	92:8
1	10	16	54	65:35
2	10	17	80	>98:2
1	11	18	52	>98:2
1[d]	13	19	71	29:71
2[d]	13	20	62	20:80

[a] Crude imines were used. [b] Overall isolated yields after flash chromatography. [c] By 300-MHz ^1H-NMR spectroscopy. [d] 1 mol equiv of enolate per mol equiv of imine.

Addition of Achiral Enolates of 2-Pyridyl Thioesters to Chiral Imines.[5,6] 2-Pyridyl thioesters were

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