Lewis Acid-catalysed Reactions of 2,2,2-Trichloroethyl 6-Diazopenicillanate and Imines: Rearrangements of Spiro-6-Aziridine- and Spiro-6-oxirane-penicillanates. *X*-Ray Crystal Structures of (3*S*,6′*S*]-*2,2,2-Trichloroethyl* 3-[4-Nitrophenyl)-1-phenylspiro[aziridine-2,6′-penicillanate] and (3*S*,7a*R*)-2,2,2-Trichloroethyl 2,3,5,7a-Tetrahydro-7-methoxy-2,2-dimethyl-6-(4-nitrophenyl)-5-oxopyrrolo[2,1-*b*]thiazole-3-carboxylate

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In the presence of boron trifluoride–diethyl ether, 6-diazopenicillanate (**1**) and aromatic imines react to form aziridines, thiazolo-pyrimidinones, and, in one case, an enaminopyrrolothiazole. The structure of the spiro-aziridine penicillanate (**2**) derived from 4-nitrobenzylideneaniline was established by *X*-ray diffraction. On treatment with boron trifluoride–diethyl ether, the spiro-aziridinepenicillanates rearranged to pyrrolothiazoles, and the spiro-6-oxirane penicillanate (**21**) gave predominantly the pyrrolothiazole (**22**), whose structure was confirmed by the *X*-ray crystal analysis of the enol ether (**23**).

The preparation of penicillin analogues by the chemical modification of the penicillanate nucleus has been widely studied[1] and recently 6-diazopenicillanates have been found to be useful intermediates for the introduction of many different substituents at C-6.[2] We here report reactions between the crystalline 2,2,2-trichloroethyl 6-diazopenicillanate (**1**)[3] and imines derived from aromatic aldehydes, together with Lewis acid-catalysed rearrangements of the aziridinyl products and of related epoxides. This study parallels that between the 6-diazopenicillanate (**1**) and aromatic aldehydes described in the preceding paper;[4] related work has also been reported by Sheehan.[5,6]

Results and Discussion

Lewis Acid Catalysed Reactions of Imines.—On addition of a few drops of boron trifluoride–diethyl ether to a solution of the 6-diazopenicillanate (**1**)[3] and *N*-(4-nitrobenzylidene)aniline in dichloromethane, nitrogen evolution was observed, and two products were isolated after column chromatography. These products were identified as the spiro-aziridinepenicillanate (**2**) (17%) and the thiazolopyrimidinone (**6**) (9%). Similar behaviour was observed using benzylideneaniline, two aziridines (**3**) (23%) and (**5**) (12%) being isolated in this case together with the thiazolopyrimidinone (**7**) (13%). The analogous reaction using 4-methoxy-*N*-(4-nitrobenzylidene)aniline appeared to be more specific, only a single product, identified as the spiro-aziridinepenicillanate (**4**) (23%) being isolated. In contrast no aziridinepenicillanate product was isolated from the analogous reaction between 6-diazopenicillanate (**1**) and *N*-(4-methoxybenzylidene)aniline which gave rise instead to the thiazolopyrimidinone (**8**) (22%) together with the enaminopyrrolothiazole (**9**) (25%).

The spiro-aziridinepenicillanates (**2**), (**3**), and (**5**) are known compounds having been described by Sheehan.[5] The aziridinyl stereochemistry of penicillanate (**2**) was confirmed by *X*-ray diffraction. Figure 1 shows a projection of the molecule as determined by the *X*-ray structure which established the configuration of the aziridine ring as depicted in formula (**2**). The other aziridines (**3**)—(**5**) were identified by spectroscopic comparison with (**2**), the stereochemistry of the major isomer (**3**), and the exclusive isomer (**4**), being assigned by analogy.

The thiazolopyrimidinones (**6**)—(**8**) were identified from their spectroscopic data, and by analogy with the formation of the thiazolo-oxazinones (**10**) from the reactions between 6-diazopenicillanate (**1**) and aromatic aldehydes.[4] In each case only a single isomer was detected and was assigned the (3*S*,8a*R*)-configuration, which would be expected to be the more stable, on the basis of the lack of an n.O.e. enhancement of 3-H on irradiation of 8a-H, and *vice versa*. The 6-(4-methoxyphenyl)-8-phenylthiazolopyrimidinone (**8**) was also prepared by treatment of the 6-iminopenicillanate (**11**; Ar = *p*-$MeOC_6H_4$; Ar = Ph)[4] with boron trifluoride–diethyl ether. This rearrangement was very fast and is consistent with this imine being an intermediate in the formation of the thiazolopyrimidinone (**8**) from the 6-diazopenicillanate (**1**) and *N*-(4-methoxybenzylidene)aniline (see below).

The enaminopyrrolothiazole (**9**) was identified by comparison with related products formed by the boron trifluoride–diethyl ether-catalysed rearrangement of aziridines (**2**)—(**4**), see below.[7]

The formation of products (**2**)—(**9**) from the BF_3·Et_2O-catalysed reaction between 6-diazopenicillanate (**1**) and the aromatic imines can be explained in terms of the reaction pathways outlined in Scheme 1. Electrophilic attack by the imine onto the less hindered α-face of the 6-diazopenicillanate would provide the zwitterionic intermediate (**12**). Cyclization with inversion of configuration at C-6 would then provide the aziridines (**2**)—(**5**). Alternatively migration of the aryl group would give the 6-iminopenicillanates (**11**) which could ring-expand to provide the thiazolopyrimidinones (**6**)—(**8**). The rapid rearrangement of the *N*-phenyliminopenicillanate (**11**; Ar′ = Ph; Ar = *p*-$MeOC_6H_4$), prepared by treatment of the 6-formylpenicillanate with aniline, to the corresponding thiazolopyrimidinone in the presence of a trace of BF_3·Et_2O, is consistent with these mechanistic proposals.

Although only modest yields of products were isolated from these reactions the yield of thiazolopyrimidinone would appear to increase with the electron density of the benzylidene ring

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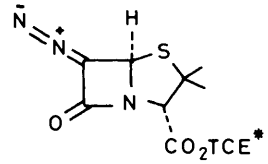
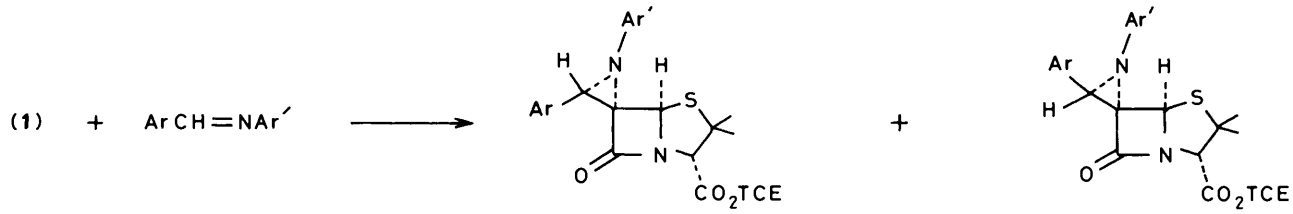
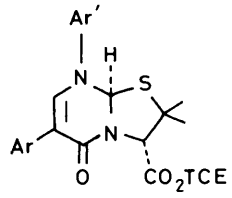


(1)

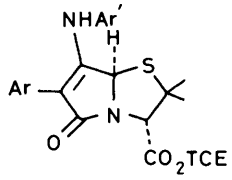


(2) Ar = $p-NO_2C_6H_4$, Ar′ = Ph
(3) Ar = Ar′ = Ph
(4) Ar = $p-NO_2C_6H_4$, Ar′ = $p-MeOC_6H_4$

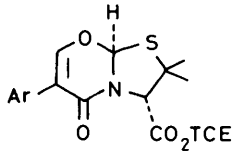
(5) Ar = Ar′ = Ph



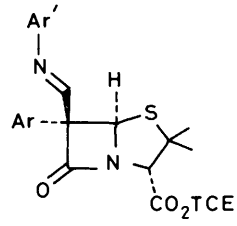
(6) Ar = $p-NO_2C_6H_4$, Ar = Ph
(7) Ar = Ar′ = Ph
(8) Ar = $p-MeOC_6H_4$, Ar′ = Ph



(9) Ar = $p-MeOC_6H_4$, Ar′ = Ph



(10)



(11)

*TCE = CH_2CCl_3

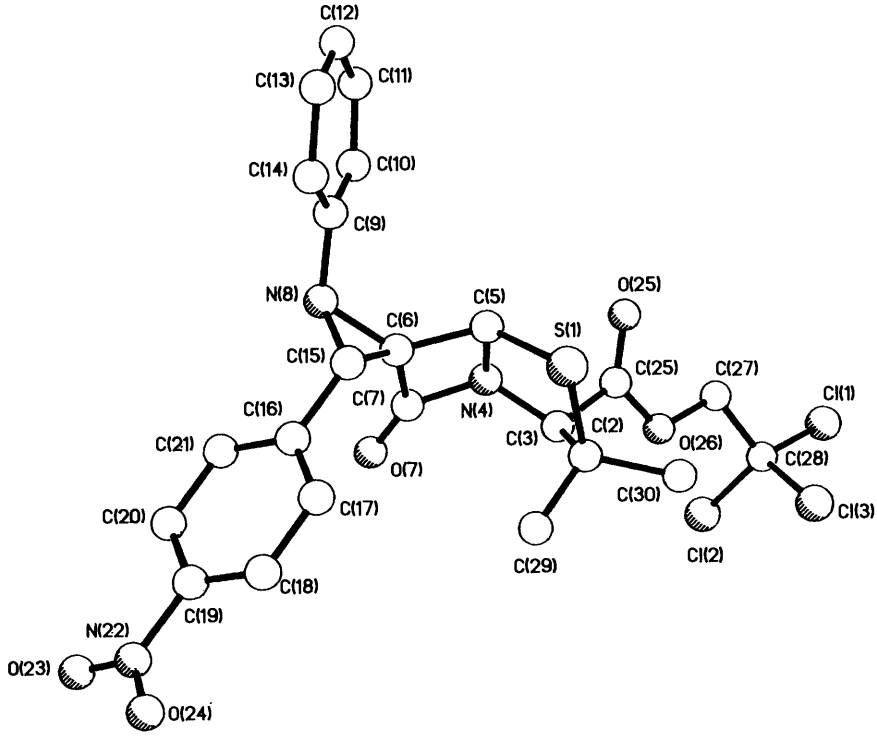
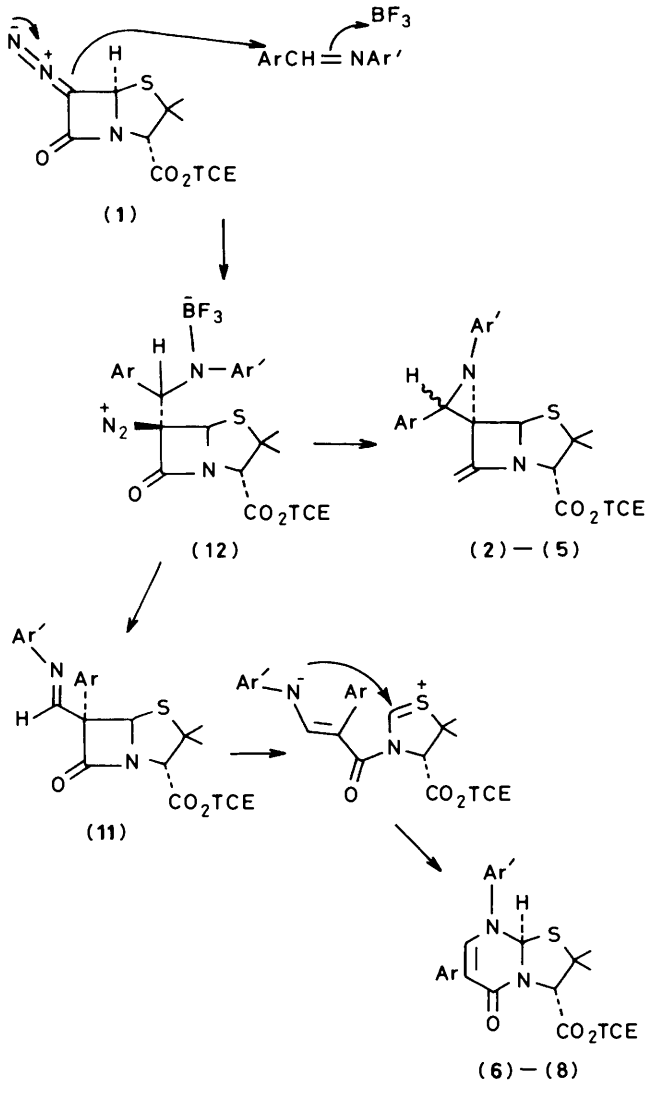


Figure 1. Molecular structure of aziridine (2) showing the crystallographic numbering scheme used

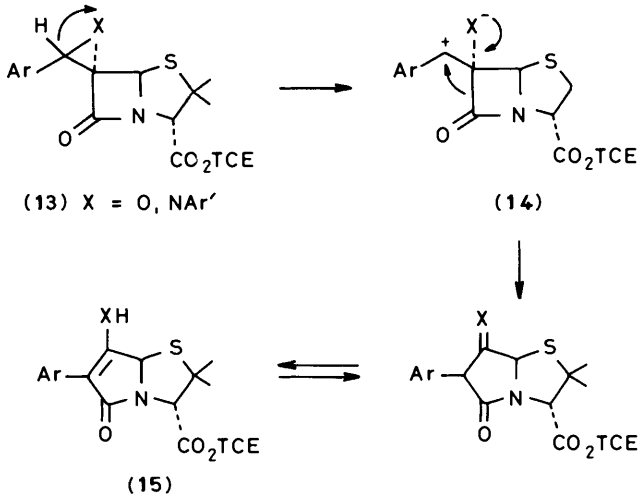


Scheme 1.

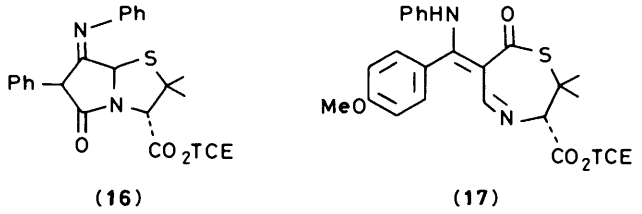
(Ar = p-$NO_2C_6H_4$, 8%; Ph, 13%; p-$MeOC_6H_4$, 22%) which is in keeping with the usual migration aptitude of these systems in electron-deficient rearrangements, and which would also lend support to the proposed mechanisms. No products were isolated which could have been formed by hydride migration in the zwitterionic intermediates (**12**).

The formation of the enaminopyrrolothiazole (**5**) can be explained as outlined in Scheme 2. It is suggested that the 6-aziridinylpenicillanate (**13**; X = NPh; Ar = p-$MeOC_6H_4$) is, as usual, formed in the imine diazopenicillanate reaction. However in this case the aziridine is unstable in the presence of the BF_3·Et_2O catalyst because of the 4-methoxy substituent. Acid-catalysed aziridine cleavage generates the methoxy stabilised zwitterionic intermediate (**14**) which can undergo the 1,2-shift shown to provide the enaminopyrrolothiazole (**9**) after tautomerisation.

In his study of the BF_3·Et_2O-catalysed reactions between imines and 6-diazopenicillanate (**1**), Sheehan does not report the isolation of thiazolopyrimidinones. Instead he assigns the pyrrolothiazole structure (**16**) to the non-β-lactam product from the benzylideneaniline reaction, and the iminothiazepine structure (**17**) to the sole product he isolated from the 4-methoxybenzylideneaniline reaction. However the spectroscopic data reported for the pyrrolothiazole (**26**) and the

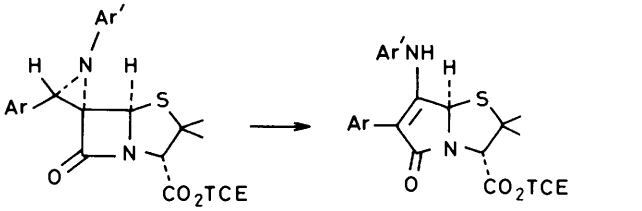


Scheme 2.

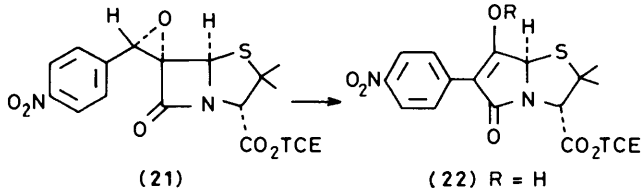


iminothiazepine (**17**) are very similar to our data for the thiazolopyrimidinone (**7**) and the enaminopyrrolothiazole (**9**), respectively.[5]

Lewis Acid-catalysed Rearrangements of 6-Aziridinyl- and 6-Epoxy-penicillanates.—It was found that treatment of the 6-aziridinylpenicillanates (**2**)—(**4**) with boron trifluoride–diethyl ether at room temperature gave rearranged products identified as the pyrrolo[2,1-*b*]thiazoles (**18**)—(**20**). Similar treatment of the stereoisomeric aziridine (**5**) gave a complex mixture of products which included a low yield of (**19**), although the other products from this reaction could not be identified. Finally, the



(18) Ar = p-$NO_2C_6H_4$, Ar′ = Ph
(19) Ar = Ar′ = Ph
(20) Ar = p-$NO_2C_6H_4$, Ar′ = p-$MeOC_6H_4$



(22) R = H
(23) R = Me

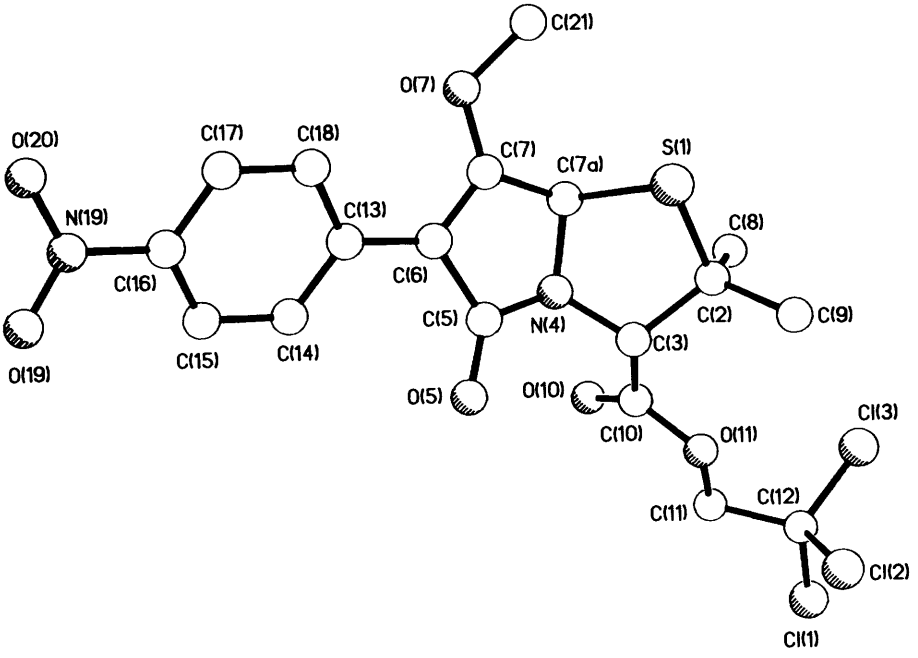


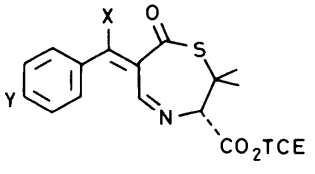
Figure 2. Molecular structure of enol ether (23) showing the crystallographic numbering scheme used

analogous rearrangement of the 6-epoxypenicillanate (**21**) was examined.[4] In this case rearrangement was much faster and led to the formation of two products in excellent yield. The major isolated product was found to be the pyrrolothiazole (**22**) but the minor product could not be unambiguously identified.

The epoxide rearranged product, the pyrrolothiazole (**22**), was the first rearrangement product to be unambiguously identified. Although it proved to be a rather polar oil that was difficult to handle, treatment with diazomethane gave a crystalline material which was amenable to *X*-ray crystallography. Figure 2 shows a projection of the molecule as determined by the *X*-ray examination which clearly shows the structure to be the enol ether represented by formula (**23**). The structure of the epoxide rearrangement product was then deduced to be the corresponding enol (**22**), this tautomer being preferred on spectroscopic grounds (see Experimental section).

The pyrrolothiazoles (**18**)—(**20**) were identified by comparison of their spectroscopic data with those of (**22**). In each case a single diastereoisomer was isolated which was assumed to be the more stable one shown.

These rearrangements of aziridines (**2**)—(**4**) and epoxide (**21**) into the pyrrolothiazoles can be rationalised in terms of the reaction pathway outlined in Scheme 2. The rate of this rearrangement would be expected to increase with the stability of the zwitterionic intermediate (**14**). Thus the rearrangement of the epoxide (**21**) is faster than that of the analogous aziridines (**2**) and (**4**), and the rearrangement of the *p*-methoxyaziridine (**13**; X = NPh; Ar = 4-$MeOC_6H_4$; not isolated) is faster than that of the analogous *p*-nitroaziridine (**2**).



(**24**) X = NPh, Y = NO_2
(**25**) X = NPh, Y = H
(**26**) X = OH, Y = NO_2

The rearrangement products isolated from aziridines (**2**) and (**3**) and epoxide (**21**) in our work, would appear to be the same as those isolated by Sheehan who identified the pyrrolothiazoles (**18**), (**19**), and (**22**), as the thiazepines (**24**), (**26**), and (**25**), respectively.[5] Our structural assignments for these compounds are based upon the *X*-ray structure of the enol ether (**23**), and spectroscopic correlation within the series of rearrangement products, as discussed above.

Experimental

For general experimental details see preceding paper.

Lewis Acid-catalysed Reactions of 6-*Diazopenicillanate* (**1**) *and Imines.*—*With* N-(4-*nitrobenzylideneaniline*). Boron trifluoride-diethyl ether (2 drops) was added to a solution of 6-diazopenicillanate (**1**) (500 mg, 1.39 mmol) and *N*-(4-nitrobenzylidene)aniline (315 mg, 1.39 mmol) in dichloromethane at 0—5 °C. After 25 min the mixture was concentrated under reduced pressure and the residue chromatographed on silica gel using ethyl acetate–light petroleum (1:9) as eluant. The first eluted material was identified as the aziridine (**2**) (136 mg, 17%), after recrystallization from dichloromethane–light petroleum, m.p. 146—147 °C (lit.,[5] m.p. 99—101 °C); $\nu_{max.}$($CHCl_3$) 1 780, 1 760, 1 600, 1 520, and 1 345 cm^{-1}; δ_H($CDCl_3$) 1.44 and 1.53 (each 3 H, s, Me), 3.88 (1 H, s, aziridine H), 4.64 (1 H, s, 3-H), 4.74 and 4.83 (each 1 H, d, *J* 12 Hz, *H*$CHCCl_3$), 5.64 (1 H, s, 5-H), 7.03—7.39 (5 H, m, ArH), and 7.78 and 8.26 (each 2 H, m, ArH); δ_C($CDCl_3$) 25.58 and 34.07 (each q, Me), 51.57 (d, Ar*C*HN), 64.06 (s, 2-C), 66.12 (d, 3-C), 66.93 (s, 6-C), 70.15 (d, 5-C), 75.00 (t, CH_2CCl_3), 94.14 (s, CCl_3), 120.25 and 123.89 (each d, ArC), 124.72, 128.28 and 129.92 (each d, ArC), 141.22, 147.48, and 148.22 (each s, ArC), 165.94 (s, CO_2), and 172.03 (s, 7-C); *m/z* 555 (M^+). The second eluted material was identified as (3S,8aR)-2,2,2-*trichloroethyl* 2,3,8,8a-*tetrahydro*-2,2-*dimethyl*-6-(4-*nitrophenyl*)-5-*oxo*-8-*phenyl*-5H-*thiazolo*[3,2-a]*pyrimidine*-3-*carboxylate* (**6**) (67 mg, 9%), a pale yellow oil; $\nu_{max.}$ (film) 1 765, 1 660, 1 650, 1 600, 1 580, 1 510, and 1 340 cm^{-1}; δ_H($CDCl_3$) 1.58 and 1.70 (each 3 H, s, Me), 4.82 and 4.89

(each 1 H, d, *J* 12 Hz, *H*CHCCl$_3$), 5.31 (1 H, s, 3-H), 7.14—7.51 (7 H, m, ArH + 8a-H and 7-H), and 7.77 and 8.17 (each 2 H, m, ArH); δ_C(CDCl$_3$) 25.35 and 33.75 (each q, Me), 52.83 (s, 2-C), 70.75 (d, 3-C), 75.00 (t, *C*H$_2$CCl$_3$), 80.15 (d, 8a-C), 94.22 (s, CCl$_3$), 106.81 (s, 6-C), 122.21, 123.59, 127.02, 127.67, and 129.78 (each d, ArC), 141.79 and 142.88 (each s, ArC), 144.57 (d, 7-C), 146.02 (s, ArC), 161.46 (s, 5-C), and 167.67 (s, CO_2); *m/z* 555 (M^+).

With N-*benzylideneaniline*. As described above, 6-diazopenicillanate (**1**) (250 mg, 0.7 mmol) and benzylideneaniline (126 mg, 0.7 mmol) in dichloromethane (10 ml) were treated with boron trifluoride–diethyl ether (2 drops) at 0—5 °C for 30 min. The crude product was chromatographed on silica gel using ethyl acetate–light petroleum (1:19) as eluant. The first fraction off the column was a mixture of the aziridines (**3**) and (**5**) (167 mg, 47%) which were separated by repeated chromatography on silica using dichloromethane–carbon tetrachloride (1:4) as eluant. The faster-moving isomer was identified as the (*R*)-aziridine (**5**) (42 mg, 12%), pale yellow platelets, m.p. 165—167 °C (lit.,[5] m.p. 175—176 °C) (Found: M^+, 510.0345, $C_{23}H_{21}{}^{35}Cl_3N_2O_3S$ requires M^+, 510.0337); $\nu_{max.}$(CHCl$_3$) 1 780, 1 770, 1 595, and 1 485 cm^{-1}; δ_H(CDCl$_3$) 1.47 and 1.56 (each 3 H, s, Me), 3.87 (1 H, s, aziridine H) 4.50 (1 H, s, 3-H), 4.71 and 4.87 (each 1 H, d, *J* 12 Hz, *H*CHCCl$_3$), 5.56 (1 H, s, 5-H), and 7.03—7.41 (10 H, m, ArH); δ_C(CDCl$_3$) 26.54 and 30.36 (each q, Me), 48.96 (d, aziridine C), 63.09 (s, 2-C), 64.89 (s, 6-C), 69.11 (d, 3-C + 5-C), 74.93 (t, *C*H$_2$CCl$_3$), 94.12 (s, CCl$_3$), 119.55, 123.97, 127.19, 128.48, 128.73 and 129.26 (each d, ArC), 134.12 and 148.44 (each s, ArC), 166.45 (s, CO_2), and 171.62 (s, 7-C); *m/z* 510 (M^+). The slower-moving isomer was identified as the (*S*)-aziridine (**3**) (83 mg, 23%) (Found: M^+, 510.0336. $C_{22}H_{21}{}^{35}Cl_3N_2O_3S$ requires *M*, 510.0337); white needles, m.p. 132—133 °C (from CHCl$_3$–CCl$_4$) (lit.,[5] m.p. 131—132 °C); $\nu_{max.}$(CHCl$_3$) 1 780, 1 760, 1 600, and 1 595 cm^{-1}; δ_H(CDCl$_3$) 1.46 and 1.52 (each 3 H, s, Me), 3.82 (1 H, s, 9-H), 4.64 (1 H, s, 3-H), 4.73 and 4.83 (each 1 H, d, *J* 12 Hz, HC*H*CCl$_3$), 5.63 (1 H, s, 5-H), and 7.03—7.62 (10 H, m, ArH); δ_C(CDCl$_3$) 25.53 and 33.97 (each q, CH$_3$), 52.89 (d, 9-C), 63.59 (s, 2-C), 66.22 (d, 3-C), 66.35 (s, 6-C), 70.03 (d, 5-C), 74.85 (t, *C*H$_2$CCl$_3$), 94.07 (s, CCl$_3$), 120.19, 123.98, 127.18, 128.39, and 129.53 (each d, ArC), 133.63 and 148.15 (each s, ArC), 165.97 (s, CO_2), and 172.60 (s, 7-C); *m/z* 510 (M^+). The second fraction off the column was identified as (3S,8aR)-2,2,2-*trichloroethyl* 2,3,8,8a-*tetrahydro*-2,2-*dimethyl*-5-*oxo*-6,8-*diphenyl*-5H-*thiazolo*[3,2-a]*pyrimidine*-3-*carboxylate* (**7**) (47 mg, 13%), a colourless oil (Found: M^+, 510.0338. $C_{23}H_{21}{}^{35}Cl_3N_2O_3S$ requires *M*, 510.0337); $\nu_{max.}$(CHCl$_3$) 1 760, 1 655, 1 645, 1 590, and 1 390 cm^{-1}; δ_H(CDCl$_3$) 1.59 and 1.70 (each 3 H, s, Me), 4.80 and 4.87 (each 1 H, d, *J* 12 Hz, *H*CHCCl$_3$), 5.37 (s, 3-H), and 7.13—7.56 (12 H, m, 7-H, 8a-H, + ArH); *m/z* 510 (M^+).

With 4-*methoxy* N-(4-*nitrobenzylidene*)*aniline*. As described above diazopenicillanate (**1**) (700 mg, 1.95 mmol) and 4-methoxy-*N*-(4-nitrobenzylidene)aniline (500 mg, 1.95 mmol) were treated with boron trifluoride–diethyl ether (3 drops) in dichloromethane (30 ml) at 0—5 °C for 25 min. Chromatography on silica gel, using ethyl acetate–light petroleum (1:9), as eluant, gave (3S,6′S)-2,2,2-*trichloroethyl spiro*[N-(4-*methoxyphenyl*)-3-(4-*nitrophenyl*)[*aziridine*-2,6′-*penicillanate*] (**4**) (264 mg, 23%), white needles, m.p. 130—131 °C (from ethyl acetate–light petroleum) (Found: M^+, 585.0278. $C_{24}H_{22}{}^{35}Cl_3N_3O_6S$ requires *M*, 585.0294); $\nu_{max.}$(CHCl$_3$) 1 780, 1 760, 1 520, 1 500, and 1 340 cm^{-1}; δ_H(CDCl$_3$) 1.44 and 1.53 (each 3 H, s, Me), 3.80 (3 H, s, OMe), 3.83 (1 H, s, aziridine H), 4.63 (1 H, s, 3-H), 4.74 and 4.83 (each 2 H, d, *J* 12 Hz, *H*CHCCl$_3$), 5.57 (1 H, s, 5-H), and 6.88, 6.98, 7.77, and 8.25 (each 2 H, m, ArH); *m/z* 585 (M^+).

With N-(4-*methoxybenzylidene*)*aniline*. As described above 6-diazopenicillanate (**1**) (500 mg, 1.39 mmol) and *N*-(4-methoxybenzylidene)aniline (294 mg, 1.39 mmol) in dichloromethane (20 ml) were treated with boron trifluoride–diethyl ether (8 drops) at 0—5 °C. After 30 min the reaction mixture was concentrated under reduced pressure. The residue was dissolved in dichloromethane (80 ml), and the solution washed with saturated, aqueous sodium hydrogen carbonate and water, dried (MgSO$_4$), and concentrated under reduced pressure. Chromatography on silica gel using ethyl acetate–hexane (1:9) as eluant, gave two product fractions. The first eluted product was identified as (3S,8aR)-2,2,2-*trichloroethyl*-2,3,8,8a-*tetrahydro*-6-(4-*methoxyphenyl*)-2,2-*dimethyl*-5-*oxo*-8-*phenyl*-5H-*thiazolo*[3,2-a]*pyrimidine*-3-*carboxylate* (**8**) (166 mg, 22%) (Found: M^+, 540.0440. $C_{24}H_{23}{}^{35}Cl_3N_2O_4S$ requires *M*, 540.0042); $\nu_{max.}$(CHCl$_3$) 1 760, 1 650, 1 595, 1 510, and 1 495 cm^{-1}; δ(CDCl$_3$) 1.59 and 1.69 (each 3 H, s, Me), 3.80 (3 H, s, OMe), 4.79 and 4.86 (each 1 H, d, *J* 12 Hz, *H*CHCCl$_3$), 5.37 (1 H, s, 3-H), 6.88 and 7.45 (each 2 H, m, ArH), and 7.11—7.41 (7 H, m, 7-H, 8a-H, and ArH); *m/z* 540 (M^+). The second eluted product was identified as (3S,7aR)-2,2,2-*trichloroethyl*-7-*anilino*-2,3,5,7a-*tetrahydro*-6-(4-*methoxyphenyl*)-2,2-*dimethyl*-5-*oxopyrrolo*[2,1-b]*thiazole*-3-*carboxylate* (**9**) (191 mg, 25%) (Found: M^+, 540.0433. $C_{24}H_{23}{}^{35}Cl_3N_2O_4S$ requires *M*, 540.0442); $\nu_{max.}$(CHCl$_3$) 1 760, 1 680, 1 630, and 1 600 cm^{-1}; δ_H(CDCl$_3$) 1.505 and 1.515 (each 3 H, s, Me), 3.82 (3 H, s, OMe), 4.78 and 4.83 (each 1 H, d, *J* 12 Hz, *H*CHCCl$_3$), 4.97 (1 H, s, 3-H), 6.10 (1 H, s, 7a-H), 6.89 (1 H, br s, exchanges with D$_2$O, N*H*Ar), 6.95 and 7.46 (each 2 H, m, ArH), and 7.07—7.35 (5 H, m, ArH); *m/z* 540 (M^+).

Lewis Acid-catalysed Rearrangements of 6-*Aziridinyl- and* 6-*Epoxy-penicillanates*.—(3S,6′S)-2,2,2-*Trichloroethyl*[3-(4-*nitrophenyl*)-1-*phenylspiro*[*aziridine*-2,6′-*penicillanate*] (**2**). Boron trifluoride–diethyl ether (20 drops) was added to the 6-aziridinyl penicillanate (**2**) (76 mg, 0.14 mmol) in chloroform (10 ml), and the mixture was stirred for 2.75 h at room temperature before being concentrated under reduced pressure to leave a dark oil. The oil was dissolved in chloroform, and the chloroform solution was washed with saturated, aqueous sodium hydrogen carbonate and water, dried (MgSO$_4$), and concentrated under reduced pressure. Chromatography using ethyl acetate–light petroleum (1:9) as eluant gave (3S,7aR)-2,2,2-*trichloroethyl*-7-*anilino*-2,3,5,7a-*tetrahydro*-2,2-*dimethyl*-6-(4-*nitrophenyl*)-5-*oxopyrrolo*[2,1-b]*thiazole*-3-*carboxylate* (**18**) (34 mg, 45%), a yellow oil (Found: M^+, 555.0196. $C_{23}H_{20}{}^{35}Cl_3N_3O_5S$ requires *M*, 555.0188); $\nu_{max.}$(CHCl$_3$) 1 750, 1 660, 1 615, 1 590, and 1 335 cm^{-1}; δ_H(CDCl$_3$) 1.52 (6 H, s, 2 × Me), 4.79 and 4.84 (each 1 H, d, *J* 12 Hz, *H*CHCCl$_3$), 4.95 (1 H, s, 3-H), 6.10 (1 H, s, 7a-H), 7.11—7.37 (6 H, m, NH and ArH), and 7.69 and 8.19 (each 2 H, m, ArH); δ_C(CDCl$_3$) 26.33 and 33.31 (each q, Me), 61.30 (s, 2-C), 65.93 (d, 3-C), 68.34 (d, 7*a*-C), 74.97 (t, *C*H$_2$CCl$_3$), 94.19 (s, CCl$_3$), 100.80 (s, 6-C), 123.94, 124.56, 127.02, 128.54, and 129.73 (each d, ArC), 137.36, 138.41, and 146.02 (each s, ArC), 161.51 (s, 7-C), 167.49 (s, 5-C), and 173.41 (s, CO_2); *m/z* 555 (M^+).

(3S,6′S)-2,2,2-*Trichloroethyl* 1,3-*diphenylspiro*[*aziridine*-2,6′-*penicillanate*] (**3**). The 6-aziridinylpenicillanate (**3**) (100 mg, 0.19 mmol) was dissolved in chloroform (10 ml) and boron trifluoride–diethyl ether (3 drops) added at room temperature. After 5 min the solution was concentrated under reduced pressure, and the residue chromatographed on silica using ethyl acetate–light petroleum (1:9) as eluant to give (3S,7aR)-2,2,2-*trichloroethyl* 7-*anilino*-2,3,5,7a-*tetrahydro*-2,2-*dimethyl*-5-*oxo*-6-*phenylpyrrolo*[2,1-b]*thiazole*-3-*carboxylate* (**19**) (85 mg, 85%) (Found: M^+, 510.0335. $C_{23}H_{21}{}^{35}Cl_3N_2O_3S$ requires *M*, 510.0338); $\nu_{max.}$(CHCl$_3$) 1 760, 1 680, 1 620, 1 600, 1 500, and 1 410 cm^{-1}; δ_H(CDCl$_3$) 1.51 and 1.52 (each 3 H, s, Me), 4.78 and 4.84 (each 1 H, d, *J* 12 Hz, *H*CHCCl$_3$), 4.99 (1 H, s, 3-H), 6.11 (1 H, s, 7a-H), 6.97 (1 H, br s, NH), and 7.11—7.58 (10 H, m, ArH); *m/z* 510 (M^+).

Table 1. Atom co-ordinates (× 10^4) for compound (**2**)

Atom	*x*	*y*	*z*
S(1)	7 887(4)	725(1)	9 432(1)
C(2)	7 049(13)	1 343(5)	8 933(3)
C(3)	4 566(13)	1 447(4)	9 000(3)
N(4)	3 738(10)	699(3)	9 159(2)
C(5)	5 194(13)	297(4)	9 492(3)
C(6)	4 672(13)	−441(4)	9 222(3)
C(7)	3 330(12)	44(4)	8 887(3)
O(7)	2 396(10)	−41(3)	8 527(2)
N(8)	4 158(11)	−1 233(3)	9 383(2)
C(9)	4 189(13)	−1 389(4)	9 888(3)
C(10)	2 597(16)	−1 078(5)	10 178(3)
C(11)	2 532(17)	−1 284(6)	10 638(3)
C(12)	4 076(18)	−1 775(6)	10 821(3)
C(13)	5 722(17)	−2 051(5)	10 546(3)
C(14)	5 758(16)	−1 884(5)	10 067(3)
C(15)	6 174(13)	−1 104(4)	9 123(3)
C(16)	6 450(12)	−1 453(4)	8 646(3)
C(17)	8 392(14)	−1 364(5)	8 424(3)
C(18)	8 721(15)	−1 696(6)	7 981(3)
C(19)	7 114(17)	−2 090(6)	7 774(3)
C(20)	5 126(17)	−2 183(6)	7 981(3)
C(21)	4 805(15)	−1 855(6)	8 433(3)
N(22)	7 523(19)	−2 447(6)	7 313(3)
O(23)	6 015(19)	−2 732(7)	7 101(3)
O(24)	9 375(17)	−2 450(7)	7 155(3)
C(25)	3 922(13)	2 058(4)	9 333(3)
O(25)	3 608(12)	1 997(4)	9 747(2)
O(26)	3 745(11)	2 735(3)	9 111(2)
C(27)	3 115(12)	3 402(3)	9 389(2)
C(28)	3 437(11)	4 093(5)	9 080(3)
C(28′)	4 188(16)	4 131(5)	9 216(5)
Cl(1)	2 551(6)	4 922(1)	9 374(1)
Cl(2)	1 854(9)	3 966(2)	8 574(1)
Cl(3)	6 185(6)	4 209(2)	8 936(2)
Cl(2′)	6 829(16)	4 133(11)	9 457(7)
Cl(3′)	4 321(24)	4 122(10)	8 596(4)
C(29)	7 559(13)	962(5)	8 470(3)
C(30)	8 332(14)	2 120(5)	8 977(4)
C(40)	7 307(26)	5 331(17)	7 695(11)
C(41)	7 119(25)	4 445(16)	7 655(10)
C(42)	5 569(25)	5 601(16)	7 818(10)
C(43)	9 043(24)	5 765(14)	7 936(8)

Table 2. Atom co-ordinates (× 10^4) for compound (**23**)

Atom	*x*	*y*	*z*
S(1)	9 296(4)	2 442(2)	1 856(1)
C(2)	8 499(14)	1 603(6)	1 331(3)
C(3)	6 908(13)	2 300(5)	1 046(3)
N(4)	7 541(11)	3 342(4)	1 097(2)
C(5)	6 044(14)	4 090(6)	1 162(2)
O(5)	4 255(9)	4 032(4)	989(2)
C(6)	6 970(12)	4 899(6)	1 485(2)
C(7)	8 829(12)	4 539(6)	1 650(3)
O(7)	10 144(9)	5 054(5)	1 941(2)
C(7a)	9 344(13)	3 529(6)	1 427(3)
C(8)	10 373(15)	1 330(7)	1 020(3)
C(9)	7 432(19)	680(6)	1 557(3)
C(10)	6 640(13)	1 972(5)	495(3)
O(10)	7 240(9)	2 453(4)	138(2)
O(11)	5 731(10)	1 063(4)	478(2)
C(11)	5 394(15)	636(5)	−10(3)
C(12)	5 263(14)	−501(6)	63(3)
Cl(1)	4 531(5)	−1 039(2)	−528(1)
Cl(2)	3 373(5)	−839(2)	510(1)
Cl(3)	7 679(5)	−1 013(2)	228(1)
C(13)	5 960(13)	5 862(5)	1 605(3)
C(14)	4 350(17)	6 243(6)	1 302(3)
C(15)	3 371(17)	7 140(6)	1 413(4)
C(16)	3 913(16)	7 671(5)	1 829(3)
C(17)	5 479(18)	7 310(7)	2 143(4)
C(18)	6 489(15)	6 421(6)	2 038(3)
N(19)	2 862(18)	8 607(6)	1 953(3)
O(19)	1 272(17)	8 831(7)	1 726(4)
O(20)	3 596(13)	9 163(5)	2 278(3)
C(21)	11 878(14)	4 522(8)	2 172(3)

(3S,6′S)-2,2,2-*Trichloroethyl* 1-(4-*methoxyphenyl*)-3-(4-*nitrophenyl*)*spiro*[*aziridine*-2,6′-*penicillanate*] (**4**). Boron trifluoride–diethyl ether (17 drops) was added to the 6-aziridinyl penicillanate (**4**) (150 mg, 2.56 mmol) in chloroform (10 ml) at room temperature. After being stirred for 1.5 h, the solution was washed with saturated aqueous sodium hydrogen carbonate and water, dried ($MgSO_4$), and concentrated under reduced pressure to leave an oil. This was chromatographed on silica using ethyl acetate–light petroleum as eluant, to give (3S,7aR)-2,2,2-*trichloroethyl* 2,3,5,7a-*tetrahydro*-7-(4-*methoxyphenylamino*)-2,2-*dimethyl*-6-(4-*nitrophenyl*)-5-*oxopyrrolo*[2,1-b]-*thiazole*-3-*carboxylate* (**20**) (81 mg, 54%), a pale yellow oil (Found: M^+, 585.0299. $C_{24}H_{22}{}^{35}Cl_3N_3O_6S$ requires *M*, 585.0294); $\nu_{max.}$($CHCl_3$) 1 750, 1 670, 1 610, and 1 590 cm^{-1}; δ_H($CDCl_3$) 1.485 and 1.495 (each 3 H, s, Me), 3.81 (3 H, s, OMe), 4.75 and 4.82 (each **1** H, d, *J* 12 Hz, *H*$CHCCl_3$), 4.91 (1 H, s, 3-H), 5.91 (1 H, s, 7a-H), 6.86 and 7.12 (each 2 H, m, ArH), 7.32 (1 H, br s, exchanges with D_2O, NH), and 7.70 and 8.17 (each 2 H, m, ArH); *m*/*z* 585 (M^+).

(3S,6′S)-2,2,2-*Trichloroethyl* 3-(4-*nitrophenyl*)*spiro*[*oxirane*-2,6′-*penicillanate*] (**21**).—Boron trifluoride–diethyl ether (18 drops) was added to a solution of the epoxypenicillanate (**21**) (300 mg, 0.62 mmol) in ethanol-free chloroform (15 ml) at room temperature. The clear colourless solution rapidly turned cloudy, and gradually became yellow. After 5 min the solution was concentrated under reduced pressure and the residue chromatographed on silica using ethyl acetate–light petroleum as eluant. The first product off the column was rechromatographed on silica using dichloromethane as eluant to give white crystals (89 mg), m.p. 152—154 °C from ethyl acetate–light petroleum, which could not be identified and which were too disordered for *X*-ray analysis. The second product off the column was identified as the enolic *pyrrolo*[2,1-b]*thiazole* (**22**) (230 mg) (Found: M^+ 479.9725. $C_{17}H_{15}{}^{35}Cl_3N_2O_6S$ requires *M* 479.9715); δ_H[$(CD_3)CO$] 1.50 and 1.54 (each 3 H, s, Me), 4.93 (1 H, s, 3-H), 4.98 and 5.0 (each 1 H, d, *J* 12 Hz, *H*$CHCCl_3$), 5.55 (1 H, s, 7a-H), and 8.04 and 8.62 (each 2 H, m, ArH); *m*/*z* 480 (M^+). This product, a viscous oil, was difficult to purify. Instead a sample (76 mg, 0.16 mmol) was dissolved in ethyl acetate (10 ml) and treated with an excess of diazomethane. After concentration under reduced pressure, the residue was chromatographed on silica gel using dichloromethane as eluant to provide (3S,7aR)-2,2,2-*trichloroethyl* 2,3,5,7a-*tetrahydro*-7-*methoxy*-2,2-*dimethyl*-6-(4-*nitrophenyl*)-5-*oxopyrrolo* [2,1-b]-*thiazole*-3-*carboxylate* (**23**) (54 mg, 69%), m.p. 175—177 °C (from dichloromethane–light petroleum) (Found: M^+, 493.9882. $C_{18}H_{17}{}^{35}Cl_3N_2O_6S$ requires *M*, 493.9872); $\nu_{max.}$($CHCl_3$) 1 760, 1 700, 1 620, 1 590, 1 510, and 1 340 cm^{-1}; δ_H($CDCl_3$) 1.59 and 1.65 (each 3 H, s, Me), 4.08 (3 H, s, OMe), 4.82 and 4.92 (each 1 H, d, *J* 12 Hz, *H*$CHCCl_3$), 4.99 (1 H, s, 3-H), 6.04 (1 H, s, 7a-H), and 8.18 and 8.22 (each 2 H, m, ArH); δ_C($CDCl_3$) 26.50 and 32.72 (each q, Me), 59.22 (q, OMe), 63.25 (s, 2-C), 63.74 (d, 3-C), 67.84 (d, 7a-C), 75.00 (t, CH_2CCl_3), 94.17 (s, CCl_3), 105.02 (s, 6-C), 123.31 and 128.24 (each d, ArH), 136.86 and 146.30 (each s, ArC), 167.29 (s, CO_2), 172.80 (s, 7-C), and 174.27 (s, 5-C); *m*/*z* 494 (M^+).

Crystal Data.—Compound (**2**) $C_{23}H_{20}Cl_3N_3O_5S$ M = 569,* orthorhombic, a = 6.135(1), b = 17.301(3), c = 28.257(9) Å, U = 2 999 Å^3, μ(Cu-K_α) = 38 cm^{-1}, λ = 1.541 78 Å, space group $P2_12_12_1$, Z = 4, D_c = 1.26 g cm^{-3}*, F(000) = 1 168. Approximate crystal dimensions 0.22 × 0.15 × 0.40 mm; Compound (**23**) $C_{18}H_{17}Cl_3N_2O_6S$, M = 495.7, orthorhombic, a = 6.310(2), b = 13.140(6), c = 26.567(5) Å, U = 2 203 Å^3, μ(Cu-K_α) = 51 cm^{-1}, λ = 1.541 78 Å, space group $P2_12_12_1$, Z = 4, D_c = 1.50 g cm^{-3}, F(000) = 1 016. Approximate crystal dimensions 0.07 × 0.13 × 0.20 mm.

Data Collection and Processing.—Compound (**2**) 2 017 independent observed reflections [$|F_o| > 3\sigma(|F_o|)$, $\theta < 56°$], (**23**) 1 388 independent observed reflections ($\theta < 58°$) were measured on a Nicolet R3m diffractometer with Cu-K_α radiation (graphite monochromator) using ω-scans.

Structural Analysis and Refinement.—Both structures were solved by direct methods and all the non-hydrogen atoms were refined anisotropically. The hydrogen atom positions were idealised (C–H = 0.96 Å), assigned isotropic thermal parameters [U(H) = 1.2U_{eq} (C)], and allowed to ride on their parent carbon atoms. The methyl groups were refined as rigid bodies. Refinement was by block-cascade full-matrix least-squares and converged to give for (**2**) R = 0.081, R_w = 0.086, [$w^{-1} = \sigma^2(F) + 0.002F^2$] and for (**23**) R = 0.061, R_w = 0.064, [$w^{-1} = \sigma^2(F) + 0.0012F^2$]. In compound (**2**) the terminal CH_2CCl_3 group has two discrete orientations with estimated occupancies of 0.85 and 0.15. This structure also contains an unidentified solvent fragment with an estimated occupancy of 0.4. Computations for both structures were carried out on an Eclipse S140 computer using the SHELXTL program system.[8]

Fractional atomic co-ordinates for the non-hydrogen atoms for compounds (**2**) and (**23**) are given in Tables 1 and 2 respectively. Bond lengths, bond angles, the fractional co-ordinates of the hydrogen atoms, the isotropic thermal parameters, and the anisotropic thermal parameters for the non-hydrogen atoms for compounds (**2**) and (**23**) are available on request from the Cambridge Crystallographic Data Centre.†

* Contains contributions from unidentified solvent fragments.

† See Instructions for Authors (1986), para. 5.6.3 in, *J. Chem. Soc., Perkin Trans. 1*, 1986, issue 1.

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