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Chromatography with silver nitrate

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Contents

1. Introduction

Electron donor–acceptor complexes, or π complexes, have been used extensively in various types of chromatography.[1] These complexes are considered to be formed from a π acceptor, or π acid, and a π donor, or π base. A requirement for a good acceptor in chromatography is that there must be more than one strongly electronegative or electron-withdrawing group attached to the carbon atoms of the π bond. The main requirements of donor molecules for chromatographic use are that steric hindrance and electron-withdrawing groups should be minimal.[2]

Silver nitrate has had a long history of use as a chromatographic support (π acceptor), after Lucas[3,4] and Nichols[5] reported that silver ions can complex with alkenes (π donor). These studies led the way for complexation recrystallisation,[6] which was simplified by washing non-polar solutions with aqueous silver nitrate, ('counter-current distribution').[7] Silver salts were then introduced into adsorbents by Morris,[8] de Vries,[9] Dutton[10] and Barrett,[11] who fully realised the potential of silver nitrate as a chromatographic adsorbent (argentation chromatography). Surprisingly this method has been patented only recently.[12]

The theory, spectroscopy and physical nature[13] behind the capabilities of silver nitrate have been investigated,[3,4,5,14] reviewed[15,21] and discussed elsewhere,[16,17] and will not be discussed in this review.

Although there was a period of intense activity in the 1960s, the following decades saw a decline in the use of this reagent. With this article, therefore, it is aimed to revive the awareness of synthetic chemists regarding the utility of argentation chromatography.

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Table 1. HPLC SN separation of alkenes

Compound	References	Compound	References
(*E*) and (*Z*)-9-tetradecen-1-ol acetate	22–26	1-Octene	27
(*E*) and (*Z*)-3-decene		1,7-Octadiene	
(*E*) and (*Z*)-9-dodecen-1-ol acetate		1,9-Decadiene	
(*E*) and (*Z*)-7-dodecen-1-ol acetate		(*E*)-1,4,9-Decatriene	
(*Z*,*E*) and (*Z*,*Z*)-9,12-tetradecadien-1-ol acetate		(*E*/*Z*)-2-Pentene	
(*E*,*E*) and (*Z*,*E*)-3,13-octadecadien-1-ol acetate		(*E*/*Z*)-2-Octene	
(*Z*,*E*) and (*Z*,*Z*)-3,13-octadecadien-1-ol acetate		(*E*/*Z*)-2-Decene	
		(*E*/*Z*)-1,4-Octadiene	
Methyl (*E*)-9-octadecenoate			
Methyl (*Z*)-9-octadecenoate		1,3,5,7-Cyclooctatetraene	
Methyl (*Z*)-9-(*Z*)-12-octadecadienoate		1,3,5-Cyclooctatriene	
Methyl (*Z*)-6-(*Z*)-9-(*Z*)-12-octadecatrienoate		1,3-Cyclooctadiene	
		1,4-Cyclooctadiene	
(*Z*)-cyclodecene	28	1,5-Cyclooctadiene	
(*Z*,*Z*)-1,6-cyclodecadiene		Cyclooctene	
(*Z*,*Z*)-1,5-cyclodecadiene			
(*Z*,*E*)-1,5-cyclodecadiene		(*Z*,*Z*,*Z*)-1,5,9-Cyclododecatriene	
		(*Z*,*Z*,*E*)-1,5,9-Cyclododecatriene	
		(*Z*,*E*,*E*)-1,5,9-Cyclododecatriene	
		(*E*,*E*,*E*)-1,5,9-Cyclododecatriene	

Abbreviations used in this article for various adsorbents are given in parenthesis for silver nitrate (SN), SN impregnated upon silica gel (SNIS), upon alumina (SNIA), upon amberlyst resin (SNIAR), upon sephadex (SNISe), and gas chromatography mobile or stationary phases will be discussed throughout the review when appropriate.

2. Alkanes

The utmost purities of the hydrocarbon solvents, cyclohexane, *n*-hexane, *n*-pentane, 3-methylpentane, 2,2,4-trimethylpentane and methylcyclohexane, were required for investigation of niobium and tantalum halids in non-aqueous systems. The usual procedures for purification were tried with little success. Columns filled with SNIA, however, were found to give spectroscopically pure solvents, removing all aromatic and olefinic impurities on a litre scale.[18] Isopentane and 3-methylpentane have been successfully purified using SNIA for use in high grade spectrochemical studies.[19]

In the ongoing attempts to find SN-containing stationary phases for gas chromatography of high selectivity and negligible tendency to bleed, in order to be compatible with flame ionisation detectors and on-line mass spectrometers, Dautzenberg[20] was able to separate a mixture of *n*-pentane, *n*-hexane, *n*-heptane, methylcyclohexane, *n*-octane and *n*-nonane using both tetraethylene glycol/SN and naphthyl-1-acetonitrile/SN stationary phases.

3. Alkenes and alkynes

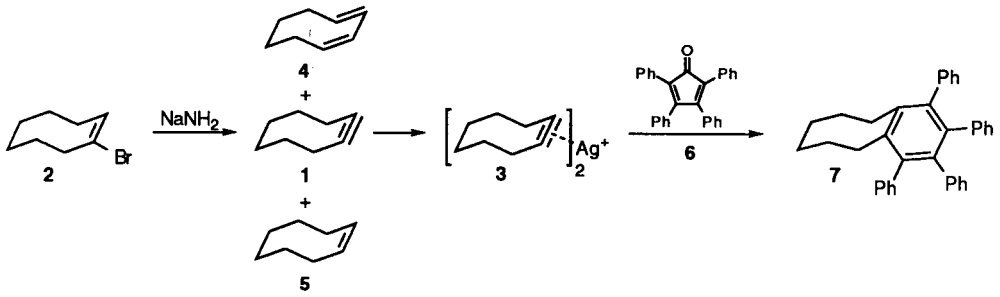
High pressure SN and silver perchlorate liquid chromatography is highly efficient in the separation of a large number of geometrical isomers (Table 1). Two reviews of this topic have been published and these should also be consulted.[21]

SN complexes were found to be very useful for the separation of a mixture of 1,3-, 1,4- and 1,5-cyclooctadienes obtained by sodium–alcohol reduction of cyclooctatetraene.[29] The three adducts differ in stability in aqueous silver nitrate; for example, the 1,3- adduct dissociates at 30°C, the 1,4- adduct at 60°C and the 1,5-complex at 90–100°C. The pure dienes are then recovered by steam distillation. A mixture of *cis*- and *trans*-cyclooctene was similarly separated by complexation. Surprisingly, aqueous silver nitrate selectively extracted the *trans*-isomer as a water soluble complex from a pentane solution containing the *cis*- and *trans*- isomers, while the *cis*-isomer remained in the *n*-pentane. Decomplexation using cold concentrated ammonium hydroxide solution afforded the pure *trans*-isomer.[30,31]

In the preparation of cyclooctyne (**1**) from 1-bromocyclooctene (**2**), Wittig and Dorsch[32] isolated the product as a crystalline SN complex **3** in 30% yield after aqueous extraction, whereas 1,3-cyclooctadiene (**4**), cyclooctene **5** and residual 1-bromocyclooctene **2** remained in the solvent. Treatment of the SN complex **3** with ammonium hydroxide liberated pure cyclooctyne (**1**), while treatment with tetraphenylcyclopentadienone (**6**) in benzene for 24 h at room temperature gave the decarbonylated cycloaddition product **7** in 87% yield (Scheme 1).

The separation of a mixture of isoprene, *cis*- and *trans*-penta-1,3-diene, penta-1,4-diene and cyclopentadiene was easily accomplished using gas chromatography on an SN/ethylene glycol stationary phase, whilst hexa-1,5-diene was retained irreversibly by the column.[33] Utilising the same system, the authors were also able to separate a mixture of ethene, propene and allene as well as a mixture of 2-methylbut-1-ene and 2-methylbut-2-ene.

The chromatographic behaviour of 89 synthetic *Z*,*Z*- and *E*,*Z*- diene standards, of 18–38 carbon atoms, has been studied by HPLC (SNIS) and the retention times compared to those developed by multiple regression models.[34] A series of methyl- and ethyl- substituted cyclopentenes and cyclohexenes have been investigated using high-speed liquid chromatography with SN/ethylene glycol as the stationary phase,[35] while the unsubstituted cyclic systems were investigated using TLC (SNIS).[36]



Scheme 1.

Table 2. Gas chromatography of exocyclic alkenes

Compound	Bp (°C)	References	Compound	Bp (°C)	References
Vinylcyclohexane	127.0	37	1(7)-*p*-Menthene	174.0	37
Ethylidenecyclohexane	136.8		8-*p*-Menthene	168.5	
1-Ethylcyclohexene	136.3		4(8)-*p*-Menthene	173.0	
3-Ethylcyclohexene	134.5		1-*p*-Menthene	174.5	
4-Ethylcyclohexene	132.5		*trans*-2-*p*-Menthene	166.6	
			3-*p*-Menthene	175.0	
i-Propylidenecyclohexane	160.5				
1-*i*-Propylcyclohexene	155.0				
3-*i*-Propylcyclohexene	149.6				
4-*i*-Propylcyclohexene	154.0				

Gas chromatography has proved to be especially efficient in partitioning closely-related cyclohexanes, cyclohexenes and structurally similar monoterpenes, using a variety of SN stationary phases (Table 2).

Convenient large-scale (1–3 g) separations of mixtures of (*E*)- and (*Z*)-8-heptadecene and (*Z*,*E*)- **8** and (*Z*,*Z*)-α-farnesene (**9**) have been achieved using argentation medium pressure liquid chromatography.[38,39] The four isomers of farnesol were effectively partitioned by the same authors under the same conditions,[38] but difficulties were encountered with a mixture of (*E*)-**10** and (*Z*)-7-methyl-6-nonen-3-one (**11**) which gave only partial separation[39] (Fig. 1).

Abidi[40] has reported a preparative reverse phase HPLC separation, using SN as the mobile phase, of the *cis*- and *trans*- isomers of the allylic *N*-terpenyl-*N*-hydroxyethyl-nitrosamines **12**–**15** derived from allylic terpenyl ethanolamines (experimental fish toxicants) (Fig. 2).

The total synthesis of pheromones has relied on the very important Wittig reaction for useful synthetic transformations, but this process is invariably complicated by the formation of both *E*- and *Z*-isomers. When the hexa-1,6-diylid **16** was generated in the presence of heptan-7-one (**17**) and 5-acetoxypentanal (**18**), two geometrical isomers, **19** and **20**, were obtained, and these were subsequently partitioned using SNIS[41] (Scheme 2).

Stilbenes[42] partition well using SN, as do dimethylcinnamic acids.[43] Normal phase HPLC (5% SN/Partisil 10) was required for the stilbenes *E*-**21** and *Z*-**23** where X=Br, Cl, F, OH and OCH_3, and R=methyl, ethyl and *n*-butyl, whereas the stilbenes *E*-**22** and *Z*-**24** could be separated by reverse phase HPLC using 5 and 10% SN as the

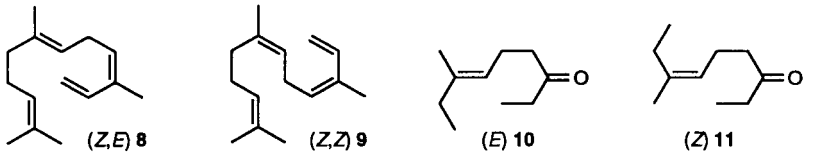


Figure 1.

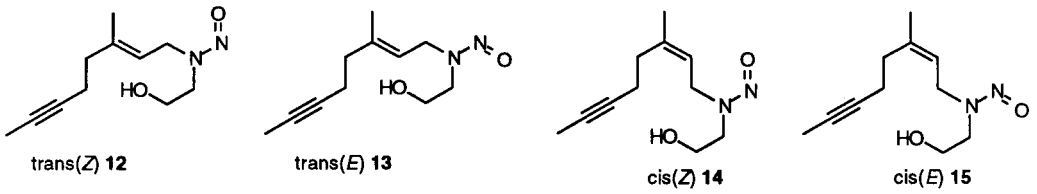
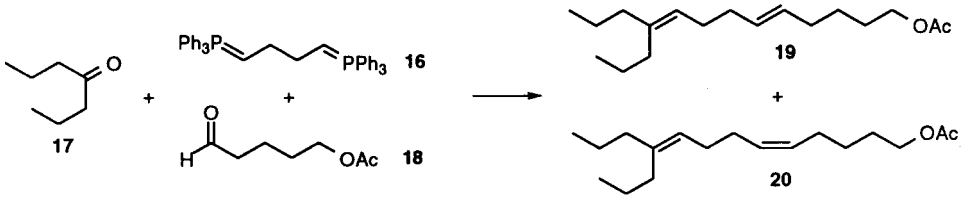


Figure 2.



Scheme 2.

eluent (Fig. 3). Lam[44] observed a good separation of *cis*- and *trans*-stilbene, *trans*-fumarate and *cis*-maleate derivatives using silver loaded aluminosilicate as the stationary phase.

When subjecting stilbenes to SNIA, caution must be taken, as epoxidation of the double bond can occur as a side reaction to separation. Kumari et al.[45] observed that when a mixture of 2,4,5-trimethoxybenzyl 2′-methoxy styrene (**25**) and latifolin (**26**), the isomeric allyl compound, were eluted slowly through an SNIA column, considerable amounts of **25** were retained. The use of a more polar solvent gave a new compound, not present in the original mixture, which was eluted and determined to be the epoxide **27**. Further confirmation of the formation of **27** was obtained when this compound was heated in the presence of triphenylphosphine to afford the starting styrene **25** (Fig. 4).

In the search for antimalarial derivatives, Rücker[46] utilised SNIS in both the purification of the starting γ-curcumene (**28**) from the essential oil *Helichrysum italicum* as well as in the separation of the desired peroxide targets **29** and **30**. Formation of the ketone **33** was observed as a side reaction, however, when the bicyclic peroxides **31** and **32** were subjected to SNIS (Scheme 3).

The normally difficult isomer separation of **35** and **36** resulting from the acid-catalysed degradation of 3-hydroxy-α-ionol **34** can easily be performed with SNIS[47] (Scheme 4).

A similar separation of the dimethylcyclohexadienes,[48] **38**

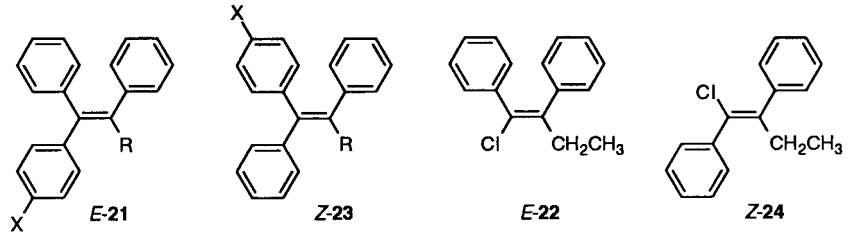


Figure 3.

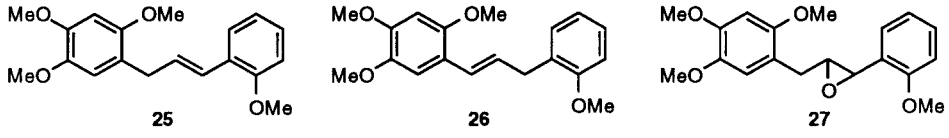
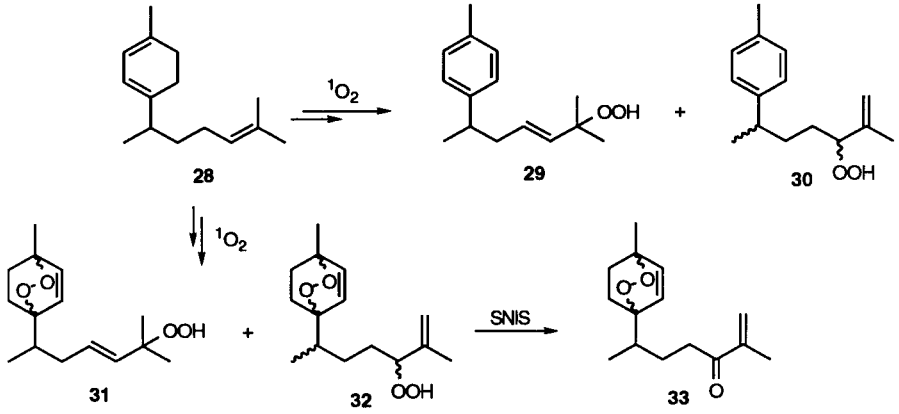
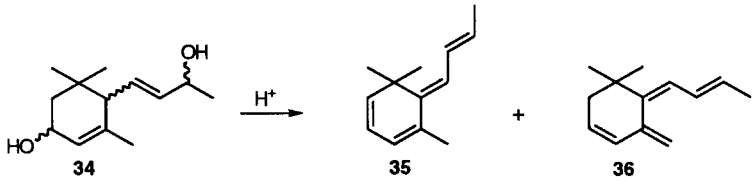


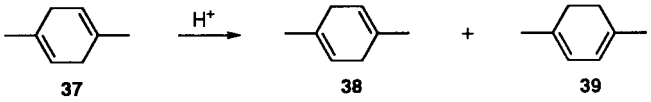
Figure 4.



Scheme 3.



Scheme 4.



Scheme 5.

and **39**, formed by treatment of 1,4-dimethylcyclohexa-1,4-diene (**37**) with acid, was achieved using identical conditions to those described above (Scheme 5).

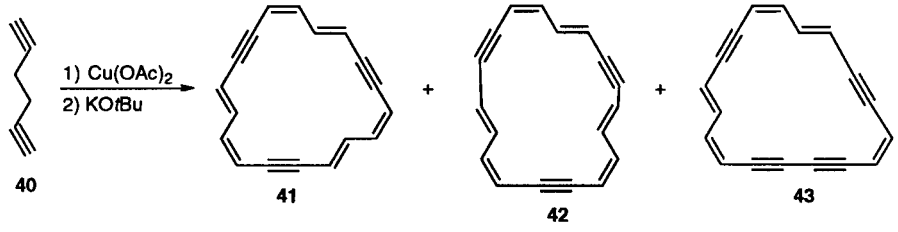
The ability of SNIA to resolve mixtures of annulenes allowed Wolovsky[49] to utilise non-regio and non-specific chemical synthesis which would otherwise require intensive and time-consuming sequential syntheses. 1,5-Hexadiyne (**40**) was oxidatively coupled with cupric acetate and the product mixture then subjected to prototropic rearrangement with potassium *t*-butoxide. This afforded the annulenes **41**–**43** combined with a number of polymeric products that were partitioned on a preparative scale (Scheme 6). Other annulenes have been subjected to SNIS, but these derivatives rapidly equilibrated, making isolation of the pure compounds impossible.[50]

Humulene (**44**) is readily purified as an SN complex and may then be regenerated, either by steam distillation or by treatment with aqueous ammonia[51] (Fig. 5). Synthesis of the humulene epoxide **45** has previously been accomplished in four steps in a very low total yield, with the final step requiring a difficult separation from the isomer **46** upon SNIS. Hayano and Shirahama[52] reported a more efficient synthesis of **45** by first treating humulene (**44**) with two equivalents of *m*-chloroperbenzoic acid followed by selective titanium(II) reduction, which afforded the desired major product **45** and the minor product **47**. Separation was effected by the formation of a crystalline SN complex of **45** which was decomplexed using hydroxylamine.

Isolation of the naturally occurring polyacetylenes **48**–**53** from immature safflower seeds required the help of SNIS (Fig. 6). In addition, changes in the amounts of the polyacetylenes during maturation were discovered and the quantities were determined using this method.[53]

$\Delta^{1,11}$-Dodecadiene (**55**), prepared from 3-chloro-1-propene (**54**), presents a particular difficulty because it co-distills with 1,6-dichlorohexane, a byproduct of the reaction. On addition of the crude oily diene to aqueous SN a solid complex formed that could be recrystallised from hot ethanol.[54] The complex was decomposed with water, and the hydrocarbon extracted with ether and distilled (Scheme 7).

Allylic derivatives of benzene or cyclohexene were separated from their propenylic isomers by means of SNIS methodology. Only the allylic isomers formed complexes with SN, since the propenyl derivatives showed about the same R_f values both on silica and impregnated silica[55] (Table 3).



Scheme 6.

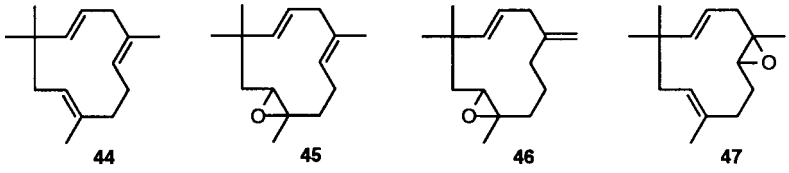


Figure 5.

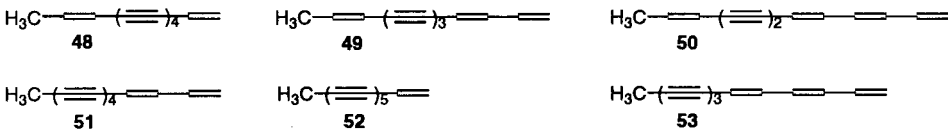
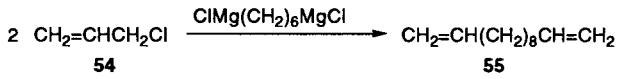


Figure 6.



Scheme 7.

Table 3. Allyl and propenyl partitioning

Compound	R_f		Eluent
	SiO_2	SNIS	
Pulegone	0.37	0.41	Benzene–Methanol (1:3)
i-Pulegone	0.43	0.18	
Estragole	0.66	0.51	Benzene
Anethole	0.68	0.67	
Eugenol	0.42	[a]	Benzene–Methanol (99:1)
i-Eugenol	0.42	[a]	
Eugenyl acetate	0.51	0.32	Benzene–Methanol (99:1)
i-Eugenyl acetate	0.51	0.51	
Safrole	0.57	0.29	Petroleum ether–Benzene (1:1)
i-Safrole	0.57	0.57	

[a] The compounds react with SN and reduce Ag^+ on the plate.

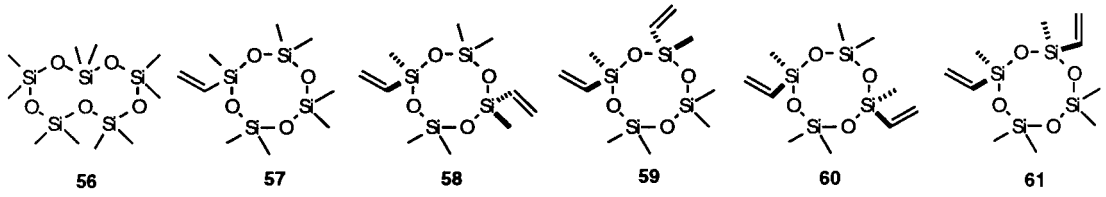
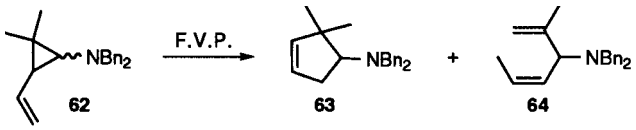


Figure 7.

A mixture of nongeminal divinylhexamethylcyclotetrasiloxanes obtained from the product of co-hydrolysis of dichlorodimethylsilane and dichloromethylvinylsilane was separated into five fractions by means of TLC (SNIS). Column chromatography on the same adsorbent gave five fractions: (1) 1,1,3,3,5,5,7,7,9,9-decamethylcyclopentasiloxane (**56**), (2) 1-vinyl-1,3,3,5,5,7,7-heptamethylcyclotetra siloxane (**57**), (3) *trans*-1,5-divinyl-1,3,3,5,7,7-hexamethylcyclotetrasiloxane (**58**), (4) a mixture of *trans*-1,3-divinyl-1,3,5,5,7,7-hexamethylcyclotetrasiloxane (**59**) and *cis*-1,5-divinyl-1,3,3,5,7,7-hexamethylcyclotetra siloxane (**60**), and (5) *cis*-1,3-divinyl-1,3,5,5,7,7-hexamethylcyclotetrasiloxane (**61**)[56] (Fig. 7).

Flash vacuum pyrolysis of the ethenylaminocyclopropane **62** afforded an aminocyclopentene **63** (6%) and a diene **64** (36%). The first product, **63**, was derived from a [1,3]-sigmatropic rearrangement while the second compound, **64**, was derived from a competing homo-1,5-hydrogen shift. Both products could not be resolved from one another on silica gel, but were successfully isolated using SNIS column chromatography (Scheme 8).[57]



Scheme 8.

4. Aromatics

A highly efficient chromatographic column consisting of glass beads coated with solid SN and modified by water vapour in the carrier gas was developed by Wasik.[58] The column could be used at room temperature to analyse mixtures containing aromatic hydrocarbons having boiling points of up to 180°C. To demonstrate column performance, a mixture of 14 benzenoid derivatives was separated into its individual components (Table 4). This method of water vapour utilisation was adopted by Viktorova[59] for the separation of alkenes.

Urushiol diacetate, derived from urushiol [a major component of the sap of Japanese lac trees (*Rhus vernicifera*)], containing a mixture of 3-substituted catechols with pentadecyl, 8-pentadecenyl, 8,11-pentadecadienyl and 8,11,13-pentadecatrienyl groups, was separated by HPLC on 10% SN-coated LiChrosorb Si-60 and LiChroprep Si-60 columns.[60]

The unsaturated components of anacardic acid, the principle constituent of cashew nut-shell oil (*Anarcardium occidentale*), have been examined using chromatography and it was demonstrated that, on SNIS, three spots developed that coincided with unsaturated 2-hydroxy-3-alkylbenzoic acid derivatives.[61,62] This mixture was decarboxylated to give the phenols **65**–**68** (cardanol)[62–64] which, together with their methylated derivatives **69**–**72**, were partitioned on SNIS and later epoxidised[65] (Fig. 8).

The capsaicin family of compounds are the active constituents isolated from red peppers. Even though the alkyl side chain contains a polar amide functionality, capsaicin **73** could be separated cleanly (SNIS) from dihydrocapsaicin (**76**), nordihydrocapsaicin (**75**), homocapsaicin (**74**) and homodihydrocapsaicin (**77**)[66] (Fig. 9).

Table 4. The separation of aromatic hydrocarbons given in order of elution

Elution order	Compound	Elution order	Compound
1	Benzene	9	1-methyl-3-ethylbenzene
2	Toluene	10	1,3,5-trimethylbenzene
3	Ethylbenzene	11	1-methyl-2-ethylbenzene
4	*p*-Xylene	12	1,2,4-trimethylbenzene
5	*m*-Xylene	13	*n*-butylbenzene
6	*o*-Xylene	14	1,2,3-trimethylbenzene
7	*n*-Propylbenzene		
8	1-Methyl-4-ethylbenzene		

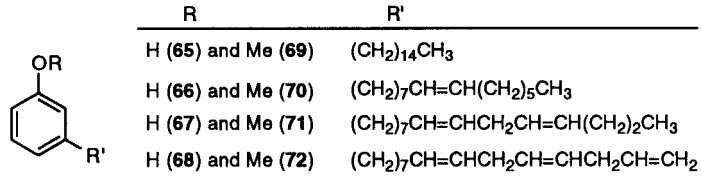


Figure 8.

The antibiotic, ascochlorin (**78**), when isolated from *Nectria coccinea*, was contaminated with a number of other metabolites. Although most of these compounds could be separated by crystallisation and chromatography on normal absorbents, SNIS was employed to remove small amounts of the dihydro contaminant **79** from ascochlorin (**78**)[67] (Fig. 10).

The isomers of the dihydroanthracenes **80** could not be separated by crystallisation, but they were partitioned upon SNIA[68] (Fig. 11). Cannabinolic acids, mainly cannabinol **81**, tetrahydrocannabinol **82** and cannabidiol **83** (Fig. 11), are widely studied by analytical chemists since unequivocal identification is important for forensic purposes. Normally, silica gel is impregnated with dimethylformamide (DMF), but the time-consuming nature of the preparation has prevented a general acceptance of this method. Caddy and Fish[69] have overcome some of these problems using SNIS; the chromatograms were clear with no tailing or smearing and the time taken to impregnate silica gel with silver nitrate is rapid in comparison to DMF. This observation was supported by Grlic[70] and was later applied to 'Dry-Column' chromatography.[71]

5. Bicycles

In a search for the prostaglandin analogues **88**, Portoghese[72] obtained and separated (SNIS) a mixture of regioisomers of bicyclo[2.2.1]heptadiene **86** and **87**, after reaction of the

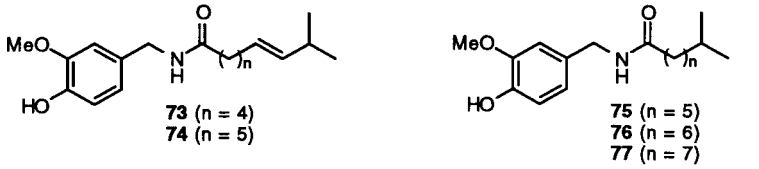


Figure 9.

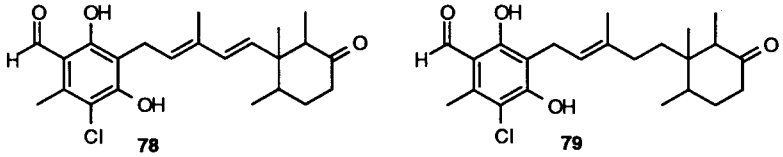


Figure 10.

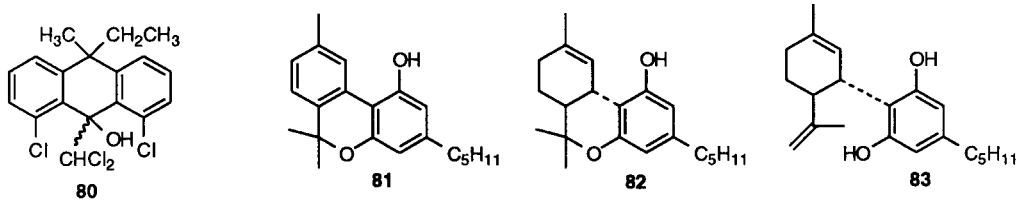
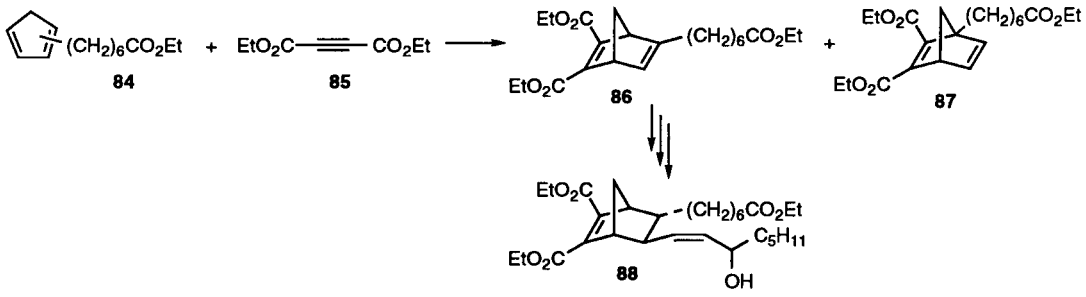
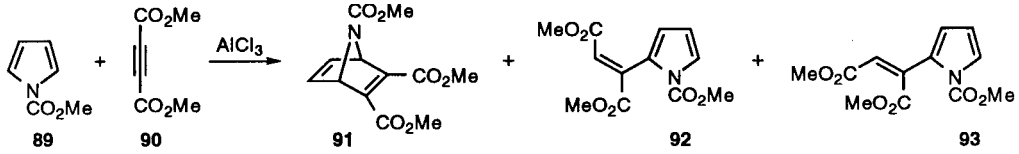


Figure 11.



Scheme 9.



Scheme 10.

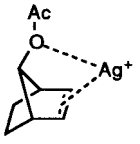
substituted cyclopentadiene **84** with diethyl acetylenedicarboxylate (**85**) (Scheme 9).

Aluminium trichloride dramatically influenced the outcome of the Diels–Alder reaction between *N*-methoxycarbonylpyrrole (**89**) and dimethyl acetylenedicarboxylate (**90**) (Scheme 10). Low concentrations of the aluminium compound gave the azabicycle **91** and the *cis* **92** and *trans* **93** pyrroles, which were difficult to separate because the azabicycle **91** and the *cis* **92** pyrrole eluted together. Higher concentrations of aluminium chloride gave only the azabicycle **91** and the *trans* **93** pyrrole which were separable (SNIS).[73]

Treatment of the hydrazone **94** with sodium acetamide gave 75% of the carbene insertion product, the olefin **95**, and 15% of the carbene insertion product, cyclopropane **96**, both of which were separable by SNIS[74] (Scheme 11).

Stille and Frey[75] investigated the Diels–Alder addition of norbornadiene and cyclopentadiene and obtained the adduct **97** as the major product, along with small amounts of other adducts and cyclopentadiene dimers, trimers and tetramers. Distillation gave the major product in about 97% purity but absolute purity was obtained by SN complex formation, by adding aqueous SN to the hydrocarbon while stirring. A hard gel formed which was collected by filtration and recrystallised from ethanol. The hydrocarbon was then recovered by continuous extraction. The dihydro derivative **98** was purified in a similar manner (Fig. 12).

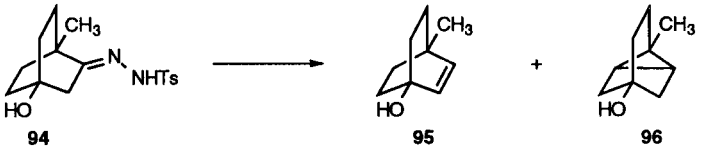
Catalytic hydrogenation of 7-acetoxynorbornadiene yields primarily *syn*-7-acetoxynorbornene together with some of the *anti*-isomer. Franzus et al.[76] found that the *syn*-7-acetate forms a silver complex (**99**) which is about ten times more stable than that of the *anti*-7-acetate. This difference is sufficient to permit separation of the isomers. The effect is attributed to chelation of the silver ion with both the double bond and the acetoxy group. Surprisingly, the complex **99** is even more stable than the complex with norbornene, but the effect appears to be general. Thus, *cis*-4-cycloocten-1-ol is superior to *cis*-cyclooctene in its coordinating ability. In acyclic terminally unsaturated alcohols, the complexing ability is highest when the double bond is in a Δ^4-relationship to the hydroxyl group, but a Δ^3- or Δ^6- relationship additionally enhances complexation.[77]



Shiner[78] employed (−)-*N*,*S*-dimethyl-*S*-phenylsulfoximine to optimise the enantiomeric purity of camphenilone (**100**) (ca 18% ee). Generation of the *C*-lithio sulfoximine **101** gave exo addition to **100** which afforded two diastereomeric alcohols and these were cleanly separated by flash chromatography on SNIS, furnishing **102** as the major diastereomer. Thermolysis of the diastereomer **102** gave **100** in >99.9% ee (Scheme 12).

6. Cyclophanes

SNIS has been employed as a crucial technique during the



Scheme 11.

Figure 12.

synthesis of certain cyclophane derivatives, e.g. **105**. Birch reduction of the intermediate indan derivative **103** afforded a mixture of the dihydro product **104** and starting material. Reduction could not be driven to completion and the product **104** slowly rearomatises, complicating the separation. SNIS successfully separated the two compounds so that the dihydro product **104** could be used immediately in the next step of the sequence[79] (Scheme 13).

7. Cyclopropanes and analogues

An early report by Shabtai[33] showed that cyclopropane could be separated from spiropentane by gas chromatography on an SN/glycol stationary phase. *Cis*- **106** and the *trans*-carboxycyclopropanes **107** (*cis*- and *trans*-permethrin)were eventually separated but this involved a silver aluminosilicate stationary phase prepared by treating silica gel with sodium aluminate to give a polyanionic surface which was readily exchanged with the counter ions, for example, silver ions, giving an effective silver support[43] (Fig. 13).

The aminocyclopropanes **108** and **109** have been separated using normally prepared SNIS. The fully saturated aminocyclopropane **108** was eluted from the column while the unsaturated analogue **109** was strongly bound to the column, presumably forming the complex **110**. **109** was easily isolated, however, after treatment of the absorbent with aqueous ammonia followed by extraction with organic solvents[80] (Fig. 14).

The diethenyl analogue **111** surprisingly underwent a [3,3]-sigmatropic rearrangement catalysed by SN, affording an aminocycloheptadiene **112**[57] when purification was attempted on SNIS (Scheme 14).

Successful separations of the diastereomeric cyclopropylidenes **113** and **114** have been achieved with SN/ethylene glycol-impregnated Corasil[35] (Fig. 15).

8. Cyclobutanes and cyclobutenes

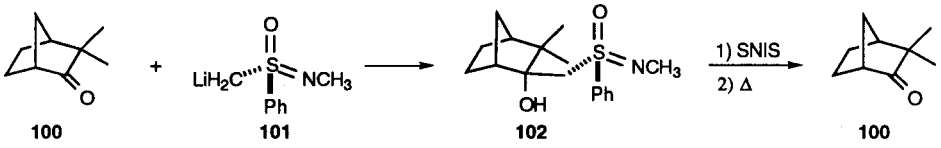
The separation of a mixture of methylenecyclobutane (**115**), 1-methylcyclobutene (**116**) and 3-methylcyclobutene (**117**) was performed using gas chromatography on an SN/ethylene glycol stationary phase[33] (Fig. 16). No rearrangements or isomerisations were observed.

9. Heterocycles

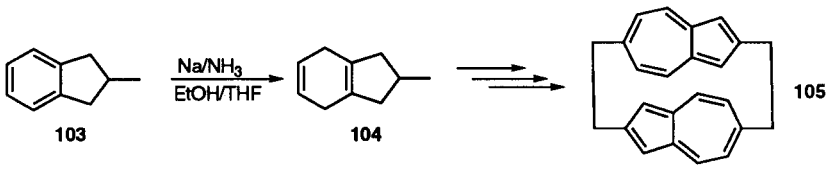
Many impressive separations on SNIS for determining quantitative drug mixture assays have been demonstrated.[81] Nicotinic acid (**118**), for example, was separated from etofylline (**119**), and cyclobarbital **120** from pentobarbital (**121**) (Fig. 17).

Silver complexation proved to be the method of choice for the separation of the ethynylpyridine **122** from the ethenylpyridine **123**. The mixture was treated with alcoholic SN giving a sparingly soluble silver complex of **122**, which was isolated by filtration and decomposed upon treatment with sodium cyanide, thereby affording the pure ethynylpyridine **122**[82] (Fig. 18).

The aromatic and nonaromatic heterocyclic compounds **124**–**135** have been separated using HPLC silver ion chromatography.[27,83] As expected, *N*-heterocycles show strong complexation with silver, resulting in longer retention



Scheme 12.



Scheme 13.

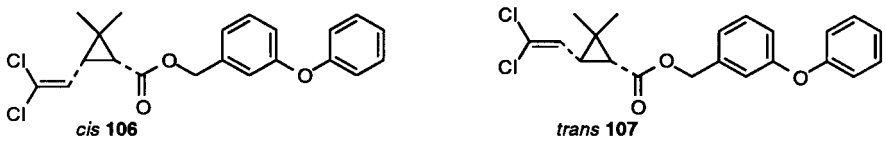


Figure 13.

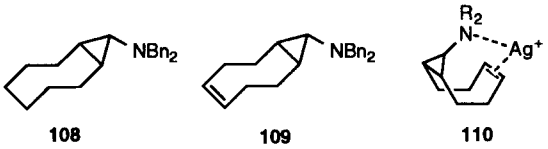
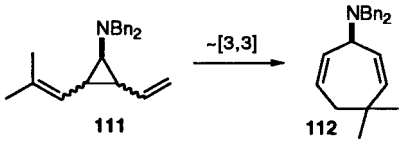


Figure 14.



Scheme 14.

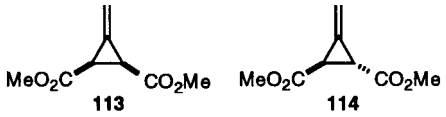


Figure 15.

Figure 16.

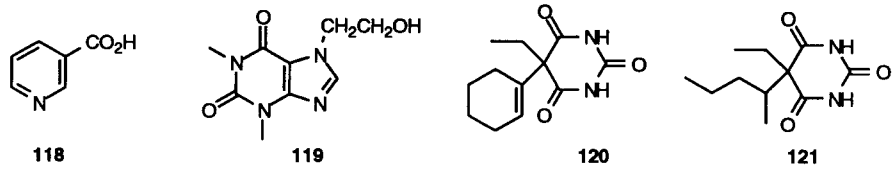


Figure 17.

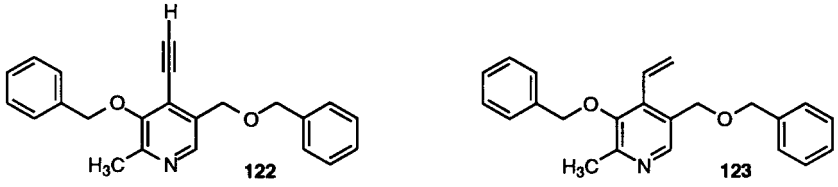


Figure 18.

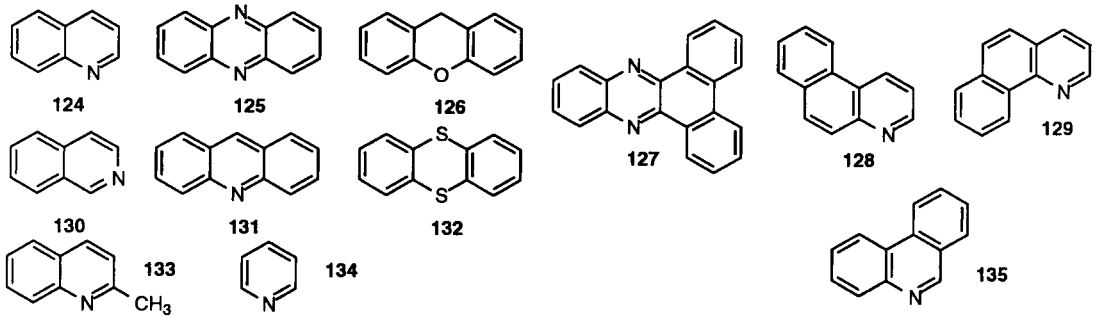


Figure 19.

times. Phenazine (**125**), which contains two nitrogen atoms, unexpectedly exhibits weaker complexation than acridine (**131**), presumably because the second nitrogen atom is electron withdrawing and decreases the overall basicity of phenazine (**125**) in comparison with acridine (**131**) (Fig. 19).

The three isomers of picoline **136**–**138** that vary only in the position of the methyl group have been successfully partitioned by SNIS HPLC[84] (Fig. 20).

The effect of solvent polarity on thin-layer chromatography (SNIS) of polynuclear selenium and sulfur heterocycles **139**–**142** was investigated by Ghe et al.[85] The ability to develop π-coordination by the aromatic systems was found to be related to the retention times. For example, **139** has a slower retention time than **140** (Fig. 21).

10. Hydrazones

The separation of carbonyl compounds can sometimes be extremely difficult and conversion to the corresponding hydrazones can facilitate the separation, either for detection or isolation. Denti[86] treated various aldehydes and ketones with 2,4-dinitrophenylhydrazine, affording the 2,4-dinitrophenylhydrazones. The hydrazones were then mixed, and partition was demonstrated upon either SNIS or SNIA (Table 5). Many other hydrazone derivatives have been examined by Urbach,[87] Johnson,[88] de Jong[89] and Meijboom.[90]

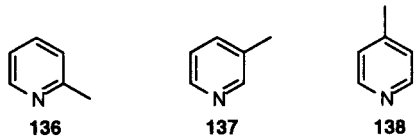


Figure 20.

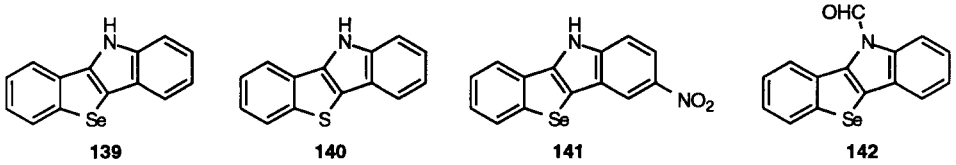
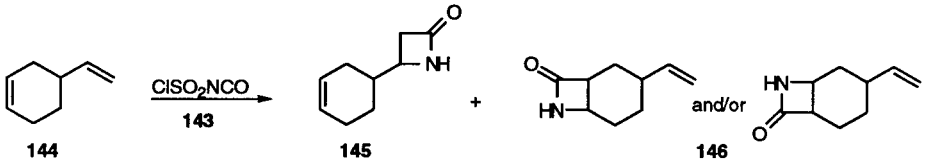


Figure 21.

Table 5. Silver nitrate chromatography of dinitrophenylhydrazones (R_{for}=R_f (2,4-DNPH of compound)/R_f (formaldehyde 2,4-DNPH); (I) the R_f of formaldehyde 2,4-DNPH was unity)

2,4-Dinitrophenylhydrazone of	R_{for}	
	(SNIS)	(SNIA)
Formaldehyde	(I)	(I)
Propionaldehyde	1.46	1.10
Butyraldehyde	1.81	1.14
i-Butyraldehyde	1.96	1.19
Methyl ethyl ketone	1.43	1.12
n-Valeraldehyde	1.90	1.18
3-Pentanone	1.83	1.22
2-Pentanone	1.73	1.19
Cyclopentanone	0.90	0.86
n-Caproaldehyde	2.13	1.19
α-Methyl-*n*-valeraldehyde	0.78	0.85
4-Methyl-2-pentanone	2.12	1.20
2-Hexenal	1.90	1.11
5-Hexen-2-one	0.18	0.20
Cyclohexanone	0.98	0.74
Oenanthaldehyde	2.46	1.19
Benzaldehyde	1.75	0.95



Scheme 15.

Cis- and *trans*-aldehydes have been separated using the above technique, i.e. conversion to the dinitrophenylhydrazone followed by partition on SNIS[91]

11. β-Lactams

When *N*-chlorosulfonyl isocyanate (**143**) was reacted with 4-vinylcyclohexene (**144**), two β-lactams were formed,[92] the first (**145**) resulting from addition to the exocyclic double bond and the second (**146**) resulting from addition to the endocyclic double bond (Scheme 15).

Although the two β-lactams **145** and **146** were easily separated (SNIS), it could not be determined with confidence whether **146** was actually a mixture of two isomers or a single compound.

12. Lipids and fatty acids

Lipids,[9,93–96] including glycerides,[11] glycerols, acylglycerols, acylglycerides and triacylglycerols,[97] have been reviewed or discussed elsewhere, as have fatty acids and long chain unsaturated acids,[8,10,96,98–101] all of which are therefore beyond the scope of this review. There are, however, some publications that are relevant to this article, particularly those of Spencer[102] and of Lam[44] who, reported that *cis*- and *trans*-4-decene-1,10-dioic acids could easily be separated by SNIS. Chan and Levett later found that the *p*-bromophenacyl esters gave improved results.[103]

Frankel and co-workers[104] discovered that the iron tricarbonyl complex of methyl linoleate **147** was amenable to SNIS or SNIAR and that the retention time was the same as that of methyl stearate **148** (Fig. 22).

13. Natural products and precursors

Schreiber[105] dimerised the immunosuppressant FK-506 (**149**), using the newly-developed Grubb's alkene metathesis catalyst, to create small molecule dimers. This procedure afforded a mixture of the *E* (**150**) and *Z* (**151**) isomers of the dimer which were separated by SNIS with retention of all stereogenic centres (Scheme 16).

For the preparation of **154**, a key intermediate in the synthesis of the natural product, borrelidin **155**, Haddad[106] found that SNIS allowed isolation of the pure precursor **153** derived from Lindlar reduction of the diyne generated

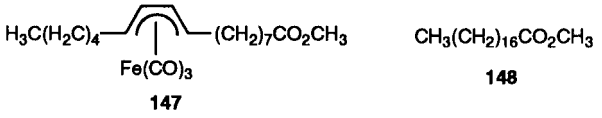
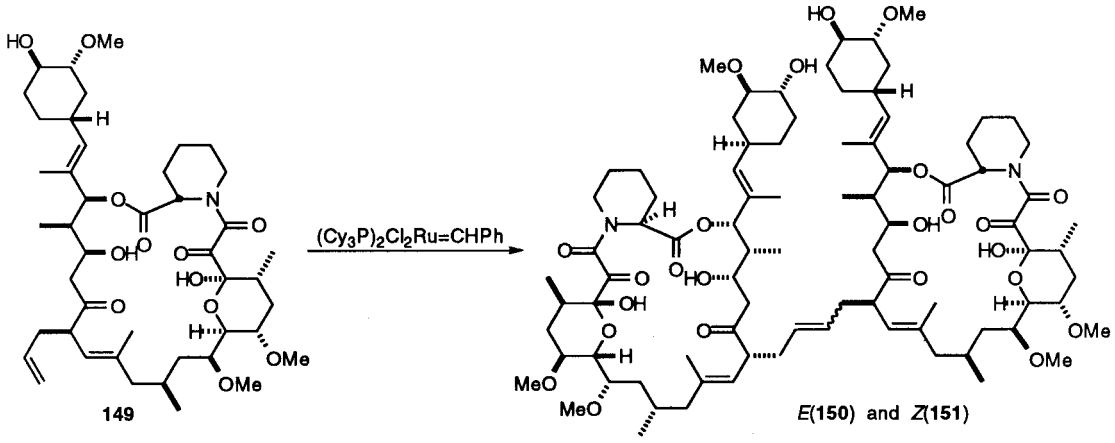


Figure 22.



Scheme 16.

from the diol **152**. Transformation of **153** by Sharpless epoxidation and methylation afforded the intermediate **154** (Scheme 17).

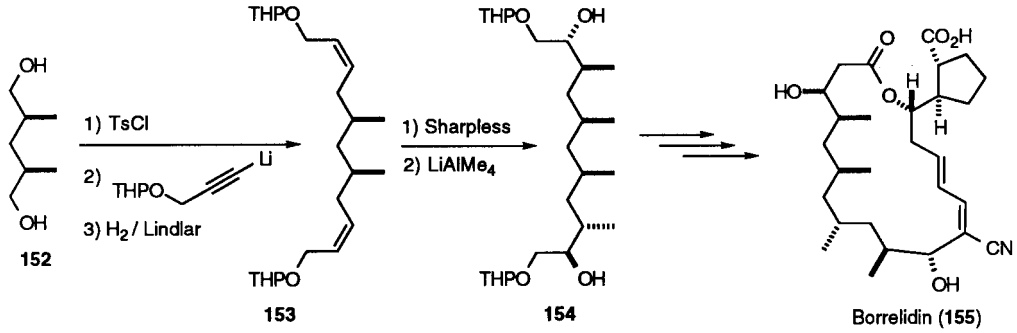
Other important synthetic intermediates have been purified utilising SNIS. For example, Heathcock[107] synthesised a degradation product of zaragozic acid A (**158**) by attaching the SNIS-purified (β,γ-isomer impurity removed) side chain **157** to the dioxo[1.2.3]bicycle **156** (Scheme 18).

The vitamin K analogues **159**–**162** were amenable to separation by SNIS[108] (Fig. 23), but the dihydric phenols, catechol and hydroquinone, are susceptible to oxidation to the corresponding quinones and, when these were separated on thin layers of SNIS, the *ortho*- and *para*- quinones were formed.[109]

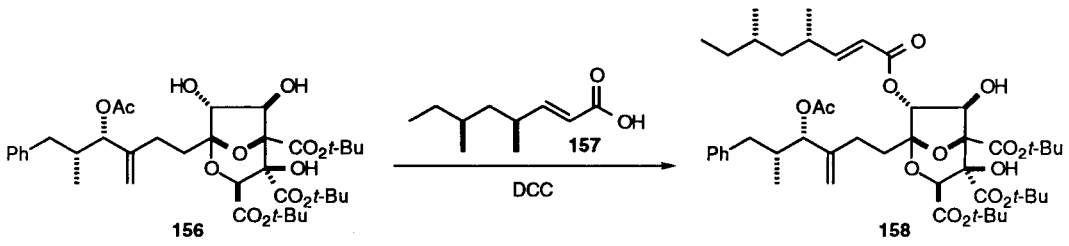
The minor aggregation pheromone produced by male broad-horned flour beetles was investigated by Tebayashi et al.[110] The volatiles from 3.5 million males were applied to silica gel and SNIS followed by preparative gas liquid chromatography to yield the major pheromone component (acoradiene **163**) and the minor pheromone component [α-cedren-14-al (**164**)] (Fig. 24).

To identify sex pheromone components in *Drosophila ananassae*, the cuticular hydrocarbons were obtained after SNIS chromatography, affording bioactive fractions of (*Z*,*Z*)-5,25- (**165**) and (*Z*,*Z*)-4,26-hentriacontadiene (**166**) (Fig. 25). Both hydrocarbons were found to elicit male courtship behaviour, the former being product.[111]

In samples of 1,2-[^{3}H]-gibberellin A_1, prepared by partial reduction of gibberellin A_3 with tritium, the fully saturated dihydrogibberellin A_1 isomers are frequent contaminants (Fig. 26). 1,2-[^{3}H]-Gibberellin A_1 can be purified by chromatography on silica gel but separation from the dihydro derivatives is difficult. Impregnating the adsorbent with SN



Scheme 17.



Scheme 18.

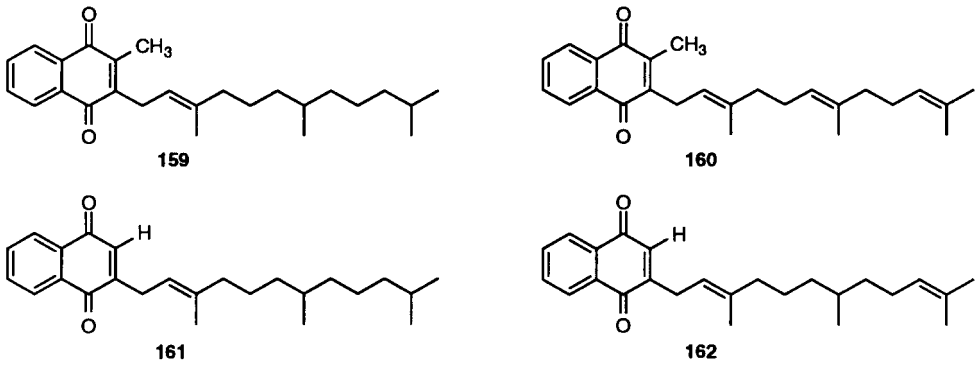


Figure 23.

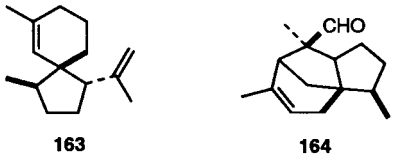


Figure 24.

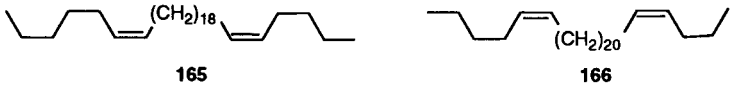


Figure 25.

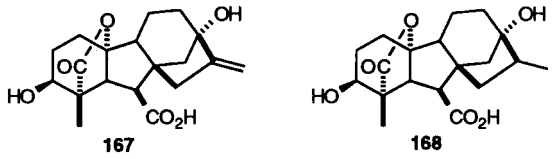


Figure 26.

improved the resolution, since gibberellin A_1 (**167**) complexed with silver ions and was more strongly adsorbed, but neither preparative thin layer chromatography nor column chromatography on SNIS proved to be satisfactory for obtaining pure gibberellin A_1 **167**. The slower-moving gibberellin A_1 (**167**) zone always contained some dihydro derivative **168**, possibly because of tailing. Large losses of gibberellins also occurred during the TLC separation. Because many gibberellins are conveniently separated by partition chromatography on sephadex columns, however, Vining[112] investigated the use of SN-impregnated sephadex and found that separation could be easily achieved.

Many years later, Heftmann was able to separate gibberellins differing from each other only by the presence or absence of a double bond on SNIS HPLC[113] and TLC[114]

The gibberellins (GA) were first converted to the *p*-nitrobenzyl esters, since the free acids are too strongly adsorbed on SNIS, this derivatisation having the added advantage that it facilitates detection by UV and identification by mass spectrometry. HPLC partitioned **169/170**, **171/172** and **173/174** *p*-nitrobenzyl ester mixtures using either *n*-hexane/methanol/dichloromethane or *n*-hexane/methanol/*i*-propanol solvent systems. Gibberellins containing a 3-hydroxyl group were eluted before those containing a 13-hydroxyl substitutent, and the more saturated analogue was always eluted before the less saturated derivative (Fig. 27).

14. Polyhydroxylated compounds

The *threo* and *erythro* isomers of 2,3-dihydroxybutyric acid (**175**) and 2,3-dihydroxy-2-methylbutyric acid (**176**) have been subjected to separation upon silica gel impregnated

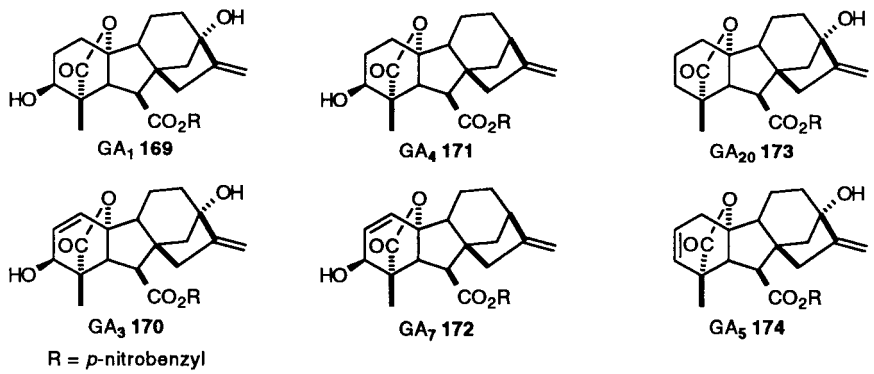


Figure 27.

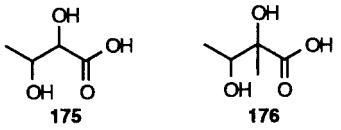


Figure 28.

with SN, boric acid and dipotassium hydrogen phosphate. SNIS methodology provided the best results[115] (Fig. 28).

15. Prostaglandins

Prostaglandins of the **177** series can be separated from those of the closely related **178** series; for example, PGE_1 (**177**) and PGE_2 (**178**), on SNIS.[116,117] Unfortunately, this method fails[118] when applied to the difficult separation of prostaglandins PGA_2 (**179**) and PGB_3 (**180**), and the use of iron(III)-impregnated silica gel has been recommended for this system[119] (Scheme 19). For the separation of hydroxylated analogues, the publications of Schurig[35] Gréen,[116] Eglinton[120] and Attallah et al.[121] should be mentioned.

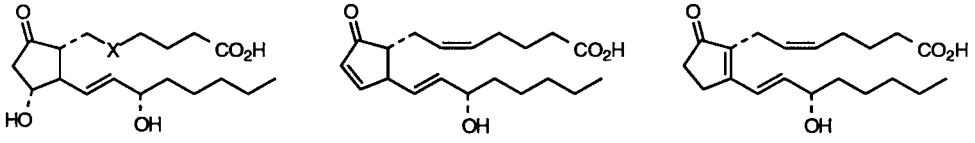
16. Steroids

Steroid separation on SNIS and SNIA[122] has been used extensively,[123–133] as indicated in Table 6, and will therefore only be discussed briefly. For ethynylated steroids, see Ercoli et al.[134] and Pellizzari et al.[135]

Meinwald[138] discovered that solvolysis of the cyclobutylmesylate **181** afforded four products **182**–**185** of which **183** and **184** could be separated on silica gel, but compounds **182** and **185** eluted as one fraction. This fraction was subjected to SNIS and the two epimers were separated, with **182** eluting first followed by **185** (Scheme 20). Solvolysis followed by SNIS purification was the method of choice for the synthesis of radiolabelled 4-[^{14}C]- and 7α[^{3}H]-androsta-4,16-dien-3-one.[139]

The steroidal alkaloids **186** and **187** could be conveniently separated (SNIS) even though the only difference was a methoxyl compared with an ethoxyl group (Fig. 29).[140] Steroidal aminal alkaloids that have structural similarities to those below have found partition success with SNIS.[141]

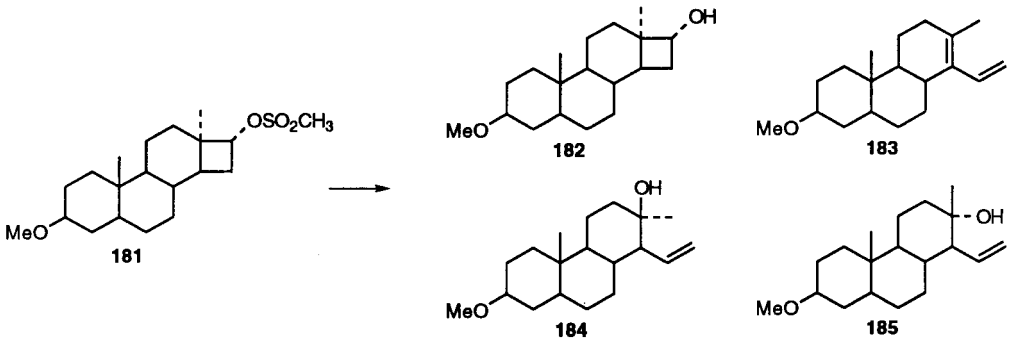
When the steroid **188** was dehydrated by heating in pyridine at reflux for 6 days, two isomeric products were isolated in 90% yield. The first compound (**189**) was the result of a methyl migration and the second (**190**) was derived from simple elimination; both compounds were easily obtained in high purity by SNIS chromatography[142] (Scheme 21). Similar compounds have been resolved by the same authors.[143]



Scheme 19.

Table 6. Separation of steroidal derivatives

Mixture	R_f	Solvent	References
Cholesterol	0.37	Hexane–ethyl acetate (3:1)	136
Cholestanol	0.47		
3β-Acetoxycholest-5-ene	0.48	Hexane–diethyl ether (10:1)	
3β-Acetoxycholestane	0.62		
3β-Acetoxycholest-8(14)-ene	0.42	Hexane–diethyl ether (5:1)	
3β-Acetoxycholest-14-ene	0.27		
4β-Methylcholest-2-ene	0.43	Hexane	
4-Methylcholest-3-ene	0.33		
4-Methylcholest-4-ene	0.55		
(20*R*)-Diacholest-13(17)-ene	0.46	Hexane–toluene (10:1)	
(20*S*)-Diacholest-13(17)-ene	0.61		
4,4-Dimethylcholest-5-ene	0.35	Hexane	
4,5α-Dimethylcholest-3-ene	0.64		
(20*R*)-4,4-Dimethyldiacholest-13(17)-ene	0.46	Hexane–toluene (10:1)	
(20*S*)-4,4-Dimethyldiacholest-13(17)-ene	0.61		
Estrone	0.67	cyclohexane–ethyl acetate (7:3)	137
Equilin	0.48		
Equilenin	0.59		
α-Estradiol	0.52		
α-Dihydroequilin	0.19		
α-Dihydroequilenin	0.36		
β-Estradiol	0.46		
β-Dihydroequilin	0.21		
β-Dihydroequilenin	0.34		



Scheme 20.

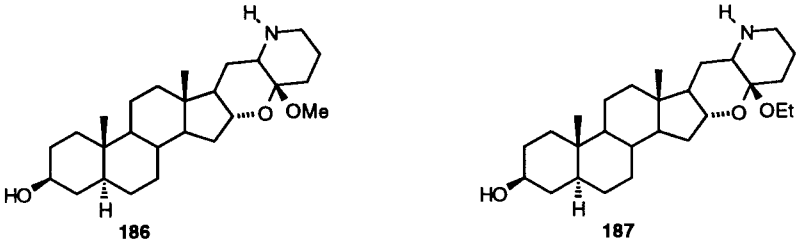
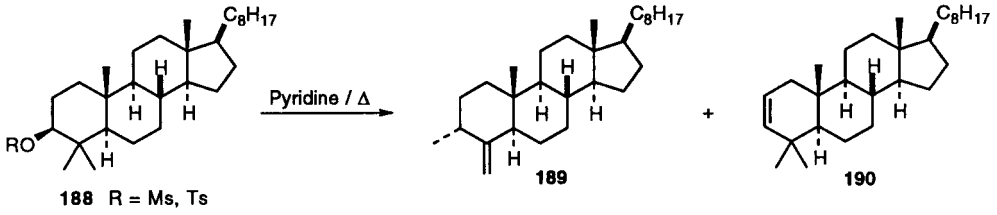


Figure 29.



Scheme 21.

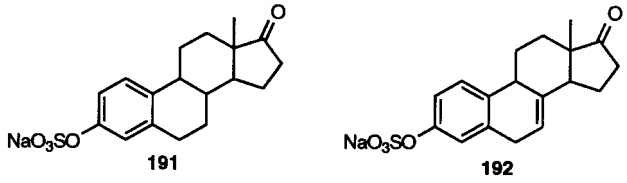


Figure 30.

Steroidal salts such as estrone (**191**) and equilin (**192**) sodium sulfate can be separated, but special polygram foils impregnated with SN are required[81] (Fig. 30).

Researchers have previously shown that the partial separation of vitamin D_2 (**193**) from vitamin D_3 (**194**) can be achieved using HPLC. These separations are, however, found to be difficult to reproduce and the use of an argentated reverse-phase HPLC system has therefore been recommended as an alternative method by Tscherne and Capitano[144] (Fig. 31).

17. Terpenes and terpenoids

A number of reports have shown that terpenes and terpenoid compounds can be easily separated using SN methodology (Table 7; see also Table 2). An extensive investigation into monoterpene esters has been described by ter Heide.[145]

Comparisons of SN to silver perchlorate retention, with and

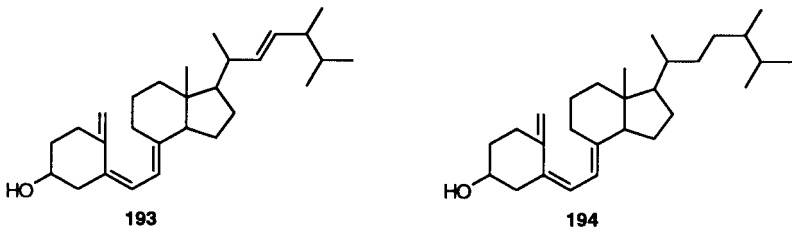


Figure 31.

without gypsum, have been undertaken with a number of terpenes[149] (Table 8). The results suggest that the use of the perchlorate counterion in the absence of gypsum is the optimum combination for terpene separation. If the silver perchlorate is not prepared correctly (i.e. acid free), however, it can catalyse unwanted terpene rearrangements.[149] Gupta[150] has reported an individual R_f study of the same and related compounds using specially prepared SNIS.

The sesquiterpenes, δ-cadinene (**195**) and γ-cadinene (**196**), when subjected to HPLC silver ion chromatography were partitioned with ease.[27] Other separable sesquiterpene mixtures include the α-gurjunene isomers[151] **197** and **198**, β-selinene (**199**) and caryophyllene (**200**),[150] bazzanene (**201**) and bazzanenol (**202**),[152] as well as *cis* **203** and *trans*-carveol (**204**)[153] (see also Gollnick,[154] Prelog,[155] Pesnelle[156] and Hara[157]) (Fig. 32).

The total synthesis of the sesquiterpene dihydrocostunolide[158] gave rise to a number of other naturally occurring side products including 3-santenolide (**206**), which was obtained after a partial hydrogenation of diene **205** with diimide. The product was isolated from the starting material in 72% yield utilising SNIS (Scheme 22).

The tetracyclic triterpenes **207**–**212**, which have a closely related structural similarity, are not separable upon alumina, but SNIS was able to drastically improve the separation and for some derivatives the R_f values were changed by 30% (Fig. 33).[159] Pentacyclic triterpenes have been similarly investigated.[160]

Two cytotoxic diterpenes have been isolated from aerial parts of the fern *Multifida*, by repeated column chromatography on silica gel and SNIS.[161] The structures were confirmed by spectroscopic methods as ent-kaurane-

Table 7. Terpenoids amenable to SN chromatography

Mixture	R_f	Solvent	References
Triterpenes			
Lupeol	0.42	Hexane–ethyl acetate (3:1)	136
Dihydrolupeol	0.53		
Betulin	0.39	Hexane–ethyl acetate (3:1)	
Dihydrobetulin	0.50		
Lup-2-ene	0.34	Hexane	
γ-Lup-3(4)-ene	0.50		
γ-Lup-3(5)-ene	0.29		
Lupa-2,20(29)-diene	0.37	Hexane–Toluene (10:1)	
γ-Lupa-3(4),20(29)-diene	0.46		
19a(H)-28-Norlup-17-ene	0.82	Hexane	
19b(H)-28-Norlup-17-ene	0.70		
28-Norlup-16-ene	0.51		
28-Norlup-17(22)-ene	0.38		
Sesquiterpenes			
Khusinol	0.32	Benzene–ethyl acetate (4:1)	146
Khusol	0.31		
Isopulegol	0.67		
Cholesterol	0.42		
Methyleugenol	0.19		
Carotol	0.52		
α-Ionone	0.59		
β-Ionone	0.32		
Carvone	0.50		
Zerumbone	0.51		
Santonin	0.26		
Costunolide	0.31		
Dehydrocostus lactone	0.23		
Δ^3-Carene	0.36		
Terpenes			
Δ^4-Carene	0.56	Benzene	147,148
Myrcene	0.20		
Sabinene	0.29		
Ocimene	0.35		
Allo-ocimene	0.58		
Limonene	0.35		
Santene	0.35		
α-Phellandrene	0.41		
β-Phellandrene	0.50		
α-Pinene	0.67		
β-Pinene	0.46		
α-Terpinene	0.49		
γ-Terpinene	0.59		
Terpinolene	0.62		
Camphene	0.53		
α-Fenchene	0.57		
Tricyclene	0.67		
p-Cymol	0.68		

Table 8. Separation comparison between SN and silver perchlorate [A: light petroleum; B: Benzene–light petroleum (1:1); C: Benzene–light petroleum (1:4); D: Ethyl acetate–benzene (3:17)]

Compound	No. of double bonds	Solvent system	R_f			
			$AgNO_3$		$AgClO_4$	
			With gypsum	Without gypsum	With gypsum	Without gypsum
Longicyclene	0	A	0.75	0.68	0.77	0.76
Isolongifolene	1	A	0.66	0.58	0.67	0.66
Longifolene	1	A	0.44	0.31	0.32	0.14
α-Gurjunene	1	B	0.82	0.80	0.79	0.78
α-Bergamotene	2	B	0.74	0.62	0.71	0.61
β-Bisabolene	3	B	0.37	0.18	0.32	0.16
α-Himachalene	2	C	0.69	0.56	0.70	0.55
β-Himachalene	2	C	0.61	0.46	0.62	0.46
Cembrene	4	D	0.85	0.81	0.86	0.83
Cembrene A	4	D	0.65	0.41	0.42	0.16

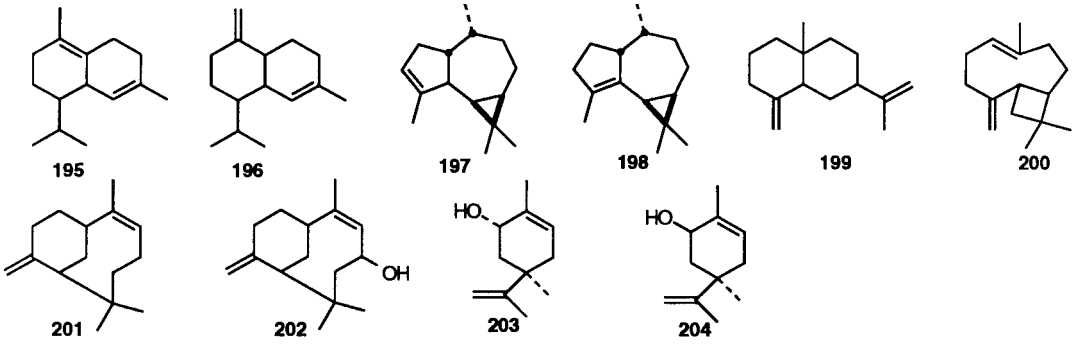
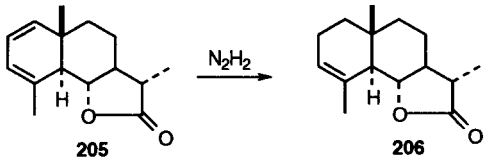


Figure 32.



Scheme 22.

2β,16α-diol (**213**) and ent-kaur-16-ene-2b,15α-diol (**214**) (Fig. 34). The furanyl diterpenes kahweol **215** (R=H) and cafestol **216** (R=H) are constituents present in the light petroleum extract of green coffee beans in the form of esters with fatty acids. Kahweol palmitate **216** [$R=CO(CH_2)_{14}CH_3$] and cafestol palmitate **215** [$R=CO(CH_2)_{14}CH_3$] have been separated using SNIS thin layer plates.[162] Extending this technique, Lam[163] developed preparative liquid chromatography SNIS cartridges to achieve complete separation of gram quantities of the diterpene esters **215** ($R=COCH_3$) and **216** ($R=COCH_3$) without extensive recycling (Fig. 34).

Finally, *cis*-**217** and *trans*-methyl communate (**218**) and methyl abietate (**219**) have been successfully separated in a mixture in relatively large amounts on SNIS[164] (Fig. 35).

18. Reactions on silver nitrate absorbents

Elgamal and Fayez[165] demonstrated that acetylation, saponification, oxidation, reduction, hydrogenation,

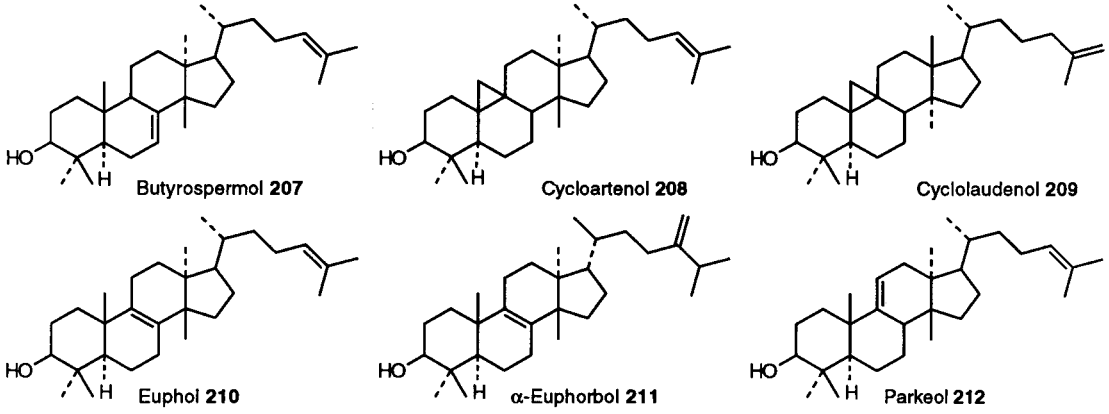


Figure 33.

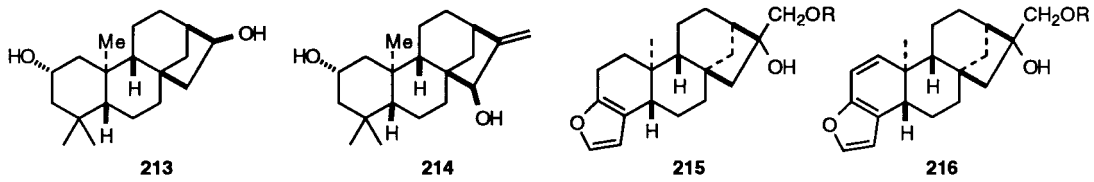


Figure 34.

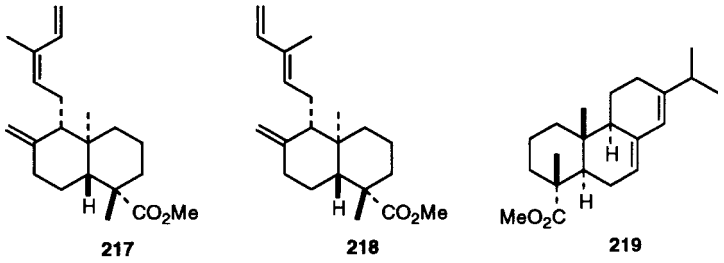


Figure 35.

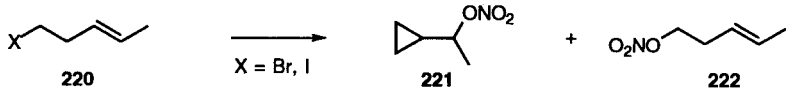
halogenation, nitration, esterification, etherification, acetonide formation and hydrazone formation could all be achieved on SNIS and the products subsequently separated.

Alkyl bromides undergo conversion to alkyl nitrates and alkenes when subjected to SNIS or SNIA. For example, methyl 11-bromoundecanoate afforded methyl 11-nitratoundecanoate (84%), 1-bromododecane gave 1-nitratododecane in 90% yield and dodecan-1-ene in 6% yield, whereas 2-bromotridodecane gave 2-nitratotridecane in 49% yield and the corresponding alkene in 39% yield.[166] Based on the above observations Smith[167] reported that, when 5-bromopent-2-ene **220** (X=Br) was eluted with pentane through a column of SNIA, a 74% yield of 1-cyclopropylethyl nitrate (**221**) was obtained along with a 2% yield of pent-3-enyl nitrate **222**. Substituting bromide for iodide gave a 94% yield of **221**, while the chloride passed through the column unchanged (Scheme 23). Contrary to this work, SNIS has been used to determine the purity of an allylic bromide.[168]

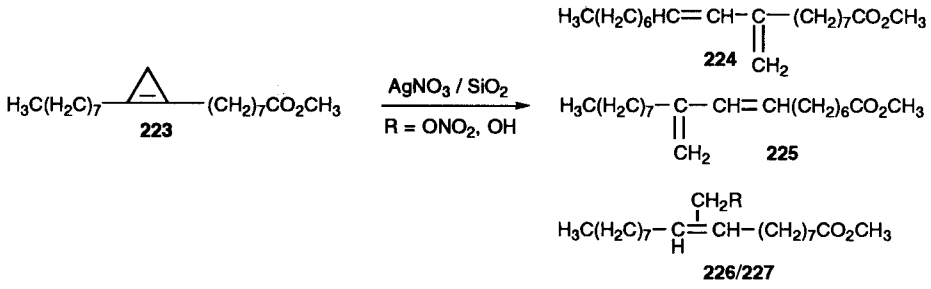
When in contact with SNIS, methyl esters of cyclopropene fatty acids undergo ring opening to yield pairs of isomers with methylene, hydroxymethyl, or nitratomethyl side chains at the original ring position.[169] The main products from methyl sterculate (**223**) were thus the methyl 9(or 10)-methylene octadec-10(or 8)-enoates **224** or **225**, and in lesser quantities, the methyl 9(or 10)-(nitratomethyl)-octadec-9-enoates **226** and the methyl 9(or 10)-(hydroxymethyl)-octadec-9-enoates **227**. Hydrogenation quantitatively converted this mixture of isomeric pairs to a mixture of methyl 9- and methyl 10-methyloctadecanoates (Scheme 24).

Crundwell and Cripps,[170] who subjected the enynoic acids **228**–**230** to SNIS, discovered that the *cis*-acid **228** undergoes cyclisation affording the furancarboxylic acid **231**, while the *trans*-acid of **229** and the isomeric *cis*-acid **230** were left unchanged after prolonged contact with SNIS (Scheme 25).

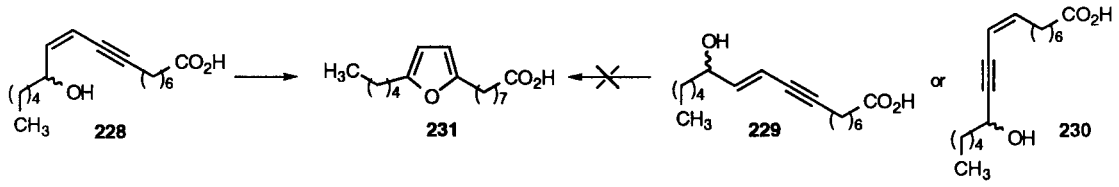
Other unexpected reactions upon SN impregnated adsorbents include epoxidation of stilbenes[45] (Fig. 3) and the conversion of hydroperoxides to ketones[46] as shown in Scheme 3.



Scheme 23.



Scheme 24.



Scheme 25.

19. Preparation of adsorbents

For column chromatography, most preparations revolve around dissolving SN in methanol or acetonitrile and adding the solution to the adsorbent followed by evaporation and drying. The only disadvantage of these procedures is that the adsorbents become light sensitive (an aluminium foil or a dark paper shroud is required) and must be used within a short period of time due to autooxidative processes. Novel preparation procedures have recently emerged which suggest that careful preparation is the key to stability,[136] while other methods have used stabilising agents, such as molybdenum,[171] to overcome the problem. Moisture content must always be taken into consideration when working with SN-impregnated adsorbents, since resolution can depend on the layers of hydration.[172]

It should be noted that other counterions[173] have been utilised as well as other metals.[172,174] For example, silver perchlorate[149]—and silver iodate[146]—doped adsorbents have found superiority to SN, but these materials are harder to use and prepare. Thallium nitrate,[174a,e] although very toxic, gives comparable results to those of SN, but because thallium is less soluble in organic solvents, polar solvents can be used without eluting the adsorbent. Lithium nitrate,[174d] and rhodium,[174f] palladium[174c] and platinum[174b] salts have been used in conjunction with SN.

Thin layer preparative and analytical silica gel plates can be impregnated by inserting the edge of the plate into a solution of 10% aqueous SN, about 1 cm high, and allowing the solution to travel the length of the plate. The plates are then air-dried, followed by drying in an oven at 110°C for 1–2 h.[175] Other improvements for thin layer chromatography have been reported.[136,176] The more common procedure, however, is to spray an aqueous solution of SN onto the plate and allow it to dry in an oven, the drawback being that the adsorption is not evenly distributed.

For gas chromatography, SN has been applied to many stationary phases mentioned to above. Some novel applications include combination with heptakis(2,3,6-tri-*O*-pentyl)-β-cyclodextrin or bentone[177] and these have been successfully applied to the separation of simple aromatics.[178,179] The solubility of SN in stationary phases[180] should be considered, and is useful for determining the amount of SN on the column support. A review on the use of SN in gas chromatography has been reported.[181]

Various adsorbents have been discussed throughout this review when applicable, such as silica gel (SNIS), alumina (SNIA), amberlyst resin (SNIAR) and sephadex (SNISe). Florisil has additionally been coated with SN[182] and should therefore be added to the list of available adsorbents.

20. Conclusion

In conclusion, the authors wish to highlight the pioneering work by Morris,[8] de Vries,[9] Dutton[10] and Barrett[11] on revealing and developing the potential of SN as a chromatographic aid which otherwise might not have been fully realised until much later.

It is hoped that this article will encourage the synthetic community to use this simple and versatile method to effect separations which are otherwise conducted by often more difficult, less effective or tedious methods. The most significant conclusion to be made in this report is the effectiveness of these supports in separating such a wide variety of multifunctional compounds.

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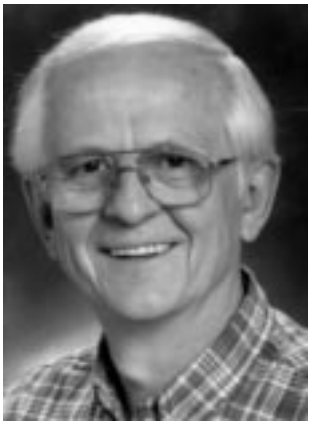
Biographical Sketch

Craig M. Williams was born in Adelaide, Australia. He received his BSc(Hons) degree in chemistry in 1994 and in 1997 was awarded his PhD from Flinders University under the supervision of Professor Rolf H. Prager. He worked as an Alexander von Humboldt Postdoctoral Fellow with Professor Armin de Meijere at the Georg-August-Universität, Göttingen, Germany until 1999 and then took up a postdoctoral fellowship at the Australian National University. He presently holds a lectureship at The University of Queensland.



Lew Mander was born in Auckland, New Zealand, completed his BSc and MSc degrees at the University of Auckland, the latter with R. C. Cambie, and obtained his PhD in 1964 at the University of Sydney under the supervision of C. W. Shoppee, E. Ritchie and W. C. Taylor. After two years of post-doctoral studies with R. E. Ireland, initially at the University of Michigan and then at the California Institute of Technology, he returned to Australia as a lecturer in organic chemistry at the University of Adelaide. He moved to the Australian National University in 1975 as a senior fellow in the Research School of Chemistry and was appointed as Professor in 1980. He was a Nuffield Fellow at Cambridge University in 1972 with A. R. Battersby, and a Fulbright Senior Scholar at the California Institute of Technology in 1977 and at Harvard University in 1986 (with D. A. Evans on both occasions). His research interests are concerned with the development of methods and strategies for the assembly and manipulation of complex organic molecules with a special interest in plant growth and development.