

Immobilization of rhodium complexes with chiral cationic water soluble ligands on Nafion–H and other strongly acidic cation exchange resins

Imre Tóth, Brian E. Hanson *

*Department of Chemistry, Virginia Polytechnic Institute and State University,
Blacksburg, VA 24061 (U.S.A.)*

and Mark E. Davis

*Department of Chemical Engineering, Virginia Polytechnic Institute and State University,
Blacksburg, VA 24061 (U.S.A.)*

(Received April 4th, 1990)

Abstract

Rhodium complexes of the chiral cationic water soluble ligands, [(*S,S*)-2,4-bis[*p*-*N,N*-dimethylammoniumphenyl]phosphino]pentane]⁴⁺, [(*S,S*)-2,3-bis[*p*-*N,N*-dimethylammoniumphenyl]phosphino]butane]⁴⁺, and [(*S,S*)-2,4-bis[*p*-*N,N,N*-trimethylammoniumphenyl]phosphino]pentane]⁴⁺, were immobilized on several cation exchange resins. All of these supported complexes catalyze the asymmetric hydrogenation of dehydroaminoacid derivatives at the appropriate conditions with no detectable loss of rhodium into the substrate phase. The rates and enantioselectivities of these hydrogenations depend not only on the ligand used but also on the nature of the exchange resin upon which the complex is immobilized. When the complexes were supported onto the acidic Nafion–H cation exchange resin the resulting catalysts were easy to handle and gave optical yields comparable to those obtained with the non-supported complexes in homogeneous solution. The results presented here show that ion exchange resins may be used in the immobilization of asymmetric catalysts with no detectable rhodium leaching under batch conditions.

The immobilization of homogeneous catalysts is of importance for the generation of new methods for the separation of products from catalyst in a homogeneous reaction. The separation is important not only to ensure the product purity but also allows the homogeneous catalyst to be recycled. Many of the recent attempts for the

immobilization of homogeneous catalysts have focused on asymmetric hydrogenation catalysts [1–7]. For example, rhodium complexes containing chiral ligands have been chemically bonded to modified polymers [1,2] and to metal oxide surfaces [3]. When the problems of reduced enantioselectivity and rhodium leaching that often plague immobilized asymmetric catalysts are overcome, these catalysts provide comparable optical yields to their homogeneous counterparts [4–7]. For example, Stille et al. have shown that the incorporation of chiral phosphinopyrrolidine ligands into a crosslinked polymer matrix leads to a highly enantioselective immobilized catalyst for dehydroaminoacid hydrogenation [6a].

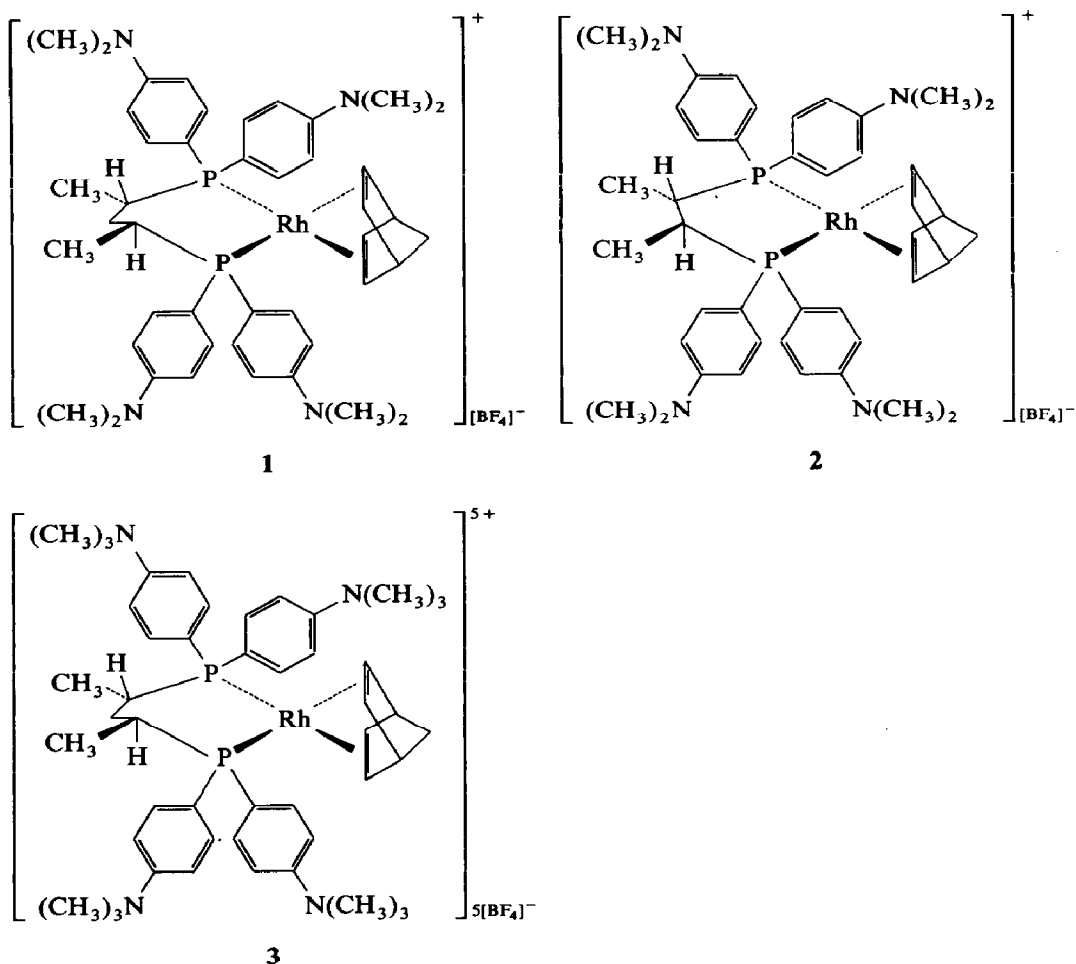
Although ion exchange resins have been used for the separation of cationic catalyst complexes [8–10] very few catalytic applications have been reported for ion-exchange resin supported catalysts [11–13]. A successful resin-supported catalyst was prepared from the rhodium complexes of the non-chiral cationic ligand, $\text{P(Ph)}_2\text{CH}_2\text{CH}_2\text{N(CH}_3)_3^+$ (amphos). When a rhodium complex of amphos was exchanged onto a macroreticular cation exchange resin the resulting material was active for the hydrogenation and hydroformylation of hexene with little loss of rhodium [12]. The cationic rhodium complex of the neutral chiral ligand, 2,3-*O,N*-bis(diphenylphosphino)-1-(α -naphthyl)-2-hydroxy-3-isopropylaminopropane, has been exchanged onto sulfonated divinyl benzene resins. These gave excellent enantioselectivities but show rhodium leaching of up to 0.5% of the total rhodium [13].

An alternative to chemically bonding the catalyst to a solid support has been made possible through the synthesis of chiral water soluble ligands. Through the use of these ligands heterogeneous catalysts can be devised in which the catalytic reaction proceeds between two immiscible phases [14,15] e.g., an aqueous catalyst containing phase and an organic substrate containing phase. In these unique systems the immiscible phases define a heterogeneous system.

More recently, we have developed a method for the systematic introduction of quaternary amino groups to the phenyl rings of various chiral ditertiary phosphines [16,17]. Rhodium complexes of the cationic water soluble ligands, [(*S,S*)-2,4-bis[bis(-*p-N,N,N*-trimethylammoniumphenyl)phosphino]pentane] $^{4+}$ and [(*S,S*)-2,3-bis(-*p-N,N,N*-trimethylammoniumphenyl)phosphino]butane] $^{4+}$, provide similar enantioselectivities [17,18] in two-phase asymmetric hydrogenation to complexes of chiral phosphines which contain bis(-*m*-sulfonatophenyl) groups [14]. The presence of quaternary amino groups on these ligands not only imparts water solubility to the rhodium complexes but also provides a potentially new way to immobilize chiral catalysts through exchange onto cation exchange resins.

We have shown previously that rhodium complexes of 2,4-bis[bis(-*p-N,N*-dimethylaminophenyl)phosphine] pentane can be selectively protonated at the amine nitrogens and not at the metal by non-coordinating acids such as fluoroboric acid [19]. The protonated *p*-dimethylammonium derivatives show similar catalytic activities and enantioselectivities to those catalysts prepared with *p*-trimethylammonium derivatives. It is reasonable to expect that other non-coordinating acids, including the acidic forms of strong cation exchange resins, would also selectively protonate at the amine nitrogens. The treatment of solutions of the rhodium complexes of [(*S,S*)-2,4-bis[bis(-*p-N,N*-dimethylaminophenyl)phosphino]butane] (**2**) [17] with the strongly acidic Nafion-NR-50-H resin [20] resulted in the quantitative removal of complex from solution. The catalytic activity of **1** and **2** and the methyl quaternized

analog of **1**, complex **3**, supported on Nafion and other ion exchange resins is reported in this paper.



Results and Discussion

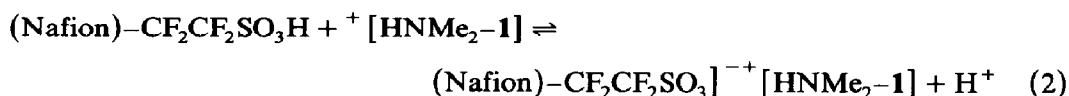
Immobilization of 1, 2, and 3 on cation exchange resins. When methanol solutions of **1** or **2** are stirred in the presence of a sufficient amount of the acid form of Nafion-NR-50 the quantitative removal of the rhodium complexes is observed. Immobilization of **1** onto Amberlyst-H proceeded in a similar manner. Simple acid-base chemistry is considered to be responsible for the removal of the complexes from solution. This is represented in equation 1 and is similar to the protonation previously observed when complexes **1** and **2** are treated with fluoroboric acid [19].



The reaction in equation 1 is not reversed by the addition of concentrated HBF_4 , in fact, even in acid solution the reaction proceeds to the right (see below).

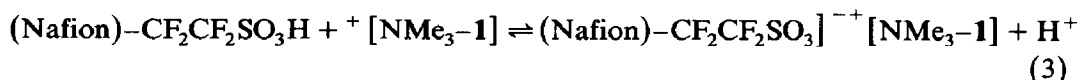
However, the addition of a base stronger than dimethylaniline, such as triethylamine, results in the quantitative removal of the exchanged complex from the resins. Solution NMR of the extracted complexes demonstrates that the complexes are unchanged.

In the presence of HBF_4 the protonated forms of **1** and **2** are obtained. When these protonated complexes are brought into contact with Nafion-H they are also adsorbed onto the resin. The exchange of the protonated complexes, represented in equation 2, appears to be qualitatively faster than the adsorption of the nonprotonated complexes.



Typical loadings consumed 50% of the exchange capacity of the Nafion [20] under the assumption that five equivalents of exchange capacity are required for the adsorption of either **1** or **2**. The maximum loading obtainable was 80 to 90% of the exchange capacity of Nafion-H. Thus there is always some residual free acid present on the rhodium exchanged Nafion-H catalysts. This has important consequences for the catalytic activity of the materials (see below).

Exchange of **3**, the methyl quaternized form of **1**, onto the acid form of Nafion was performed in aqueous methanol. Under these conditions only partial exchange of **3** could be achieved on Nafion-H; the exchange reaction is depicted in equation 3.



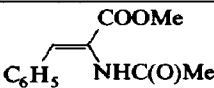
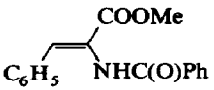
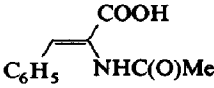
After 24 hours it was estimated from the quantity of rhodium adsorbed that ca. 10% of the exchange capacity of the Nafion-H was consumed. It appears that it is the rate of exchange that is unfavorable. The resins exchanged with **3** were treated with excess triethylamine to consume the excess acid functionality of the Nafion. Triethylamine does not displace **3** from Nafion-H since **3** has no acid functionality.

Formation of the potassium form of Nafion followed by exchange with **3** (or protonated **1**) leads to almost no adsorption of the complexes from solution over a 24 hour period. This is in contrast to the behavior observed for the sodium forms of the Dowex and Amberlite exchange resins; these quantitatively removed **3** from aqueous solution. Although the displacement of five monovalent ions by an ion with a net +5 charge from the resins is favored entropically the exchange is not observed to take place on Nafion-K. It is not clear at this time whether this is a kinetic or a thermodynamic phenomenon.

Catalytic asymmetric hydrogenation with resin-supported 1, 2, and 3. The results for the asymmetric hydrogenation of several dehydroaminoacid derivatives with **1** and **2** on Nafion-H and Amberlyst-H are shown in Table 1. For comparison the results obtained with **1** and **2** in homogeneous methanol solution are also given. It is apparent that there is virtually no loss in enantioselectivity between **2** in homogeneous solution and **2** when immobilized on Nafion-H. The rates, however, are much slower as indicated by the total reaction time required for complete conversion. This is expected in part because the Nafion-H beads used were very large, ca. 1×3 mm and have a very small surface area [20]. The rates are comparable to that observed

Table 1

Enantioselectivities (reaction times) in the homogeneous and immobilized asymmetric hydrogenation of dehydroaminoacid derivatives with complexes **1** and **2**^a

Substrate	Complexes 1			2	
	in MeOH ee (time)	on Nafion-H ee (time)	on Amberlyst-H ee (time)	in MeOH ee (time)	on Nafion-H ee (time)
	72 (33 min) ^b	50 (36 h) ^c	5 (3 h) ^c	75 (30 min)	72 (36) ^c
	57 (5.4 min) ^b	56 (24 h) ^c		53 (1 h)	56 (48 h) ^c
	54 (5 min) 87 (5.1 min) ^b	63 (24 h) ^{c,d} 41 (24 h) ^e	9.4 (3 h) ^e	82 (30 min) 87 (8 h) ^b	76 (48 h) ^{c,f} 35 (36 h) ^h

^a Catalyst concentration: 0.025 mmol in 10 ml solvent; substrate/Rh = 100:1; $P = 14$ atm H_2 , 20 °C; Conversion > 95%. All products are of the *R* configuration; optical yields were determined by polarimetry [10,21]. ^b 1 bar H_2 . ^c Solvent: MeOH. ^d Conversion for hydrogenation: 91%; esterification: 43%. ^e Solvent: THF. ^f Conversion for hydrogenation: 95%; esterification: 63%. ^g Solvent: 50% MeOH–50% H_2O . ^h Solvent: 20% MeOH–80% H_2O .

with other polymer supported hydrogenation catalysts [22]. With **1** as the catalyst on Nafion-H there is a slight drop in enantioselectivity for some substrates when compared to the homogeneously catalyzed reaction. This can be readily explained by the dependence of enantioselectivity on hydrogen pressure for skewphos derivatives; the reactions with **1** on Nafion-H were performed at 14 atm while the homogeneous reactions with **1** were done at 1 atm. With **1** adsorbed on Amberlyst-15-H, which has significantly higher surface area than Nafion-H, the rates improved significantly, however, very low optical yields were observed (Table 1).

Importantly, rhodium leaching into the substrate phase could not be detected by atomic adsorption spectroscopy for all of the resin-supported catalysts. With the instrumentation available this places an upper limit of 0.1 ppm on the rhodium concentration in solution. This is a significant improvement over the results obtained with **1** and **2** as catalysts in two-phase applications [17]. The complexes with a net +5 charge appear to be more strongly bound to the ion exchange resins than complexes with a charge of +1 [13]. As indicated in Table 2 a catalyst can be recycled without a significant change in activity and enantioselectivity. The overall slight drop in enantioselectivity observed is most likely due to traces of oxygen. The reproducible behavior of the recycled catalysts is consistent with the assumption that the catalysts do not leach rhodium and that the catalytic reactions take place on the exchange resins. A further proof for the catalytic chemistry occurring on the resin comes from a comparison of the results for Amberlyst-H and Nafion-H supported **1**. If these catalysts were to lose rhodium during the catalysis then the results for

Table 2

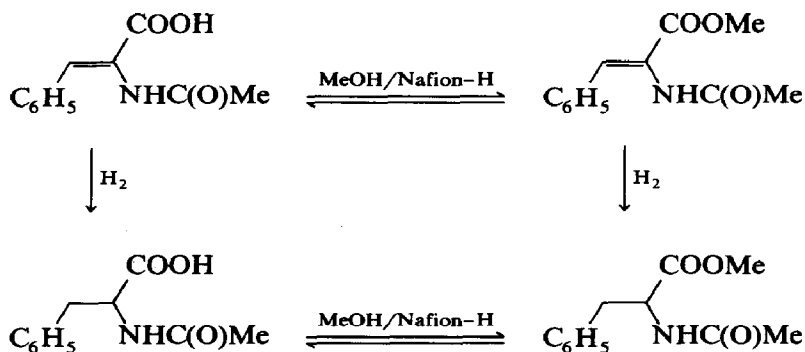
Asymmetric hydrogenation of (*Z*)-*N*-acetylaminocinnamic-acid methyl ester by recycling of Nafion-supported **2**^a

Cycles	Conversion (%)	ee (%)
1	98	73
2	98	72
3	98	73
4	92	67
5	96	64
6	97	63

^a Reaction time: 36 h, catalyst concentration 0.025 mmol on 300 mg Nafion-H; substrate/Rh = 100. Solvent: 10 ml methanol. 20 °C, 14 bar H₂. All products are of the *R* configuration.

activity and enantioselectivity would be expected to be identical since both catalysts would leach the rhodium complex into solution. Finally we note that the filtered solutions obtained during the recycling experiments showed no catalytic activity when charged with new substrate and pressurized with hydrogen. Thus the chemistry is not occurring in solution.

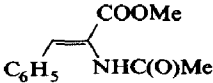
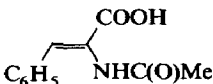
In a previous paper we showed that **1** retains its catalytic activity and selectivity even in fluoroboric acid solution below a pH of 1 [19]. However, it is still surprising that the catalysts remain unchanged on the superacidic exchange resin, Nafion-H, which has an estimated Hammett acidity parameter of -12 [20]. The enantioselectivity is essentially the same for the catalysts on the Nafion resin as in solution which suggests that no protonation occurs at rhodium. Under these strongly acidic conditions with methanol as the solvent, the acid substrate, entry 3 in Table 1, yielded not only the hydrogenated acid but also its methyl ester derivative. Scheme 1, shows the potential pathways to these products. The unsaturated acid gave very little conversion to ester in methanol (25 °C, 36 h) with rhodium free Nafion-H as the catalyst. On the other hand, a sample of pure saturated acid was esterified with a conversion of 93% under the same conditions. Thus the order of reactions is hydrogenation followed by esterification. The mixtures obtained after hydrogenation can be transformed nearly quantitatively to the pure methyl ester by the addition of rhodium free Nafion-H.



Scheme 1

Table 3

Enantioselectivities (reaction times) in the immobilized asymmetric hydrogenation of dehydroaminoacid derivatives with **3** as the catalyst ^a

Substrate	3		
	on Dowex-Na	On Amberlite-Na	on Nafion-H + Et ₃ N
	—	—	49 (36 h) ^b
	12 (48 h) ^b	36 (3 h) ^c 15 (48 h) ^d	57 (48 h) ^b 42 (24 h) ^c

^a Catalyst concentration: 0.025 mmol in 10 ml solvent; substrate/Rh = 100:1; *P* = 14 atm H₂, 20 °C; Conversion > 95%. All products are of the *R* configuration optical yields were determined by polarimetry [10,21]. ^b Solvent: MeOH. ^c Solvent: 50% MeOH–50% H₂O. ^d Solvent: 80% MeOH–20% H₂O.

Esterification could, of course, be eliminated by working in a nonalcohol solvent. Reaction selectivity is a function of solvent and may be expected to change with solvent. Unfortunately Nafion-H is not swollen by THF and Nafion-supported catalysts showed no activity with THF as solvent. Also very low rates and enantioselectivities were observed when water alone was used as solvent for Nafion-supported catalysts.

The problem of a secondary esterification reaction can be overcome by eliminating the residual acid functionality of the rhodium containing resins. Titration of the remaining acid functionality is not feasible since this removes **1** and **2** from the resins (see above). Exchange of the methyl quaternized derivative, **3**, onto Nafion-H followed by titrating the excess acid capacity with NEt₃ eliminates the potential for secondary acid-catalyzed reactions taking place on the resin. The hydrogenation results with this catalyst on the acid substrate are shown in Table 3. Also shown are the results obtained when **3** is exchanged onto the sodium form of Dowex and Amberlite-IR-116. Like the acid forms of the exchange resins reported in Table 1 none of these catalysts showed any evidence of rhodium loss.

The side reaction of esterification was eliminated for all of the catalysts reported in Table 3. The enantioselectivities obtained with **3** on Nafion-HNEt₃ are similar to those of **1** adsorbed on Nafion-H. The catalysts shown in Table 3 show a strong solvent dependence on enantioselectivity. The best results were obtained with **3** on Nafion-HNEt₃ in methanol. The swelling of Nafion is maximized in aqueous alcohol solvents; the degree of swelling may influence the observed selectivities. In principle **3** on Nafion-HNEt₃ is also suitable for substrates containing basic functional groups while **1** on Nafion-H is not.

Nafion is proposed to have a unique structure that is described as similar to a reverse micelle with sulfonate groups clustered together within a fluorocarbon matrix. The unique structure of Nafion may be responsible for allowing the good selectivity of the adsorbed catalysts on this resin compared to the other resins used.

Conclusions

Simple acid–base chemistry governs the adsorption of complexes **1** and **2** on Nafion–H and Amberlyst–H. The net +5 charge on the protonated forms of **1** and **2** and the methyl quaternized derivative **3** results in a very strong binding of the cationic complexes to all of the cation exchange resins investigated. Of the resins studied, Nafion–H is superior in terms of allowing the immobilized complexes to retain their enantioselectivity. For all of the catalysts studied, including those on Nafion, a strong dependence of enantioselectivity on solvent was observed. This may be due to the swelling properties of the resins in the various solvents chosen.

Experimental

The ion exchange resins, Dowex–H-50X2-200, Amberlyst-15–H and Amberlite–Na-IR-116, and Nafion–H-NR-50 were obtained from Aldrich, Chemical Dynamics, and DuPont respectively and used as received unless otherwise stated. The sodium form of Dowex–H-50X2-200 was prepared by treatment with 0.1 *M* NaOH for 24 h at 25°C followed by repeated washing with distilled water until the pH of the washings was ca 7. The rhodium complexes, **1** and **2**, were prepared as previously described [17,18]. Rhodium analyses were performed by atomic absorption spectroscopy on a Perkin Elmer 200A spectrometer with an air–acetylene flame. The limit of detection for rhodium was 0.1 ppm.

The immobilization of **1** or **2** on Nafion was performed in the following manner. A 2.0 g sample of prewashed and degassed exchange resin was treated with a solution of 0.160 mmol of protonated rhodium complex dissolved in 10 ml methanol. The protonation was achieved either prior to use [19] or in situ by the addition of 60 μ l of concentrated HBF₄. The colorless resin gradually turned orange red while the orange red solution became colorless over 6 h. The solution was then decanted and the gel was washed with 4 $\times$ 20 ml MeOH. After drying under vacuum the catalyst was ready to use. The immobilization of **1** onto the macroreticular resin, Amberlyst-15–H, was performed in a similar manner with acetone as the solvent.

Rhodium–norbornadiene complexes of the *p*-trimethylammonium derivative, **3**, were supported onto the sodium forms of Dowex and Amberlite in a similar manner from aqueous solution to give the same rhodium loading as above. Complex **3** could only be partially exchanged onto Nafion–H. In this case only about $\sim$ 0.06 mmol complex could be supported on a 2.0 g sample of Nafion–H from 10 ml 90% MeOH solution after 24 h. After the repeated washing of the catalyst with MeOH, 1.0 ml of Et₃N was allowed to react with the resin for 14 h. The catalyst was then repeatedly washed with MeOH and dried under vacuum.

The hydrogenation of dehydroaminoacids with the rhodium exchanged resins was performed as follows. A 300 mg sample of rhodium containing resin (0.025 mmol Rh) was transferred into a pressure reactor which was charged with 10 mL of methanol and 2.5 mmol of substrate. The reactor was then pressurized with hydrogen and the mixture stirred magnetically under the conditions indicated in Table 1. To give a comparable rhodium concentration, 800 mg of the 3–Nafion–HEt₃N catalyst was used for the hydrogenation reactions.

After the hydrogenation reactions were complete the colorless solutions were removed by syringe and the solvents evaporated under vacuum. The conversions

were checked by NMR and the optical yields were determined by polarimetry by comparison with the literature values [10,21]. In the cases when the reaction yielded mixtures of the acid and the methyl ester form of the product the optical yield was determined by first transforming the acid to the methyl ester by the addition of rhodium free Nafion-H to methanol solutions of the mixture. The optical purity of the ester was then measured by optical rotation (for the optically pure ester, $[\alpha]_{\text{D}}^{20} = -101.5^\circ$ (c 5.00, CHCl_3) [10]. Alternatively, the composition of the mixture could be determined by NMR and the expected average rotation could be calculated (for the optically pure acid, $[\alpha]_{\text{D}}^{20} = -46.0^\circ$ (c 5.00, EtOH) [21], and for the optically pure methyl ester $[\alpha]_{\text{D}}^{20} = -12.7^\circ$ (c 5.00, EtOH). The values obtained in this manner agreed with those from the pure ester.

The esterification of saturated and unsaturated amino acids were performed with 300 mg unmodified Nafion-H-NR50 with 2.5 mmol substrate for 36 h at 25°C .

Acknowledgements

We thank the precious metals loan program of Johnson Matthey Inc. for a generous loan of $\text{RhCl}_3 \cdot 3\text{H}_2\text{O}$. We thank R.W. Van Scoyoc of E.I. DuPont de Nemours and Company for a gift of Nafion-H-NR50 and helpful discussions regarding the chemistry of Nafion. Financial support for this work was provided by NSF (CBT-8719560).

References

- 1 W. Dumont, J.-C. Poulin, T.-P. Dang, H.B. Kagan, *J. Am. Chem. Soc.*, 8295 (1973) 95.
- 2 (a) J.K. Stille, *Pure Appl. Chem.*, 54 (1982) 99; (b) C.U. Pittman, Jr., in *Comprehensive Organometallic Chemistry* Vol. 8, G. Wilkinson, F.G.A. Stone, E.W. Abel, (Eds.), Pergamon Press, Oxford, 1982; p. 553.
- 3 I. Kolb, M. Cerny, V. Hetflejš, *React. Kinet. Catal. Lett.*, 7 (1977) 199.
- 4 N. Takaishi, H. Imai, C.A. Bertelo, J.K. Stille, *J. Am. Chem. Soc.*, 98 (1976) 5400.
- 5 N. Takaishi, H. Imai, C.A. Bertelo, J.K. Stille, *J. Am. Chem. Soc.*, 100 (1978) 264.
- 6 (a) G.L. Baker, S.J. Fritschel, J.R. Stille, J.K. Stille, *J. Org. Chem.*, 46 (1981) 2954; (b) G.L. Baker, S.J. Fritschel, J.K. Stille, *J. Org. Chem.*, 46 (1981) 2960.
- 7 P.D. Sybert, C.A. Bertelo, W.B. Bigelow, S. Varaprath, J.K. Stille, *Macromolecules*, 14 (1981) 502.
- 8 S. Ahrland, J. Chatt, N.R. Davies, A.A. Williams, *J. Chem. Soc.*, (1958) 1403.
- 9 T.D. Madden, P.J. Quinn, *Biochem. Soc. Trans.*, 6 (1978) 244.
- 10 M.D. Fryzuk, B. Bosnich, *J. Am. Chem. Soc.*, 99 (1977) 6262.
- 11 (a) S.C. Tang, T.E. Paxson, L. Kim, *J. Mol. Catal.*, 9 (1980) 313; (b) L. Kim, T.E. Paxson, S.C. Tang, U.S. Patents, 4,179,402; 4,179,403; 4,317,936.
- 12 R.T. Smith, R.K. Ungar, M.C. Baird, *Transition Met. Chem.*, 7 (1982) 288.
- 13 R. Selke, K. Haupke, H.W. Krause, *J. Mol. Catal.*, 56 (1989) 315.
- 14 (a) F. Alario, Y. Amrani, Y. Colleuille, T.P. Dang, J. Jenck, D. Morel, D. Sinou, *J. Chem. Soc., Chem. Commun.*, 202 (1986); (b) Y. Amrani, L. Lecomte, D. Sinou, J. Bakos, I. Tóth, B. Heil, *Organometallics*, 8 (1989) 542.
- 15 U. Nagel, E. Kinzel, *Chem. Ber.*, 119 (1986) 1731.
- 16 I. Tóth, B.E. Hanson, M.E. Davis, *Organometallics*, 9 (1990) 675.
- 17 I. Tóth, B.E. Hanson, M.E. Davis, *Tetrahedron Asymmetry* (submitted).
- 18 I. Tóth, B.E. Hanson, M.E. Davis, *Catal. Lett.*, 5 (1990) 183.
- 19 I. Tóth, B.E. Hanson, M.E. Davis, *J. Organomet. Chem.*, 396 (1990) 363.
- 20 F.J. Waller, R.W. Van Scoyoc, *Chem. Tech.*, 17 (1987) 438.
- 21 R. Glaser, S. Geresh, *Tetrahedron*, 35 (1979) 2381.
- 22 R. Deschenaux, J.K. Stille, *J. Org. Chem.*, 50 (1985) 2299.