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Article

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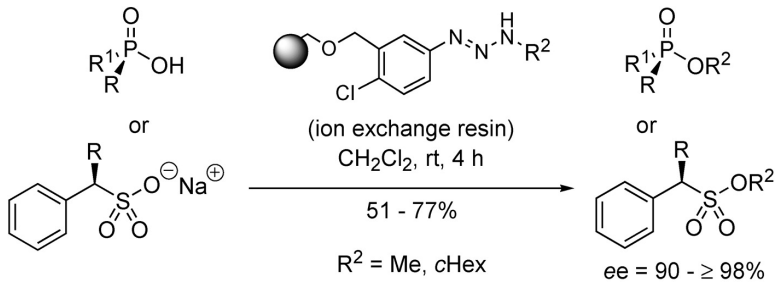

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Efficient Synthesis of Sulfonic, Phosphoric, and Phosphinic Esters Employing Alkylating Polymer-Bound Reagents

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Received September 3, 2002

The efficient esterification of various sulfonic acids and sulfonates using polymer-bound triazenes based on the triazene T2* linker is described. Esterification of enantiopure α-substituted sodium sulfonates was performed in the presence of an alkylating resin without racemization. Racemization is a serious drawback in the esterification route via sulfonyl chlorides because of intermediate sulfene formation. To demonstrate the versatility of this protocol, phosphoric and phosphinic acids have been converted into the corresponding esters as well. All products were obtained in good yield and excellent purities without any further purification steps.

Sulfonic esters are commonly known as alkylating agents.[1] They are thus often used in nucleophilic displacement reactions wherein leaving groups of moderately high reactivity are desired.[2] Because of their alkylating ability in biological systems, alkyl sulfonates possess a certain mutagenic activity,[3] but they also exhibit interesting pharmacological properties.[4] For example, numerous methyl arylalkanesulfonates have been synthesized as reagents for selective methylation of subtilisin BPN′,[5] a serine protease with a wide range of substrate specificity.[6] In other studies, 2-haloethyl sulfonates and related derivatives displayed significant activity against P388 leukemia in mice,[7] especially the chiral α-substituted 2-chloroethyl-α-cyanoethane sulfonate.[8]

The reaction of sulfonyl chlorides[9] with alcohols in the presence of a base provides a well-established access to alkyl sulfonates.[10,11] In the case of the reaction of alkylsulfonyl chlorides, the intermediate sulfene formation is a serious drawback, especially when enantiopure α-substituted sulfonyl chlorides are used.[12,13] Other methods include the reaction of sulfonic acids with ortho esters[14] and other electrophiles such as epoxides[15] or aziridines.[16] A mild and clean method for the synthesis of sulfonic esters is the reaction of sulfonic acids with diazomethane[17] or further functionalized diazoalkanes.[18] Although synthetically useful, the drawback of this method is the lack of a general accessibility of suitable diazoalkanes. In addition, the parent compound for this transformation, diazomethane, and its higher homologues are considered to be highly toxic and explosive.[19] Similarly, the well-known precursors for diazomethane (such as Diazald) are also irritants.[20]

In several communications, we demonstrated the use of triazenes as linker moieties in solid-phase organic synthesis to detach amines,[21] guanidines,[22] ureas, and amides.[23] In addition, we have demonstrated that immobilized primary triazenes derived from an aromatic diazonium ion and primary amines are suitable for the alkylation of acids and for the synthesis of alkyl halides.[24] In this case, the triazene moiety serves as a capped diazoalkane equivalent delivering the alkyl group upon protonation.

In a related context, the ability of polymer-bound triazene linkers as alkylating agents was demonstrated by another group in the synthesis of various carboxylic esters starting from the corresponding acids.[25]

In a preceding communication, we have described the use of polymer-bound triazenes based on the T2* linker in the synthesis of alkyl sulfonates starting from the corresponding sulfonic acid and in extension from sodium sulfonates.[26] To the best of our knowledge, no practical approach for a one-step esterification of sodium sulfonates has been reported before. Herein, we present in detail the development of this methodology and further extensions.

Results and Discussion

The aim of our project was to examine the use of polymer-bound triazenes as alkylating reagents for the esterification of sulfonic acids. The triazenes of type **3a**−**c** were synthesized according to a previous report[27] from the bench-stable polymer-bound diazonium salt T2* (**1**) by simple treatment with the amines **2a**−**c** to give the triazenes **3a**−**c** in excellent yields (Scheme 1). The treatment of the diazonium salt with an aqueous solution of methylamine (**2a**) was also successful.

As test substrate for the esterification, toluene-4-sulfonic acid was chosen and examined in the dependency of the yield on the reaction time. According to our standard reaction conditions, the acid **4a** was treated with 3 equiv of the solid-phase-bound triazene **3a** at room temperature (Scheme 2, Table 1).

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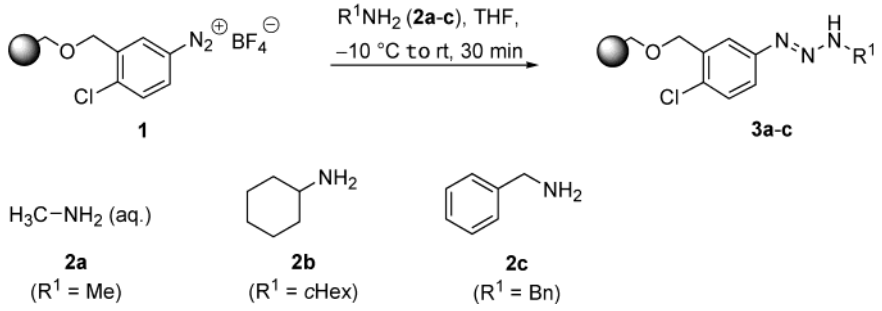
Scheme 1. Synthesis of the Polymer-Bound Triazenes **3a**−**c**



Scheme 2. Synthesis of the Sulfonic Ester **5a**

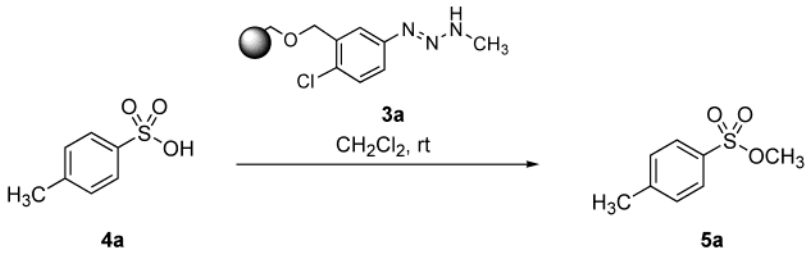
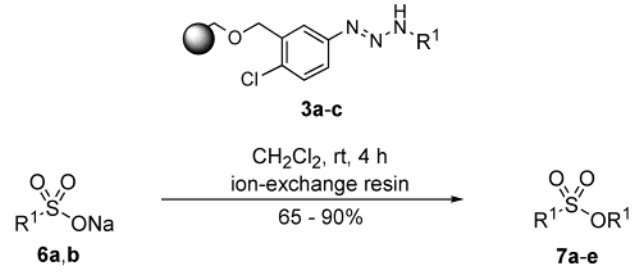


Table 1. Esterification of Toluene-4-sulfonic Acid **4a** with Variation of the Reaction Time

entry	**4a** mmol	resin **3a** g	reaction time h	yield %	purity %[a]
1	0.1	0.5	2	71	97
2	0.1	0.5	4	86	97
3	0.1	0.5	6	85	96
4	0.1	0.5	24	82	96

[a] Determined by GC.

Scheme 3. Direct Esterification of the Sodium Sulfonates **6a**,**b**

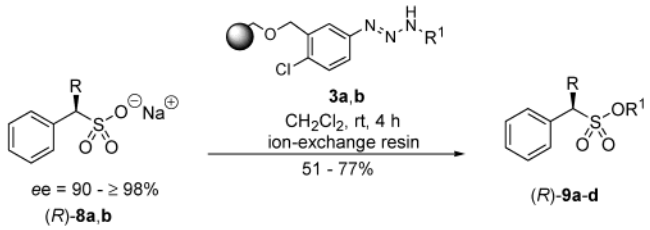


As shown in Table 1, a reaction time of 4 h was optimal in terms of yield. A longer reaction time led to a slight decrease of yield and purity. Under these acceptable reaction conditions, various sulfonic acids **4** were converted to the corresponding esters using the triazene resins **3a**−**c** to yield the sulfonic esters **5** (Table 2). Different sulfonates **5a**−**e** were prepared in excellent yields and purities, which were determined by GC and NMR methods.

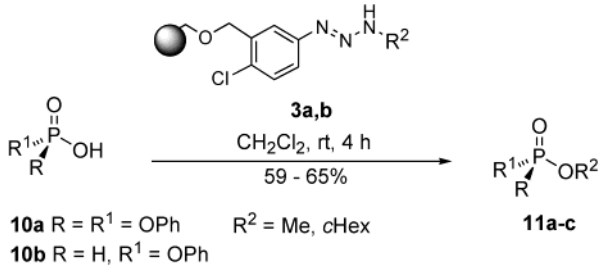
Similarly, it was also possible to use sodium sulfonates as starting material, provided that the synthesis was conducted in the presence of an acidic ion-exchange resin (Lewatit SP 120 H form). In this case, the ion-exchange resin protonates the sulfonate to give the active sulfonic acid and also retains the sodium ion. Two different sodium sulfonates **6a**,**b** were converted into an array of sulfonates **7a**−**e** (Scheme 3, Table 3).

According to this general procedure, five further sulfonic esters **7a**−**e** were obtained in good yields and purities using our new method. This result prompted us to use enantioenriched α-substituted sodium sulfonates. In general, sodium sulfonates are transformed into esters by first converting them into sulfonyl chlorides and letting them subsequently react with alcohols in the presence of base. Because of intermediate sulfene formation by preliminary elimination of hydrochloric acid, this mechanism does not allow the reaction of enantio-enriched sulfonates without racemization. Using our method, two enantio-enriched α-substituted sodium sulfonates, (*R*)-**8a**,**b**, synthesized via asymmetric synthesis[28] were transformed into esters without loss of enantiomeric excess (Scheme 4, Table 4).

Scheme 4. Esterification of Enantioenriched α-Substituted Sodium Sulfonates *(R)*-**8a**,**b**



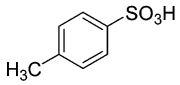
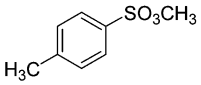
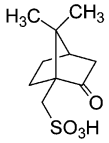
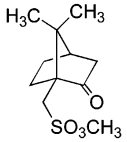
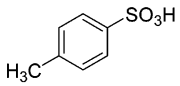
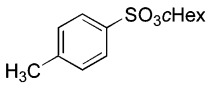
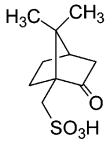
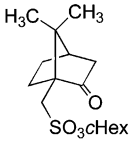
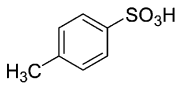
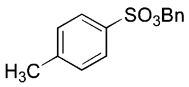
Scheme 5. Esterification of Phosphor-Based Acids **10a** and **b**



The purities and enantiomeric excesses of the products (*R*)-**9a**−**d** are in general excellent.

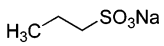
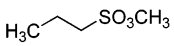
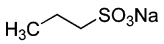
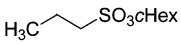
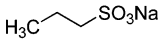
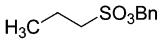
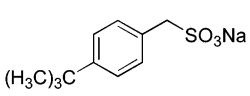
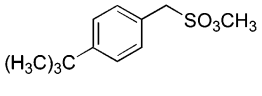
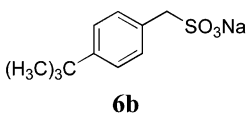
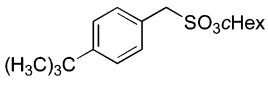
To demonstrate the versatility of our method, esterifications were also performed with phosphorus-based acids. As starting materials, phosphoric acid diphenyl ester **10a** and

Table 2. Preparation of Sulfonic Esters **5a**−**e**

Starting material	Resin	Product	Yield [%]	Purity [%]
 **4a**	**3a**	 **5a**	86	97[a]
 **4b**	**3a**	 **5b**	89	96[a]
 **4a**	**3b**	 **5c**	91	>95[b]
 **4b**	**3b**	 **5d**	87	>95[b]
 **4a**	**3c**	 **5e**	84	>90[b]

[a] Determined by GC. [b] Determined by ^{1}H NMR spectroscopy.

Table 3. Preparation of the Sulfonic Esters **7a**−**e**

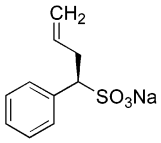
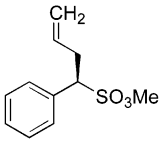
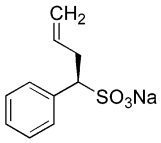
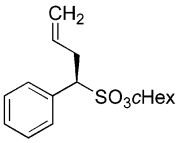
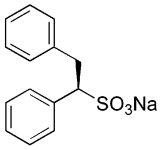
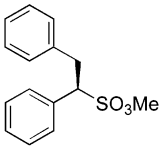
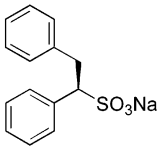
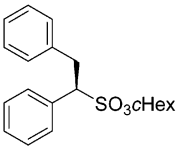
Starting material	Resin	Product	Yield [%]	Purity [%]
 **6a**	**3a**	 **7a**	77	95[a]
 **6a**	**3b**	 **7b**	76	>95[b]
 **6a**	**3c**	 **7c**	65	>90[b]
 **6b**	**3a**	 **7d**	90	97[a]
 **6b**	**3b**	 **7e**	81	>95[b]

[a] Determined by GC. [b] Determined by ^{1}H NMR spectroscopy.

the phenyl-phosphinic acid **10b** were chosen. Thus, after treatment of the acids **10** under the conditions applied before, the esters **11** were isolated in excellent purities and good yields.

With respect to the common methods to synthesize phosphoric acid esters[29] or esters of phosphinic acid,[30] this method is advantageous in terms of yields and purities obtained.

Table 4. Preparation of the Chiral Sulfonic Esters **9a**−**d**

Starting material	Resin	Product, *ee*, $[\alpha]_D$[a][b]	Yield [%]	Purity [%]
	**3a**		56	93[b]
(*R*)-**8a** *ee* ≥ 90%		(*R*)-**9a** *ee* ≥ 90% $[\alpha]_D = -5.40$ ($c = 1.0$)		
	**3b**		51	95[c]
(*R*)-**8a** *ee* ≥ 90%		(*R*)-**9b** *ee* ≥ 90% $[\alpha]_{436} = +1.2$ ($c = 1.0$)		
	**3a**		77	95[c]
(*R*)-**8b** *ee* ≥ 98%		(*R*)-**9c** *ee* ≥ 98% $[\alpha]_D = -77.4$ ($c = 1.0$)		
	**3b**		65	90[c]
(*R*)-**8b** *ee* ≥ 98%		(*R*)-**9d** *ee* ≥ 98% $[\alpha]_D = -47.8$ ($c = 0.45$)		

[a] All optical rotations were measured in Uvasol grade $CHCl_3$ at room temperature. [b] Determined by HPLC using a chiral stationary phase: for **9a,c**, (*S,S*)-Whelk-O1; for **9b**,**d**, Daicel OJ; for **9c**, Daicel OD. [c] Determined by ^{1}H NMR spectroscopy.

Conclusion

In conclusion, a general technique for the synthesis of several types of organic acid esters is presented. A great advantage is the direct esterification of sodium sulfonates, because the esterification of enantiopure α-substituted sodium sulfonates can be performed without racemization, a serious drawback via alcoholysis of sulfonyl chlorides in the presence of a base.

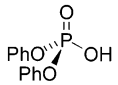
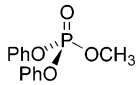
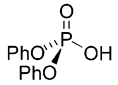
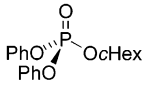
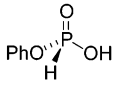
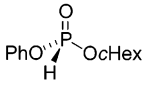
Experimental Section

Starting materials and reagents were purchased from commercial suppliers and used without further purification. Solvents were dried and purified by conventional methods prior to use. Optical rotation values were measured on a Perkin-Elmer P241 polarimeter. Microanalyses were obtained with a Vario EL element analyzer. Mass spectra were acquired on a Finnigan SSQ7000 (CI 100 eV; EI 70 eV) spectrometer. High-resolution mass spectra were recorded on a Finnigan MAT95 spectrometer. IR spectra were taken on a Perkin-Elmer FT-IR 1760. ^{1}H and ^{13}C NMR spectra were recorded on Gemini 300 or Varian Inova 400, and all measurements were performed with tetramethylsilane as internal standard. Melting points were determined on a Tottoli melting point apparatus and are uncorrected.

General Procedure for the Preparation of Alkyl Esters Starting from the Corresponding Acids (Protocol A). The acid (0.10 mmol) was added to the resin **3** (0.50 g/0.10 mmol of the acid, synthesized according ref 27, 1.1 mmol/g), and the mixture was suspended in 5 mL of dichloromethane. After 4 h, the mixture was filtered by using a filtration setup consisting of a 5-mm glass pipet filled with a plug of glass wool and a small layer of silica (10 mm). The resin was washed twice with dichloromethane, and the combined filtrates were concentrated in vacuo.

General Procedure for the Preparation of Alkylsulfonates Starting from the Corresponding Sodium Salts (Protocol B). The sodium sulfonate was added to a mixture

Table 5. Preparation of the Phosphorus-Based Acid Esters **11a−c**

Starting material	Resin	Product	Yield [%]	Purity [%]
 **10a**	**3a**	 **11a**	59	>95[b]
 **10a**	**3b**	 **11b**	65	97[a]
 **10b**	**3b**	 **11c**	62	99[a]

[a] Determined by GC. [b] Determined by ^{1}H NMR spectroscopy.

of the resin (0.5 g/0.1 mmol of the sulfonate salt) and the acidic ion-exchange resin (0.5 g/0.1 mmol of the acid). The mixture was suspended in 10 mL of dichloromethane and stirred for 4 h. The resins were then separated by simple filtration using a paper filter, and the solution was then filtered again according to protocol A.

Toluene-4-sulfonic Acid Methyl Ester (5a). According to protocol A, 17 mg of the toluene-4-sulfonic acid **4a** (0.1 mmol) and 0.5 g of the resin **3a** (3 equiv) afforded 16 mg of **5a** (86%).[31]

Camphor-10-sulfonic Acid Methyl Ester (5b). According to protocol A, 23 mg of the camphor-10-sulfonic acid **4b** (0.1 mmol) and 0.5 g of the resin **3a** (3 equiv) afforded 20 mg of **5b** (89%).[32]

Toluene-4-sulfonic Acid Cyclohexyl Ester (5c). According to protocol A, 17 mg of the toluene-4-sulfonic acid **4a** (0.1 mmol) and 0.5 g of the resin **3b** (3 equiv) afforded 23 mg of **5a** (91%).[28]

Camphor-10-sulfonic Acid Methyl Ester (5d). According to protocol A, 69 mg of the camphor-10-sulfonic acid **4b** (0.3 mmol) and 1.5 g of the resin **3a** (3 equiv) afforded 80 mg of **5d** (87%) as a white solid. mp 58 °C; $[\alpha]^{25}_D$ = +32.1 (c = 1.0, $CHCl_3$). ^{1}H NMR ($CDCl_3$) δ = 0.89 (s, 3H), 1.14 (s, 3H), 1.26−2.6 (m, 17H), 2.99 (d, 1H, J = 15.1 Hz), 3.60 (d, 1H, J = 15.1 Hz), 4.75 (m, 1H) ppm. ^{13}C NMR ($CDCl_3$) δ = 19.7, 20.0, 23.0, 32.7, 32.8, 42.5, 42.7, 47.9, 48.0, 58.1, 81.5, 214.6 ppm. IR (KBr) 1160, 1353, 1747 cm^{-1}. MS (EI) m/z = 314 [M$^+$]. Microanal. calcd for $C_{16}H_{24}SO_4$: C, 61.12; H, 8.33. Found: C, 60.81; H, 8.60.

Toluene-4-sulfonic Acid Benzyl Ester (5e). According to protocol A, 17 mg of the toluene-4-sulfonic acid **4a** (0.1 mmol) and 0.5 g of the resin **3c** (3 equiv) afforded 22 mg of **5e** (84%).[33]

Propane-1-sulfonic Acid Methyl Ester (7a). According to protocol B, 15 mg of the sodium sulfonate **6a** (0.1 mmol), 0.5 g of the resin **3a** (3 equiv) and 0.25 g of the ion-exchange resin (Lewatit SP 120 H form) afforded 10 mg of **7a** (77%).[34]

Propane-1-sulfonic Acid Cyclohexyl Ester (7b). According to protocol B, 15 mg of the sodium sulfonate **6a** (0.1 mmol), 0.5 g of the resin **3b** (3 equiv), and 0.25 g of the ion-exchange resin (Lewatit SP 120 H form) afforded 16 mg of **7b** (76%) as a colorless oil. ^{1}H NMR ($CDCl_3$) δ = 1.08 (tr, 3H, J = 7.41 Hz), 1.2−2.1 (m, 12H), 3.05 (m, 2H), 4.70 (m, 1H) ppm. ^{13}C NMR ($CDCl_3$) δ = 12.9, 17.4, 23.5, 24.9, 32.8, 53.2, 80.8 ppm. IR (neat) 939, 1166, 1358, 1454, 2939 cm^{-1}. MS (EI) m/z = 207 [M$^+$]. HR-MS m/z calcd for $C_9H_{18}SO_3$, 206.0977; found, 206.0977.

Propane-1-sulfonic Acid Benzyl Ester (7c). According to protocol B, 15 mg of the sodium sulfonate **6a** (0.1 mmol), 0.5 g of the resin **3c** (3 equiv), and 0.25 g of the ion-exchange resin (Lewatit SP 120 H form) afforded 16 mg of **7b** (65%) as a colorless oil. ^{1}H NMR ($CDCl_3$) δ = 1.00 (tr, 3H, J = 7.41 Hz), 1.85 (m, 2H), 2.99 (m, 2H), 5.23 (s, 2H), 7.41 (m, 5H) ppm. ^{13}C NMR ($CDCl_3$) δ = 12.8, 17.2, 52.8, 70.89, 128.7, 129.1, 133.3 ppm. IR (neat) 1165, 1357 cm^{-1}. MS (EI) m/z = 214 [M$^+$]. HR-MS m/z calcd for $C_{10}H_{14}SO_3$, 214.0664; found, 214.0663.

(4-*tert*-Butyl-phenyl)-methanesulfonic Acid Methyl Ester (7d). According to protocol B, 50 mg of the sodium sulfonate **6b** (0.2 mmol), 1.0 g of the resin **3b** (3 equiv), and 0.5 g of the ion-exchange resin (Lewatit SP 120 H form) afforded 44 mg of **7d** (90%) as a white solid. mp 71−72 °C. ^{1}H NMR ($CDCl_3$) δ = 1.32 (s, 9H), 3.78 (s, 3H), 4.33 (s, 2H), 7.34 (d, 2H, J = 8.24 Hz), 7.42 (d, 2H, J = 8.24 Hz) ppm. ^{13}C NMR ($CDCl_3$) δ = 31.2, 34.7, 55.8, 56.6, 124.6, 125.9, 130.3, 152.2 ppm. IR (KBr) 985, 1170, 1336, 1357, 2962 cm^{-1}. MS (EI) m/z = 242 [M$^+$]. HR-MS m/z calcd for $C_{12}H_{18}SO_3$, 242.0977; found, 242.0978.

(4-*tert*-Butyl-phenyl)-methanesulfonic Acid Cyclohexyl Ester (7e). According to protocol B, 50 mg of the sodium sulfonate **6b** (0.2 mmol), 1.0 g of the resin **3b** (3 equiv), and 0.5 g of the ion-exchange resin (Lewatit SP 120 H form) afforded 50 mg of **7e** (81%) as a colorless oil. ^{1}H NMR ($CDCl_3$) δ = 1.2−1.9 (m, 10H), 1.32 (s, 9H), 4.3 (s, 2H), 4.51 (m, 1H), 7.34 (d, 2H, J = 8.52 Hz), 7.41 (d, 2H, J = 8.52 Hz) ppm. ^{13}C NMR ($CDCl_3$) δ = 23.4, 24.8, 31.2, 32.6, 34.6, 57.2, 82.1, 124.9, 151.8, 125.6, 1302 ppm. IR 942, 1171, 1296, 1323, 1344, 1361, 2965 cm^{-1}. MS (EI) m/z = 310 [M$^+$]. Microanal. calcd for $C_{17}H_{26}SO_3$: C, 65.77; H, 8,44. Found: C, 65.98; H, 8.78.

(*R*)-1-Phenyl-but-3-ene-1-sulfonic Acid Methyl Ester ((*R*)-9a). According to protocol B, 23 mg of the sodium sulfonate **(*R*)-8a** (0.1 mmol), 0.5 g of the resin **3a** (3 equiv), and 0.25 g of the ion-exchange resin (Lewatit SP 120 H form) afforded 13 mg of **(*R*)-9a** (56%). $[\alpha]_D = -5.40$ ($c = 1.0$).[35]

(*R*)-1-Phenyl-but-3-ene-1-sulfonic Acid Cyclohexyl Ester ((*R*)-9b). According to protocol B, 23 mg of the sodium sulfonate **(*R*)-8a** (0.1 mmol), 0.5 g of the resin **3b** (3 equiv), and 0.25 g of the ion-exchange resin (Lewatit SP 120 H form) afforded 15 mg of **(*R*)-9b** (51%) as a colorless oil. $[\alpha]_{436} = +1.2$ ($c = 1.0$). ^{1}H NMR ($CDCl_3$) $\delta = 1.10-1.90$ (m, 10H), 2.95 (m, 1H), 3.13 (m, 1H), 3.64 (s, 3H), 4.26 (dd, 1H, $J = 4.67$, 10.99 Hz), 5.02 (ddd, 1H, $J = 1.10$, 2.47, 10.17 Hz), 5.10 (ddd, 1H, $J = 1.38$, 3.03, 17.03 Hz), 5.57 (m, 1H), 7.30−7.44 (m, 5H) ppm. ^{13}C NMR ($CDCl_3$) $\delta =$ 23.3, 24.8, 32.2, 32.9, 34.3, 67.4, 82.1, 118.4, 128.5, 128.8, 129.5, 132.0, 132.7 ppm. IR 932, 1166, 1353, 2939 cm^{-1}. MS (EI) $m/z = 310$ [$M^+ - C_6H_{11}OSO_2$]. Microanal. calcd for $C_{16}H_{22}SO_3$: C, 65.28; H, 7.53. Found: C, 65.22; H, 7.51.

(*R*)-1,2-Diphenyl-ethane-sulfonic Acid Methyl Ester ((*R*)-9c). According to protocol B, 28 mg of the sodium sulfonate **(*R*)-8b** (0.1 mmol), 0.5 g of the resin **3a** (3 equiv), and 0.25 g of the ion-exchange resin (Lewatit SP 120 H form) afforded 21 mg of **(*R*)-9c** (77%). $[\alpha]_D = -77.4$ ($c = 1.0$).[35]

(*R*)-1,2-Diphenyl-ethane-sulfonic Acid Cyclohexyl Ester ((*R*)-9d). According to protocol B, 28 mg of the sodium sulfonate **(*R*)-8b** (0.1 mmol), 0.5 g of the resin **3a** (3 equiv), and 0.25 g of the ion-exchange resin (Lewatit SP 120 H form) afforded 22 mg of **(*R*)-9d** (65%) as a colorless oil. $[\alpha]_D = -47.8$ ($c = 0.45$). ^{1}H NMR ($CDCl_3$) $\delta = 1.10-1.9$ (m, 10H), 3.39 (dd, 1H, $J = 11.26$, 14.01 Hz), 3.74 (dd, 1H, $J = 3.57$, 14.01 Hz), 4.36 (dd, 1H, $J = 3.57$, 11.54 Hz), 4.49 (m, 1H), 6.90−7.40 (m, 10H) pm. ^{13}C NMR ($CDCl_3$) $\delta =$ 23.3, 24.8, 32.1, 32.9, 36.5, 69.3, 82.2, 126.6, 128.2, 128.4, 128.7, 128.8, 129.5, 132.0, 136.5 ppm. IR 1166, 1333, 1350, 2938 cm^{-1}. MS (EI) $m/z = 181$ [$M^+ - C_6H_{11}OSO_2$]. Microanal. calcd for $C_{20}H_{24}SO_3$: C, 69.74; H, 7.02. Found: C, 69.70; H, 7.11.

Phosphoric Acid Methyl Ester Diphenyl Ester (11a). According to protocol A, 50 mg of the phosphoric acid diphenyl ester **10a** (0.2 mmol) and 1.0 g of the resin **3a** (3 equiv) afforded 30 mg of **11a** (59%) as a colorless oil. ^{1}H NMR ($CDCl_3$) $\delta = 3.93$ (d, 3H, $J = 11.81$ Hz), 7.14−7.35 (m, 10H) ppm. ^{13}C NMR ($CDCl_3$) $\delta = 55.3$ (d, $J = 6.1$ Hz), 119.8, 125.2, 129.6, 150.3 (d, $J = 6.8$ Hz) ppm. IR (neat) 953, 1051, 1191, 1295, 1489, 1591 cm^{-1}. MS (EI) $m/z =$ 264 [M^+]. HR-MS m/z calcd for $C_{13}H_{13}PO_4$, 264.0551; found, 264.0552.

Phosphoric Acid Cyclohexyl Ester Diphenyl Ester (11b). According to protocol A, 50 mg of the phosphoric acid diphenyl ester **10a** (0.2 mmol) and 1.0 g of the resin **3b** (3 equiv) afforded 43 mg of **11b** (65%) as a colorless oil. ^{1}H NMR ($CDCl_3$) $\delta = 1.2-2.0$ (m, 10H), 4.62 (m, 1H), 7.15−7.36 (m, 10H) ppm. ^{13}C NMR ($CDCl_3$) $\delta = 23.3$, 25.0 (d, $J = 4.5$ Hz), 33.1 (d, $J = 4.5$ Hz), 79.3, 120.0, 125.0, 129.5, 150.0 ppm. IR ($CHCl_3$) 949, 1018, 1193, 1288, 1489, 1592 cm^{-1}. MS (EI) $m/z = 332$ [M^+]. HR-MS m/z calcd for $C_{18}H_{21}PO_4$, 332.1177; found, 332.1177.

Phenylphosphinic Acid Cyclohexyl Ester (11c). According to protocol A, 45 mg of the phenyl-phosphinic acid **10b** (0.2 mmol) and 1.0 g of the resin **3a** (3 equiv) afforded 28 mg of **11c** (62%) as a colorless oil. ^{1}H NMR ($CDCl_3$) $\delta =$ 1.2−2.1 (m, 10H), 4.45 (m, 1H), 7.47−7.85 (m, 5H); 7.65 (d, 1H, $J = 559.1$ Hz) ppm. ^{13}C NMR ($CDCl_3$) $\delta = 23.6$, 25.1, 33.54 (d, $J = 3.4$ Hz), 33.9 (d, $J = 4.0$ Hz), 76.16 (d, $J = 6.8$ Hz), 128.7 (d, $J = 14.3$ Hz), 130.9 (d, $J = 11.4$ Hz), 131.9 (d, $J = 369$ Hz), 132.9 (d, $J = 3.4$ Hz) ppm. IR ($CHCl_3$) 960, 1127, 1232, 1440, 2936 cm^{-1}. MS (CI) $m/z =$ 225 [$M + H$]$^+$.

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