

173.34; HRMS calcd for  $C_{18}H_{33}NO_5$  343.2358, found 343.2398.

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### Convenient Route to Functionalized Styrenes via Pyrolysis of Functionalized Polystyrene

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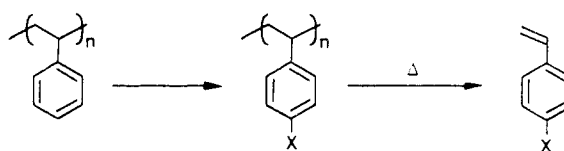
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Functionalized styrenes have been shown to be useful starting materials for a number of organic syntheses<sup>1</sup> as well as polymer syntheses.<sup>2</sup> It is important, therefore, to develop a convenient preparative method for styrene monomers or intermediates that contain functionality on the aromatic ring. So far, the conventional procedure for the preparation of functionalized styrene monomers consists of several steps involving dehydration or dehydrobromination at the last stage of the synthesis to generate the styrenic double bond.<sup>3</sup> The overall yields are usually low to moderate. Recently, Stille demonstrated an elegant procedure to prepare functionalized styrenes by palladium-catalyzed coupling of aryl bromide with vinyltin reagents. An expensive vinyltributyltin is required for this method.<sup>4</sup>

Although polystyrene is known to be thermally depolymerized to give monomer,<sup>5</sup> pyrolysis has not been used actively for the preparation of functionalized styrene monomers. Various kinds of functionalized polystyrenes have been prepared quantitatively by chemical modification of polystyrene.<sup>2,6</sup> We have found that these functionalized polystyrenes were pyrolyzed readily under reduced pressure to give the corresponding monomers, as will

Scheme I



be discussed in this paper (Scheme I).

Functionalized polystyrenes are considered to be double-bond-protected, functional styrenes that can be deprotected by pyrolysis. Protected styrene can stand exposure to vigorous reaction conditions for functionalization. The functionalized polystyrenes shown in Table I were prepared by chemical modifications of polystyrene according to the procedures given in the literature. Almost quantitative conversions were obtained in all cases. These polymeric reactions show high para selectivity in electrophilic ring substitution reactions due to steric hindrance in the ortho positions caused by the polymeric structure. This saves separation of the other ring isomers, which are sometimes unavoidable in conventional preparations. Brominated polystyrene was obtained directly from polystyrene and bromine in the presence of a catalytic amount of  $FeCl_3$  in 93% yield. The degree of bromination is easily controlled by the quantity of bromine added to the polystyrene. A gel-type copolymer of styrene-divinylbenzene was also brominated by the same procedure. Pyrolysis experiments were carried out by using a typical distillation apparatus under reduced pressure. At a temperature below 300 °C, the polystyrene derivatives degrade with no volatile products. Use of an open flame (500–650 °C) was effective for pyrolysis of the functionalized polystyrenes, to give volatile monomers. Indeed, brominated polystyrene was readily pyrolyzed to give a deep orange colored liquid, which was redistilled to give a colorless liquid of 4-bromostyrene in 78% isolated yield. Meta and ortho isomers were not detected after the redistillation.

This method has been extended to a number of functionalized polystyrenes, as summarized in Table I. Insoluble polymer beads of styrene-divinylbenzene copolymer can be utilized also for the pyrolysis (entries 2, 5, 10). Starting from partially functionalized polystyrenes, the desired monomers obtained were contaminated with styrene and other volatiles (entries 2, 11). Reduced isolated yields of the desired monomers come from their purification process. In comparison with the conventional method, the pyrolysis method appears to be a much easier and more efficient method by which to obtain functionalized styrene monomers. For example, in a conventional method, 4-cyanostyrene was prepared from dibromobenzene in an overall yield of only 6%.<sup>14</sup> Polymeric reactions such as bromination and cyanation of polystyrene have been demonstrated to proceed almost quantitatively. In the pyrolysis method, 4-cyanostyrene was obtained in 64% yield from polystyrene (run 3). In addition, the pyrolysis method needs no workup process, as is usually required in organic synthesis. In another example, many preparative routes to 4-vinylbenzyl chloride have been reported with the overall yield only up to 22%.<sup>17</sup> These routes involve the separation of the intermediates of ortho and para isomers. A greater than 50% isolated yield of 4-vinylbenzyl chloride was attained by the pyrolysis method.

(1) Meier, H.; Schmidt, M.; Eckes, H. L. *Chem. Ber.* **1989**, *122*, 1545. Lammertsma, K.; Chand, P.; Yang, S. W.; Hung, J. T. *Organometallics* **1988**, *7*, 1875. Rosenfeld, M. J.; Shankar, B. K. R.; Shechter, H. J. *Org. Chem.* **1988**, *53*, 2699. Harnos, S.; Tivakornpannarai, S.; Waali, E. E. *Tetrahedron Lett.* **1986**, *27*, 3701. Tanaka, H.; Fujiwara, Y.; Moritani, I.; Teranishi, S. *Bull. Chem. Soc. Jpn.* **1975**, *48*, 3372. Parrinello, T.; Stille, J. K. *J. Am. Chem. Soc.* **1987**, *109*, 7122. McKillop, A.; Hunt, J. D.; Kienzle, F.; Bigham, E.; Taylor, E. C. *J. Am. Chem. Soc.* **1973**, *95*, 3635.

(2) (a) Blosssey, E. C.; Ford, W. T. *Comprehensive Polymer Science*; Allen, G., Ed. Pergamon: Oxford, 1989; Vol. 6, pp 81. (b) *Syntheses and Separations Using Functional Polymers*; Sherrington, D. C., Hodge, P., Eds. Wiley: New York, 1988.

(3) *Polymer Supported Reactions in Organic Synthesis*; Hodge, P., Sherrington, D. C., Eds.; Wiley: New York, 1980.

(4) McKean, D. R.; Parrinello, G.; Renaldo, A. F.; Stille, J. K. *J. Org. Chem.* **1987**, *52*, 422.

(5) (a) *Polymer Handbook*; Brundrup, J., Immergrut, E. H., Eds.; Wiley: New York, 1975; pp II-473. (b) McNeil, I. C. In *Comprehensive Polymer Science*; Allen, G., Ed.; Pergamon: Oxford, 1989; Vol. 6, pp 451.

(6) Mathur, N. K.; Narang, C. K.; Williams, R. E. *Polymers as Aids in Organic Chemistry*; Academic: New York, 1980.

(7) (a) Farrall, M. J.; Fréchet, J. M. J. *J. Org. Chem.* **1976**, *41*, 3877. (b) Heitz, W.; Michels, R. *Makromol. Chem.* **1971**, *148*, 9.

(8) Iwatsuki, S.; Itoh, T.; Shimizu, Y.; Enomoto, T. *Macromolecules* **1989**, *22*, 38.

(9) Fréchet, J. M. J.; Schuerch, C. *J. Am. Chem. Soc.* **1971**, *93*, 492.

(10) Kenyon, W. O.; Waugh, G. P. *J. Polym. Sci.* **1958**, *32*, 83.

(11) (a) Fréchet, J. M. J.; deSmet, M. D.; Farrall, M. J. *J. Org. Chem.* **1979**, *44*, 1774. (b) Jones, G. D. *Ind. Eng. Chem.* **1952**, *44*, 2686. (c) Pepper, K. W.; Paisley, H. M.; Young, M. A. *J. Chem. Soc.* **1953**, 4097.

(12) Broos, R.; Anteunis, M. *Synth. Commun.* **1976**, *6*, 53.

(13) (a) Halpern, M.; Zahalka, H. A.; Sasson, Y.; Rabinovitz, M. *J. Org. Chem.* **1985**, *50*, 5088. (b) Kikukawa, K.; Ikenoga, K.; Kono, K.; Toritani, K.; Wada, F.; Matsuda, T. *J. Organomet. Chem.* **1984**, *270*, 277.





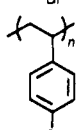
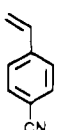
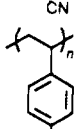
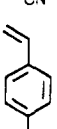
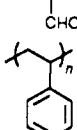
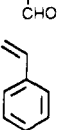
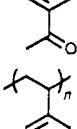
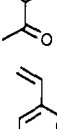
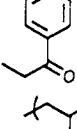
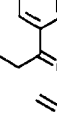
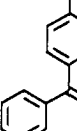
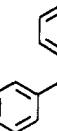
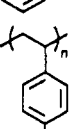
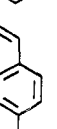
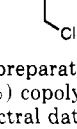
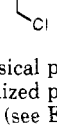
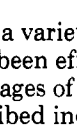
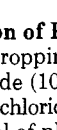
(14) Marvel, C. S.; Overberger, C. G. *J. Am. Chem. Soc.* **1945**, *67*, 2250.

(15) Dale, W. J.; Starr, L.; Strobel, C. W. *J. Org. Chem.* **1961**, *26*, 2225.

(16) Beckerbauer, R.; Baumgarten, H. E. *J. Polym. Sci., Part A* **1964**, *2*, 823.

(17) Tanimoto, S.; Miyake, T.; Okano, M. *Synth. Commun.* **1974**, *4*, 193.

Table I. Pyrolysis of Functionalized Polystyrenes

entry	functionalized polystyrene	yield from polystyrene	ref <sup>a</sup>	prod.	isol. yield	ref <sup>b</sup>
1		93	7		78	12, 13
2		99 <sup>c,d</sup>	7		48	12, 13
3		88	8		73	14
4		84	9		72	15
5		90 <sup>c</sup>	9		68	
6		95	10		80	10, 16
7		95	10		72	e
8		97	10		56	e
9		90	11		60	17
10		98 <sup>c</sup>	11		55	17
11		92 <sup>d</sup>	11		32	17

<sup>a</sup>References for preparation of the functionalized polystyrenes. <sup>b</sup>References for physical properties of the isolated products. <sup>c</sup>Styrene-divinylbenzene (2%) copolymer was used as starting resin. <sup>d</sup>Partially (50%) functionalized polystyrene was used. <sup>e</sup>Satisfactory elemental analysis, NMR spectral data, and IR spectral data were obtained for these compounds (see Experimental Section).

In conclusion, a variety of useful functionalized styrene monomers have been efficiently obtained by the pyrolysis method. Advantages of our method over other procedures previously described include higher yield, greater ease of product isolation, and minimal synthetic steps.

### Experimental Section

Melting points were obtained on a Yanagimoto micro melting point apparatus and are uncorrected. Infrared spectra were recorded on a JASCO A-3 spectrometer. NMR spectra were measured on a JEOL JNM-GX270 spectrometer in CDCl<sub>3</sub> solution with tetramethylsilane internal standard.

Polystyrene of average MW 250 000 was supplied by Mitsubishi Monsanto Chemical Co. Insoluble microporous particles of polystyrene cross-linked with 2% divinylbenzene were prepared by suspension polymerization.<sup>18</sup> Bromine, ferric chloride, copper cyanide, dimethyl sulfoxide, dimethyl sulfide, acetyl chloride, propionyl chloride, benzoyl chloride, chloromethyl methyl ether, and tin(IV) chloride were obtained from Wako Chemical Co. and used without further purification.

**Preparation of Polyvinylpropiophenone.** In a stirred flask fitted with a dropping funnel and a reflux condenser were placed carbon disulfide (100 mL), aluminum chloride (26.8 g, 0.2 mol), and propionyl chloride (13.9 g, 0.15 mol). A solution of polystyrene (10.4 g, 0.1 mol of phenyl ring) in carbon disulfide (100 mL) was then added slowly. The mixture was stirred and further refluxed gently for about 45 min, and then the mass was stirred and heated in water to remove carbon disulfide. The product was further broken up and washed in water and then dried, to yield crude product, which was dissolved in tetrahydrofuran and precipitated in methanol. After drying in vacuo, polyvinylpropiophenone (15.2 g, 95%) was obtained. Its infrared spectrum showed a large carbonyl absorption at 1685 cm<sup>-1</sup>. Anal. Calcd for C<sub>11</sub>H<sub>12</sub>O: C, 82.46; H, 7.55. Found: C, 82.55; H, 7.39.

**Pyrolysis<sup>19</sup> of Polyvinylpropiophenone.** A standard distillation apparatus was used for the pyrolysis experiments. Polyvinylpropiophenone (5 g) was pyrolyzed by heating in a distillation flask over an open flame for 20 min at 0.1 mm. The clear yellow oil obtained (4 g) was redistilled from 0.5% hydroquinone, to give 3.6 g (72%) of colorless liquid: bp 63–67 °C (0.1 mm); IR (KBr) 1685 cm<sup>-1</sup> (C=O); <sup>1</sup>H NMR (270 MHz) δ 7.89 (d, J =

(18) (a) Seidl, J.; Malinsky, J.; Dusek, K.; Mutter, M. *Adv. Polym. Sci.* **1967**, *5*, 113. (b) Guyot, A.; Bartholin, M. *Prog. Polym. Sci.* **1982**, *8*, 277. (c) Albright, R. L. *React. Polym.* **1986**, *4*, 155.

(19) **CAUTION:** Nitro derivatives of polystyrene should not be pyrolyzed. These compounds usually detonate with great violence when subjected to open flame.

8.7 Hz, 2 H), 7.43 (d,  $J = 8.7$  Hz, 2 H), 6.71 (dd,  $J = 17.5, 10.5$  Hz, 1 H), 5.83 (d,  $J = 17.5$  Hz, 1 H), 5.34 (d,  $J = 10.5$  Hz, 1 H), 2.93 (q,  $J = 7.9$  Hz, 2 H), 1.20 (t,  $J = 7.9$  Hz, 3 H). Anal. Calcd for  $C_{11}H_{12}O$ : C, 82.46; H, 7.55. Found: C, 82.49; H, 7.48.

**Pyrolysis of Polyvinylbenzophenone.** Polyvinylbenzophenone was prepared from polystyrene and benzoyl chloride by the procedure adopted for polyvinylpropiophenone: yield 97%; IR (KBr)  $1658\text{ cm}^{-1}$ . Anal. Calcd for  $C_{15}H_{12}O$ : C, 86.51; H, 5.81. Found: C, 86.42; H, 5.78.

Polyvinylbenzophenone (5 g) was pyrolyzed in a distillation flask over an open flame for 20 min at 0.1 mm. The viscous yellow liquid obtained (3.8 g) was purified by column chromatography on silica with benzene as eluent, to give a viscous colorless oil (2.8 g), which solidified on standing: mp 50–52 °C; IR (KBr)  $1655\text{ cm}^{-1}$  (C=O);  $^1\text{H NMR}$  (270 MHz)  $\delta$  7.78 (d,  $J = 8.3$  Hz, 4 H), 7.60–7.40 (m, 5 H), 6.76 (dd,  $J = 17.6, 10.5$  Hz, 1 H), 5.88 (d,  $J = 17.6$  Hz, 1 H), 5.39 (d,  $J = 10.5$  Hz, 1 H). Anal. Calcd for  $C_{15}H_{12}O$ : C, 86.51; H, 5.81. Found: C, 86.58; H, 5.73.

### A Simple and Highly Stereoselective Route to ( $\pm$ )-Podocarpic Acid

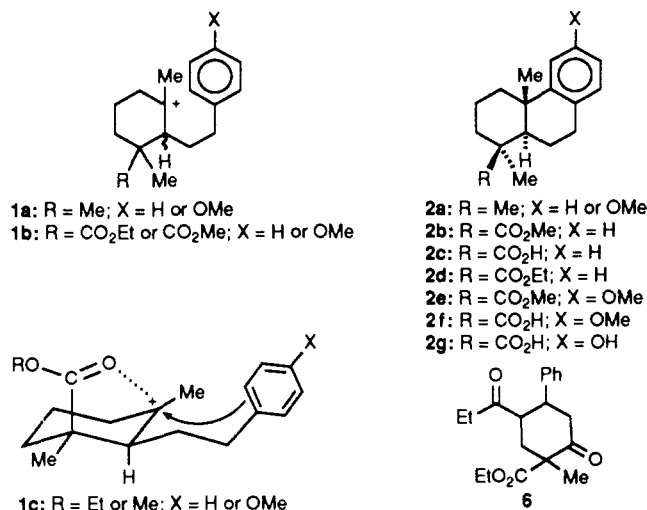
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The ring C aromatic resin acids form an important group of naturally occurring diterpenoids, which are broadly classified into two types, viz., abietane and podocarpane differing in the configuration of 4-CO<sub>2</sub>H ( $\alpha$  in the former and  $\beta$  in the latter in the natural  $5\alpha$  series). Quite a number of syntheses of both the stereoisomeric forms have been reported over the last few decades.<sup>1</sup> Of the various methods, the acid-catalyzed intramolecular cycloalkylation route presents a simple and convergent synthesis of these aromatic resin acids, particularly those related to a podocarpic acid ring system.<sup>2</sup>

Recent reports<sup>5,6</sup> have shown that by using milder conditions ( $\text{P}_2\text{O}_5\text{-MeSO}_3\text{H}$ ), the cycloalkylation reaction of 2-(2-arylethyl)-1,3,3-trimethylcyclohexyl cation **1a** (or its precursors) proceeds with high stereoselectivity, leading almost exclusively to the A/B *trans*-podocarpane derivatives **2a**. We have extended this method to the cycloalkylation of cations such as **1b**, leading to a simple and totally stereoselective synthesis of ( $\pm$ )-deoxypodocarpic acid (**2c**)<sup>7</sup> and ( $\pm$ )-*O*-methylpodocarpic acid (**2f**). It may be pointed out that these two compounds, which contain 17 of the 20 carbon atoms of the diterpenes, serve as in-



intermediates for the synthesis of a number of naturally occurring diterpenoids.

### Results and Discussion

The syntheses of both the acids **2c** and **2f** were successfully accomplished according to the sequence depicted in Scheme I. The cyclohexanonecarboxylates **7a** and **7b**, precursors of the cycloalkylation substrates **8a** and **8b**, were prepared in good yields starting with ethyl (or methyl) 2-methyl-3-oxobutylate, which was condensed with an appropriate aromatic aldehyde in pyrrolidine-acetic acid to the corresponding styryl keto ester **3a** or **3b** in addition to some high boiling products, which were not investigated further. Robinson annulation reaction of **3a** and **3b** afforded<sup>8</sup> the styrylcyclohexenone carboxylates **5a** and **5b**, which on catalytic hydrogenation yielded the cyclohexanones **7a** and **7b**, respectively, in quantitative yield. Sodium borohydride reduction of **7a** and **7b** gave a mixture of the respective cyclohexanols and  $\delta$ -lactones (**8a** and **9a** in the case of **7a**, **8b** and **9b** with **7b**). Subsequent cyclization of the individual mixture with  $\text{P}_2\text{O}_5\text{-MeSO}_3\text{H}$  (1:10) yielded ethyl ( $\pm$ )-deoxypodocarpate (**2d**) and methyl ( $\pm$ )-*O*-methylpodocarpate (**2e**), as appropriate, in 40–42% overall yield, apart from the recovered  $\delta$ -lactones **9a** and **9b** (54–55%). The esters **2d** and **2e** on alkaline hydrolysis generated the corresponding acids ( $\pm$ )-deoxypodocarpic acid (**2c**) and ( $\pm$ )-*O*-methylpodocarpic acid (**2f**). Although the  $\delta$ -lactones **9a** and **9b** were inert to  $\text{P}_2\text{O}_5\text{-MeSO}_3\text{H}$  treatment, they underwent smooth cyclization with Haworth's reagent [ $\text{H}_2\text{SO}_4/\text{AcOH}$  (1:9)] to furnish the acids **2c** and **2f** in 28% and 33% yields, respectively. The acid **2c** on treatment with ethereal diazomethane gave methyl ( $\pm$ )-deoxypodocarpate (**2b**).

The high stereoselectivity observed in the cyclization of **8a** and **8b** with  $\text{P}_2\text{O}_5\text{-MeSO}_3\text{H}$ , leading only to the respective *trans* esters **2d** and **2e** with the axial carboalkoxy function, clearly reveals that the reaction proceeds exclusively through the carbonyl-participating carbocation **1c** as suggested by Ghatak et al.<sup>4c</sup>

As the conversion of ( $\pm$ )-*O*-methylpodocarpic acid (**2f**) to ( $\pm$ )-podocarpic acid (**2g**) has already been reported,<sup>3b</sup> the present work constitutes a formal total synthesis of ( $\pm$ )-podocarpic acid (**2g**).

(8) In the case of styryl keto ester **3a** minor side product **6** was also obtained, presumably through a second intramolecular Michael reaction of the intermediate **4a**. No such product was, however, isolated in the reaction with *p*-methoxystyryl keto ester **3b**, presumably due to the relatively poor Michael acceptor character of the styryl double bond in **4b**.

(1) Ghatak, U. R. *J. Indian Chem. Soc.* **1988**, *65*, 9 and references cited therein.

(2) Acid-catalyzed cyclization using  $\text{H}_2\text{SO}_4\text{-AcOH}$  is reported<sup>3</sup> to give poor yield in this system, whereas use of polyphosphoric acid affords a stereoisomeric mixture of A/B *trans*- and A/B *cis*-podocarpic acids.<sup>4</sup>

(3) (a) Haworth, R. D.; Barker, R. L. *J. Chem. Soc.* **1939**, 1299. (b) Haworth, R. D.; Moore, B. P. *Ibid.* **1946**, 633. (c) Bhattacharyya, B. K. *J. Indian Chem. Soc.* **1945**, *22*, 165. (d) Fringuelli, F.; Manicini, V.; Taticchi, A. *Tetrahedron* **1969**, *25*, 4249.

(4) (a) King, F. E.; King, T. J.; Topliss, J. G. *Chem. Ind.* **1956**, 113. (b) Nasipuri, D.; De Dalal, I. *J. Chem. Soc., Perkin Trans. I* **1975**, 2052. (c) Ghatak, U. R.; Chatterjee, N. R.; Sanyal, B. *J. Org. Chem.* **1979**, *44*, 1992 and references cited therein.

(5) Axon, B. W.; Davis, B. R.; Woodgate, P. D. *J. Chem. Soc., Perkin Trans. I* **1981**, 2956.

(6) Banik, B. K.; Ghosh, S.; Ghatak, U. R. *Tetrahedron* **1988**, *44*, 6947.

(7) For a preliminary account see: Nasipuri, D.; Banerjee, A. K.; Pakrashi, S. C. *Indian J. Chem.* **1988**, *27B*, 875.