Polymer Bulletin 20, 427–434 (1988)

Polymer Bulletin

Novel derivatives of poly(4-hydroxystyrene) with easily removable tertiary, allylic, or benzylic ethers

Jean M. J. Fréchet*[1,2], Neil Kallman[1], Boguslav Kryczka[2], Eva Eichler[2], Francis M. Houlihan[2], and C. Grant Willson[3]

[1]Department of Chemistry, Cornell University, Ithaca, NY 14853-1301, USA
[2]Department of Chemistry, University of Ottawa, Ontario, Canada, K1N-9B4
[3]IBM Almaden Research Laboratory, San Jose, CA 95120, USA

Summary

The protection of poly(4-hydroxystyrene) and its 3,5-dimethyl analog through formation of its 2-cyclohexenyl, 1-phenyl-ethyl or t-butyl ether derivatives is easily accomplished. All of these ethers are selected as they contains structural features allowing for their facile elimination when deprotection is desired. In the case of the allylic and benzylic ethers,the monomers are easily prepared using a simple S_N2 substitution reaction on p-hydroxybenzaldehyde or its 3,5-dimethyl analog followed by a Wittig methylenation. Chemical modification of poly(4-hydroxystyrene) using etherification procedures is also done easily but usually only affords partial functionalization; the remaining hydroxyl functional groups may however be blocked in-situ by addition of a second reagent. The active ether pendant groups of the polymers can be cleaved easily and quantitatively by thermolysis, acidolysis, or acid hydrolysis suggesting that the ether protected polymers may be useful as resist materials.

Introduction

Polymers which contain reactive functionalities are finding numerous new applications in areas as varied as polymer-supported chemistry [1], chromatographic separations [2], and microlithography [3].

In recent years we have been particularly interested in polymers which can undergo facile side-chain transformations with drastic modification in their overall polarity, solubility or chemical reactivity. For example, we have used a variety of t-butyloxycarbonyl (t-BOC) protected phenolic resins in the preparation of novel separation media [4] or imaging systems [4,5] while other protected derivatives of poly(4-vinylbenzoic acid) show excellent potential as resist materials [6,7]. The success of the t-BOC group in the protection of phenolic resins [8] and our novel design [7] of easily removable ester protecting groups for polymers containing pendant carboxylic acid groups has prompted us to investigate the use of other easily removed groups for the protection of phenolic resins.

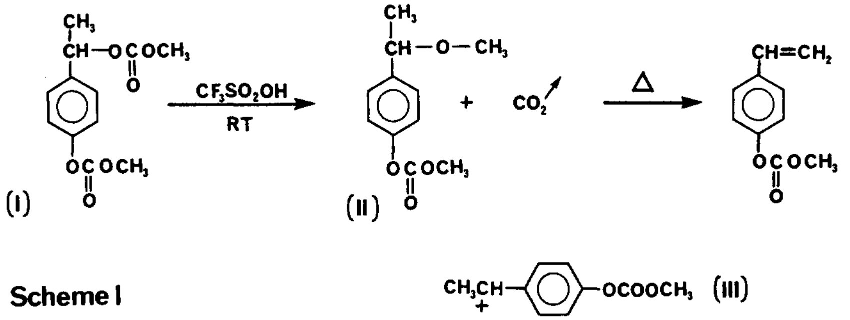
Results and Discussion

In the course of an extensive model study of the application of certain benzylic carbonates as labile protecting groups for alcohols and phenols we observed that significant yields of ethers were formed during their acid-catalyzed thermolytic cleavage. This reaction, which is outlined in Scheme I for the bis-methyl carbonate derivative of 1-(4-hydroxy-

---

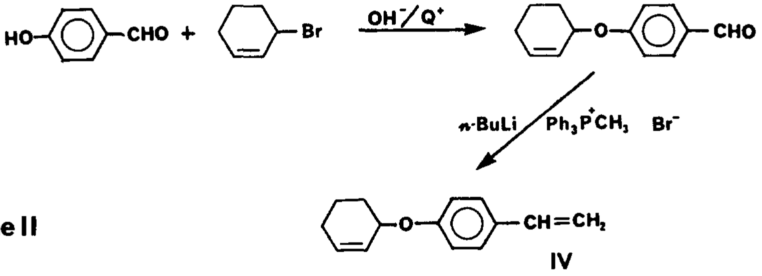
* To whom offprint requests should be sent

phenyl)-ethanol (I), proceeds at room temperature with apparent extrusion of carbon dioxide from the benzylic carbonate unit only with formation of the corresponding mono-ether mono-carbonate (II). The mechanism we propose for this cleavage reaction, which occurs at or below room temperature if a strong acid such as trifluoromethane sulfonic acid is used, involves the intermediacy of benzylic carbocation (III). Once formed, this reactive species recombines rapidly with the nucleophilic methanol, which is also produced after the initial cleavage step, to generate the benzylic ether (II). Increasing the temperature results in the cleavage of the benzylic ether (II) with formation of the substituted styrene which may then oligomerize. These findings suggest that the mechanism which prevails is an *acid-catalyzed thermolysis* of the reactive ether II. In view of this proposed mechanism it was possible to predict that other appropriately chosen ethers could undergo cleavage under thermolytic or acid-catalyzed conditions. Indeed, it is already known that t-butyl ethers are easily cleaved under acid catalysis [9,10], and it is expected that, when heated, they should also undergo thermolysis cleanly to afford alcohol or phenol and 2-methylpropene.



Scheme I

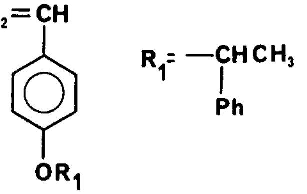
Therefore, ether protecting groups having tertiary, benzylic, or allylic structures with at least one x-hydrogen available for elimination should all prove useful and operate analogously to the t-BOC and similar carbonate-based alcohol and phenol protecting groups [8]. While t-butyl ethers are known, their difficult preparation restricts their use [9-14]; in contrast, the 2-cyclohexenyloxy group which we have developed is easily introduced on both alcohols and phenols via a simple nucleophilic displacement on 3-bromocyclohexene, a reaction which may be done either under classical homogeneous conditions or through phase-transfer catalysis. For example the synthesis of 4-(2-cyclohexenyloxy)-styrene (IV) from p-hydroxybenzaldehyde is easily performed as shown in Scheme II. Typical yields for etherification reactions involving 3-bromocyclohexene exceed 80% [15].



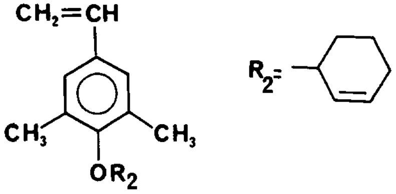
Scheme II

The same preparative route is applicable for the synthesis of secondary benzylic ethers such as 4-(1-phenylethyloxy)-styrene (V), or for more hindered ether protected vinylphenols such as 4-(2-cyclohexenyloxy)-3,5-dimethylstyrene (VI). In contrast, more complex synthetic approaches are required for the preparation of 4-t-butyloxy-substituted styrenes. The reaction of 3,5-dimethyl-4-hydroxy benzaldehyde with t-butyl bromide in pyridine [12] is extremely sluggish and only proceeds in low yield even in the presence of a large excess of the phenolic component. The reaction is only marginally better with the less hindered 4-hydroxybenzaldehyde. An interesting alternate procedure developed by Crivello et al. [14] involves the reaction of a Grignard reagent with t-butylperoxybenzoate [13]. In the case of 4-t-butoxystyrene this procedure is reported to afford the desired product in 20% yield [14]. However, a major drawback of this approach is the required use of costly 4-bromostyrene as the starting material.

V



VI

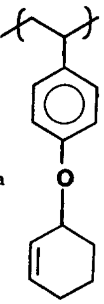


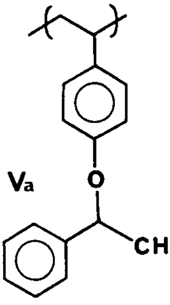
Polymerization of monomers IV-VI is easily carried out under free radical conditions. The presence of a second double bond in monomers IV and VI does not interfere with the free radical propagation. The polymers (IVa-VIa) which are obtained have a normal molecular weight distribution (1.7 to 1.9) and have Tg values which are significantly lower than that of poly(p-hydroxystyrene) [Tg=174°C] of comparable molecular weight as shown in Table 1.

Table 1: Radical Polymerization of Monomers IV-VI

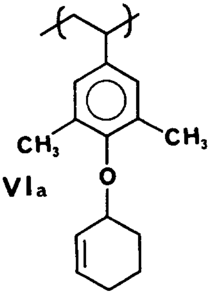
Monomer	Solvent	Conc. (wt. %)	% AIBN (wt. %)	yield	Mn[a]	Mw[a]	Tg(°C)
IV	toluene	33%	1%	76%	15,400	27,400	101
V	toluene	33%	1%	88%	17,000	31,400	74
VI	toluene	15%	1%	79%	17,600	33,500	-
VI	benzene	9%	0.6%	81%	54,200	97,500	91

[a] GPC with polystyrene calibration.

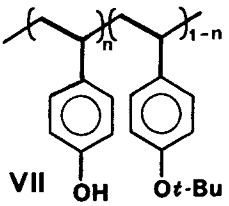

IVa



Va

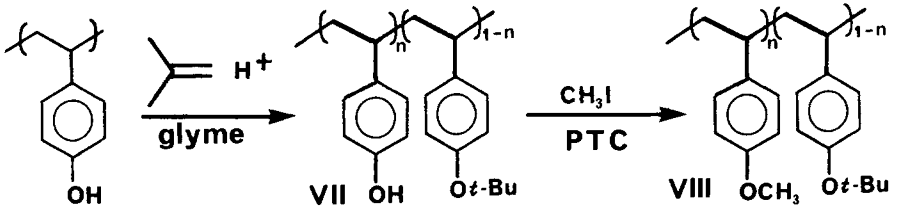


VIa



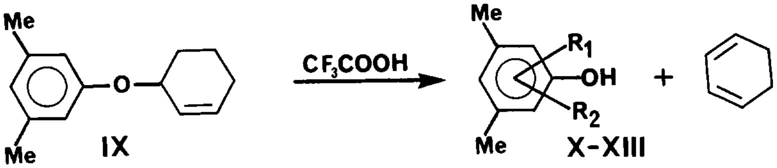
VII

The direct formation of ether protected poly(p-hydroxystyrene) by polymer modification is also successful due to the high reactivity of 3-bromocyclohexene with the phenolate derivative of poly(4-hydroxystyrene). This reaction is difficult to push to completion and the polymer which is obtained (IVa) generally contains some free hydroxyls. In contrast, the same modification using 2-bromo-2-methyl propane is unsuccessful as elimination prevails over nucleophilic substitution. It is nevertheless possible to functionalize a significant percentage of the phenolic groups of poly(p-hydroxystyrene) by treatment of the polymer with 2-methylpropene in an appropriate solvent and under acid catalysis. Thus, in 1,2-dimethoxyethane 50% of the phenolic group are etherified to afford a polymer having structure VII ($n = 0.5$); the unreacted hydroxyls of VII can then be fully protected by further reaction with reagents such as acetic anhydride, dimethyl sulfate, or di-t-butyl dicarbonate. In dichloromethane the etherification reaction does not proceed to any significant extent, as the system is heterogeneous due to the lack of solubility of the poly(p-hydroxystyrene). However, if the polymer is finely dispersed in dichloromethane and the reaction mixture is subjected to low power sonication, the polymer dissolves slowly as the t-butylation proceeds. The final product analyzed by ^{1}H NMR shows 80-85% t-butylation, but a more careful analysis by ^{13}C-NMR shows two distinct sets of peaks which can be attributed to the t-butyl groups. The major product has its quaternary t-butyl carbon at 34.5ppm and its methyl carbons at 30.7ppm. In contrast, the minor product (25% of the total t-butylation) shows its quaternary t-butyl carbon at 77.5ppm and methyl carbons at 29.0ppm. Therefore the reaction in dichloromethane results mainly in ring alkylation while etherification of only 20-25% of the starting hydroxyls is observed. Changes in reaction conditions involving shorter reaction times indicate that in dichloromethane and under sonication, the alkylation reaction is much preferred over the etherification. This is in contrast to the reaction in glyme for which little or no alkylation product is obtained. Though incomplete, this etherification procedure may nevertheless prove to be useful as it is possible to protect the unreacted hydroxyls, for example by reaction with dimethylsulfate, acetic anhydride, or di-t-butyldicarbonate. Thus, we have effected the facile one-pot synthesis of polymer VIII containing 50% of t-butyl and 50% of methyl ether groups by a simple sequential addition of reagents. In addition, the partly etherified polymer (VII) itself may prove useful as an imaging material.

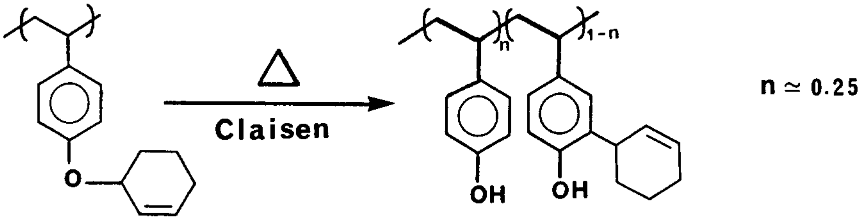


Removal of the active ether protecting groups is easily done by acidolysis, thermolysis, or acid hydrolysis. The process is facilitated by the relative stability of the carbocationic intermediates (allylic, benzylic or tertiary) which are formed. As could be anticipated from the results of our study of the acidolysis of our benzylic carbonate model (I) and of the corresponding ether II reported above, the acidolysis reaction may be slow at room temperature depending on the nature of the acid used and the structure of the ether. In general the tertiary and allylic ethers are found to be significantly more reactive in solution than their benzylic counterpart which does not cleave at any appreciable rate at 20°C. As expected the use of a strong acid such as trifluoromethane sulfonic acid results in faster deprotection than is the case with weaker trifluoroacetic acid.

Detailed model studies with 1-(2-cyclohexenyloxy)-3,5-dimethylbenzene IX and trifluoroacetic acid in dichloromethane solution show that essentially quantitative liberation of the phenolic group is achieved but that the reaction is also accompanied by significant ring-alkylation of the liberated phenol. Chromatographic monitoring of the reaction indicated up to 40% monoalkylation (Scheme II, R_1 = H and R_2 = 2-cyclohexenyl, X) and 25% dialkylation (R_1 = R_2 = 2-cyclohexenyl, ortho-ortho: XI, and ortho-para: XII) in addition to the free 3,5-dimethylphenol XIII (R_1 = R_2 = H) and some 1,3-cyclohexadiene.



With the corresponding cyclohexenyloxy-protected polymer IVa, the extent of alkylation during acidolysis with trifluoromethane sulfonic acid or trifluoroacetic acid is reduced considerably. Yet, if a purely *thermal* deprotection is attempted on polymer IVa a very significant amount of alkylated units are formed as a result of the Claisen rearrangement of the allylic ether. The resulting polymer has structure XIV in which all hydroxyls are free. In contrast, no alkylation is observed during ether removal (thermal or acid-catalyzed) for poly[4-(2-cyclohexenyloxy)-3,5-dimethylstyrene] as all reactive positions ortho and para to the phenolic group are occupied. In the case of polymer VII, quantitative removal of the t-butyloxy groups is achieved by acidolysis, thermolysis, or acid hydrolysis without any apparent alkylation side-reaction. In all cases quantitative deprotection of the phenolic groups of polymers IVa, Va, VIa, and VII is observed. With polymer VIII acidolytic or thermolytic deprotection afford a product which still contains methoxy groups.



Deprotection of the polymers in the solid state was also studied using polymer films containing a few percent of a triarylsulfonium-hexafluoroantimonate and UV-irradiation. The role of the triarylsulfonium salt in this system in the photogeneration of strong acid (H^+) *in situ* [4, 14-16]. In this case, the deprotection reaction does not occur at 20°C but is only observed upon heating near 100°C. Both the 2-cyclohexenyloxy and the t-butyloxy substituent are removed rapidly at 105°C while a longer heating period or a higher thermolysis temperature is required to remove the 1-phenyl-ethyloxy groups.

Experimental:

Preparation of 4-(methyloxycarbonyloxy)-x-(methyloxycarbonyloxy)ethylbenzene. (I).

A solution of 4.50g 1-(4-hydroxyphenyl)ethanol in 50mL dichloromethane containing 6.32g pyridine was treated dropwise at room temperature with 7.56g methyl chloroformate. After 4h stirring the reaction mixture was extracted 3 times with water, dried over magnesium sulfate and concentrated to an oil which is purified by distillation under reduced pressure to afford 7.56g (90%) of I as a colorless liquid with b.p. 153-154°C (2mm Hg).
Analysis; calculated: C, 56.69; H, 5.55. Found: C, 56.80; H, 5.46.
^{1}H-NMR ($CDCl_3$, in ppm from TMS internal standard): 1.55 (d, 3H); 3.65 (s, 3H); 3.77 (s, 3H); 5.57 (q, 1H); 7.15 (m, 4H).
Mass Spectrum: 254, 134.
IR (cm^{-1}): 2959, 1765, 1746, 1260, 1220.

Preparation of 4-(methyloxycarbonyloxy)-x-(methoxy)-ethylbenzene II by acidolysis of I at room temperature.

A mixture of 0.60g I and 1 microliter of trifluoromethanesulfonic acid is stirred for 2h at room temperature. Evolution of CO_2 is observed immediately upon addition of the triflic acid. The product is purified by preparative thin-layer chromatography (silica gel, ethyl acetate-hexane 3:7) to afford 0.37g (75% yield) of compound II.
Analysis; calculated: C, 62.85; H, 6.71. Found: C, 62.66, H,6.97.
IR (cm^{-1}): 2977, 2932, 2822, 1763, 1259, 1218.
^{1}H-NMR ($CDCl_3$, in ppm from TMS internal standard): 1.39 (d, 3H); 3.14 (s, 3H); 3.82 (s, 3H); 4.04 (q, 1H); 7.12 (m, 4H).
Mass spectrum: 210, 195.

Preparation of 4-(methyloxycarbonyloxy)-styrene and its polymer by acid-catalyzed thermolysis of I

The reaction of I (1.50g) with 2 microliters of triflic acid proceeded at room temperature (1.5h) to afford II as above. The reaction mixture was then heated to 120°C for 2h then for a few minutes under reduced pressure to remove any volatiles. The thick viscous product which was isolated (1.09g) consisted of a dimer 1,3-di-[(p-methyloxycarbonyloxy)phenyl]-1-butene obtained in 54% yield as well as a polymer containing 4-methyloxycarbonyloxystyrene units obtained in 32% yield.
Similar small-scale experiments performed with monitoring of the reaction products by GC-MS or liquid chromatography (with calibration using an authentic sample) showed the intermediacy of the 4-(methyloxycarbonyloxy)-styrene monomer.

Preparation of 3,5-dimethyl-4-(2-cyclohexenyloxy)-styrene [VI]

A solution of 36.52g of methyltriphenylphosphonium bromide in 200mL dry THF is treated with 11.42g potassium t-butoxide. To the stirred mixture is then added dropwise a solution of 19.55g 3,5-dimethyl-4-(2-cyclohexenyloxy)benzaldehyde [15] in 50mL dry THF under N_2 atmosphere. Once the addition was complete, stirring was continued for 2 hours, then enough water and ether were added to obtain a biphasic solution. After separation of phases, the water solution was extracted 3 times with ether and the combined ether phases washed 3 times with water. The washed ether solution was then dried over magnesium sulfate, filtered and evaporated to a semi-

solid from which triphenylphosphine oxide was extracted by trituration with hexane. Preparative HPLC purification on silica using 20% ethyl acetate-80% hexane afforded 18.6g (96%) of the pure monomer. The spectral analysis of the monomer (^{1}H and ^{13}C-NMR, MS) confirmed its identity.
Elemental analysis: found C, 84.58; H, 8.68; calculated: C, 84.16; H, 8.83

A similar procedure was used to prepare monomers IV and V [15].

Preparation of poly[3,5-dimethyl-4-(2-cyclohexenyloxy)styrene] (VIa)

A solution of 4.5g of the monomer prepared above in 25g toluene containing 0.045g AIBN was degassed with nitrogen then heated in an oil bath at 75°C for 24h. The polymer was precipitated twice in methanol to afford 3.55g of the desired product (70% yield) with MN 17,600 and Mw 33,500 (GPC with polystyrene calibration). Analysis: found C, 84.16; H, 8.72. The ^{1}H- and ^{13}C NMR spectra are in agreement with the proposed structure. A similar procedure was used to prepare polymers IVa and Va [14].

Reaction of poly(p-hydroxystyrene) with 2-methylpropene in the presence of acid

(a) In 1,2-dimethyoxyethane.

A solution of 6.00g poly(p-hydroxystyrene) in 100mL 1,2-dimethoxyethane in a pressure vessel was cooled to -78°C and 150mL 2-methyl-propene was condensed in. After addition of 0.5mL concentrated sulfuric acid, the reaction mixture was brought to 45°C for 1 hour while stirring. After 22h of further stirring at room temperature, the excess 2-methylpropene was removed by evaporation and the remaining solution neutralized by addition of potassium carbonate. After precipitation in water, the polymer which was obtained still contained approximately 45% free phenolic groups (55% formation of t-butyl ether groups).

(b) In 1,2-dimethoxyethane followed by acetylation of unreacted hydroxyls.

The reaction was carried out as above with 1.21g poly(p-hydroxystyrene), 20mL 1,2-dimethoxyethane, 50mL 2-methylpropene and 0.1mL sulfuric acid in a pressure vessel. After 1h stirring at 45°C and 22h at room temperature and evaporation of excess 2-methylpropene, potassium carbonate was added to neutralize the acid then 3.26mL pyridine and 5.8mL acetic anhydride were added. The light orange solution was then heated to 60°C overnight, concentrated, then precipitated into 600mL water to afford 1.60g of a light cream colored powder. NMR analyses (^{1}H and ^{13}C) indicated that the polymer contained approximately 50% of t-butyl ether and 50% of acetate groups.

(c) In dichloromethane with sonication.

The reaction was carried out as above using 1.20g of poly(p-hydroxystyrene) as a fine powder dispersed into 25mL dichloromethane, and 50mL 2-methyl propene, with 0.08mL concentrated sulfuric acid catalyst at room temperature for 23h under sonication. As the reaction proceeded, dissolution of the polymer was observed and an homogeneous solution was obtained. After evaporation of the solvent, the polymer was re-dissolved in tetrahydrofuran and precipitated in water to afford a fine, slightly colored, powder (1.4g) for which ^{1}H-NMR analysis showed that 83% of the hydroxystyrene residues had been t-butylated. Careful analysis of this and other samples (post-treated by acetylation with acetic anhydride and pyridine) by ^{13}C-NMR showed that 75% of the t-butyl groups resulted from ring alkylation, while only 25% were due to the formation of t-butyl ether functionalities. Thus, the reaction only lead to t-butyl ether formation on 21% of the polymer's phenolic residues. In the absence of sonication, less than 10% t-butylation was obtained, while a shorter reaction time (4h) under similar conditions (with sonication) lead to 56% t-butylation of which over 90% was due to ring alkylation.

Acknowledgements

Financial support of this research by IBM Corporation and the Natural Science and Engineering Research Council of Canada is gratefully acknowledged.

References:

1. J.M.J. Fréchet, D.G. Darling, S. Itsuno, P.-Z. Lu, M. Vivas de Meftahi, W.A. Rolls Jr.; Pure and Applied Chemistry, 60, 353-364 (1988).
2. W.A. Rolls Jr., J.M.J. Fréchet; Polym. Mat. Sci. Eng., 56, 745-748 (1987).
3. C.G. Willson, H. Ito, J.M.J. Fréchet, T.G. Tessier, F.M. Houlihan; J. Electrochem. Soc. 133, 181-187 (1986).
4. J.M.J. Fréchet, H. Ito, C.G. Willson; Proceedings Microcircuit Engineering, 260 (1982). C.G. Willson, H. Ito, J.M.J. Fréchet, F. Houlihan; Proceedings of IUPAC 28th Macromolecular Symposium, Amherst, Mass., 443 (1982). H. Ito, C.G. Willson, J.M.J. Fréchet; Proceedings Tokyo Conference on VLSI, Tokyo, Japan (1982); and U.S. Patent 4,491,628 (1985).
5. J.M.J. Fréchet, F. Bouchard, E. Eichler, F.M. Houlihan, T. Iizawa, B. Kryczka, C.G. Willson; Polymer Journal, 19, 31-49 (1987).
6. M. Stanciulescu; Ph.D. Thesis, University of Ottawa (1988).
7. H. Ito, C.G. Willson, J.M.J. Fréchet, Proc. SPIE, 771, 24 (1987).
8. J.M.J. Fréchet, E. Eichler, C.G. Willson, H. Ito, Polymer, 24, 995 (1983). F. Houlihan, F. Bouchard, J.M.J. Fréchet, C.G. Willson; Can. J. Chem., 63, 153-162 (1985).
9. H.C. Beyerman, J.S. Bontekoe; Recl. Trav. Chim. Pays-Bas, 81, 691 (1962).
10. J.L. Holcombe, T. Livinghouse; J. Org. Chem. 51, 111 (1986).
11. H.C. Beyerman, G.J. Heiszwolf; J. Chem. Soc., 755 (1963) and Recl.Trav. Chim. Pays-Bas, 84, 203 (1965).
12. H. Masada, Y. Oishi; Chem. Lett., 57 (1978).
13. S.O. Lawesson, N.C. Yang; J. Am. Chem. Soc., 81, 4230 (1959).
14. J. Crivello; U.S. Patent 4,603,101 (1986).
15. J.M.J. Fréchet, E. Eichler, S. Gauthier, B. Kryczka, C.G. Willson; ACS Symposium Series, "Radiation Effects on Polymeric Materials," E. Reichmanis and J. O'Donnell, Editors, (in press).
16. J.V. Crivello, Polym. Eng. and Sci., 23 (17), 953 (1983). Adv. Polym. Sci., 62, 1 (1984). J.V. Crivello, J.H.W. Lam, Macromolecules, 10, 1307 (1977).

Accepted September 1, 1988 K