

# Bifunctionalized resins. Applications to the synthesis of insect sex attractants<sup>1,2</sup>

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A 2% crosslinked divinylbenzene-styrene copolymer, incorporating benzoyl chloride groups, was used to monoprotect the symmetrical diol 1,10-decanediol. The corresponding monotrityl ether and *cis*-10-tetradecen-1-ol were prepared by this system, the latter by a Wittig reaction of a polymer-bound ylide with an aldehyde in the solution phase. A series of bifunctionalized resins containing proximally located trityl alcohol and benzoic acid groups was prepared in an attempt to prepare diol linked to the polymer via both a trityl ether and a benzoate linkage. It was established that these polymers bound 1,10-decanediol exclusively at one end only. Polymers, containing both trityl alcohol and benzoic acid groups in a random array or polymers containing proximally located trityl alcohol groups, gave mixtures of both monoprotected and doubly protected diol.

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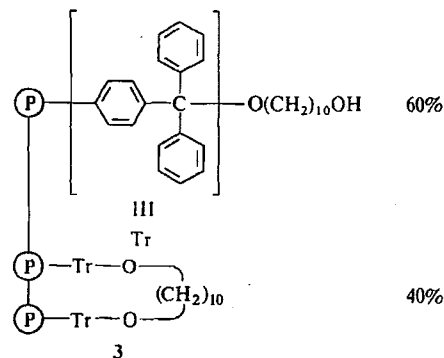
On a utilisé un copolymère divinylbenzène-styrène réticulé à 2% et incorporant des groupes chlorure de benzoyle pour protéger un seul des hydroxyles du diol symétrique décanediol-1,10. On a préparé l'éther monotritylé correspondant et le tétradécène-10 ol-1 *cis* grâce à ce système; ce dernier composé résulte d'une réaction de Wittig entre un ylure lié au polymère et un aldéhyde en solution. On a préparé une série de résines bifonctionnalisées contenant des alcools trityliques situés à proximité de groupes acides benzoïques, ces résines spéciales ont été préparées en vue de synthétiser des diols liés au polymère à la fois par un lien éther tritylique ainsi qu'à un lien benzoate. On a établi que ces polymères lient exclusivement qu'une extrémité du décanediol-1,10. Les polymères, contenant à la fois des groupes alcool tritylique et acide benzoïque au hasard et les polymères contenant des groupes alcool tritylique situé, à proximité, conduisent à des mélanges de diols mono et doublement protégés.

[Traduit par le journal]

## Introduction

Soluble bifunctional polymers have been shown to be capable of mimicking enzymatic reactions (2) by intramolecular cooperation of the two different functional groups. Insoluble bifunctional resins may even more closely approximate enzymatic systems and the studies reported herein may spur development in this area of research. Our own interest in preparing insoluble bifunctional resins lies in another sphere, namely organic synthesis on insoluble polymer supports. Our recently described syntheses of insect sex attractants on solid phases (3-5) still suffer from one minor but persistent problem. In the first step of the synthesis a 2% divinylbenzene (DVB)-styrene copolymer, incorporating trityl chloride groups (1) reacts with symmetrical diols, such as 1,10-decanediol (2) to give a monoprotected

symmetrical diol (3), the free end of which can be elaborated to insect sex attractants (3-5). Unfortunately, about 40% of the diol is actually bound to the polymer at both ends (double bound) and although this doubly-bound material does not interfere in the chemical synthesis, its presence means that it is liberated in the final cleavage step from the polymer and must be separated from the desired product.



<sup>1</sup>The use of polymer supports in organic synthesis. Part XV. For part XIV see ref. 1.

<sup>2</sup>Taken in part from the Ph.D. Thesis of T.M. Fyles.

<sup>3</sup>Holder of NRCC fellowships, 1974-1977.

Elimination of this problem would give a clean product without purification and would be more efficient in starting diol. If it were possible to actually *promote* double binding in such a way that the doubly-bound diol is bound to the polymer by two different functional groups, then the diol could be selectively cleaved from one of the functional groups liberating diol solely monoprotected by the insoluble resin. We envisioned that a polymer containing both trityl chloride and benzoyl chloride functional groups in close proximity could serve such a function. Before attempting to synthesize such a bifunctional polymer, we wished to see if it were possible to synthesize an insect sex attractant on a polymer-bound benzoyl chloride so that an attractant could be synthesized simultaneously from both functional groups of the bifunctional resin.

Leznoff and Wong (6) have described the preparation of monoethers of symmetrical diols using a polymer-bound phenylacetyl chloride as a blocking group. This polymer was not suitable for the synthesis of insect sex attractants because of the low loadings of diol previously obtained, the presence of acidic protons  $\alpha$  to the carbonyl and the inability of the polymer to be recycled. Hence a polymer-bound benzoyl chloride was sought.

### Results and Discussion

#### *Polymer-bound Benzoyl Chloride as a Blocking Group in Synthesis*

Polymer-bound phenyllithium (4) (7) was quenched with  $\text{CO}_2$  and protonated (7,8) or treated with diethyl carbonate, followed by treatment with base and protonation to give the desired polymer-bound benzoic acid (5) (7,8).

Treatment of 5 (1.0–1.5 mmol acid/g of 5) with thionyl chloride in benzene (6) gave the polymer-bound benzoyl chloride (6). The infrared (ir) spectrum of this polymer showed strong absorptions at 1810 and 1780  $\text{cm}^{-1}$  due to the acid chloride group. Polymer 6 reacted with 1,10-decanediol (2) in pyridine to give the monoprotected diol polymer 7.

The ester linkage of 7 proved to be considerably more inert to base-catalysed hydrolysis than diols bound to the previously described polymer-bound phenylacetyl chloride (6, 9).

Treatment of polymer 7, however, with 0.2 M (*n*Bu)<sub>4</sub>NOH (10) in THF for 48 h at room temperature resulted in a polymer whose ir spectrum showed no trace of residual ester absorptions. The solution phase contained 0.8–1.0 mmol of diol 2/g of polymer 7. The recovered diol was easily separated from impurities introduced by the cleavage reagent by preparative thin-layer chromatography (tlc). Although not as clean as the HCl in dioxane mixture

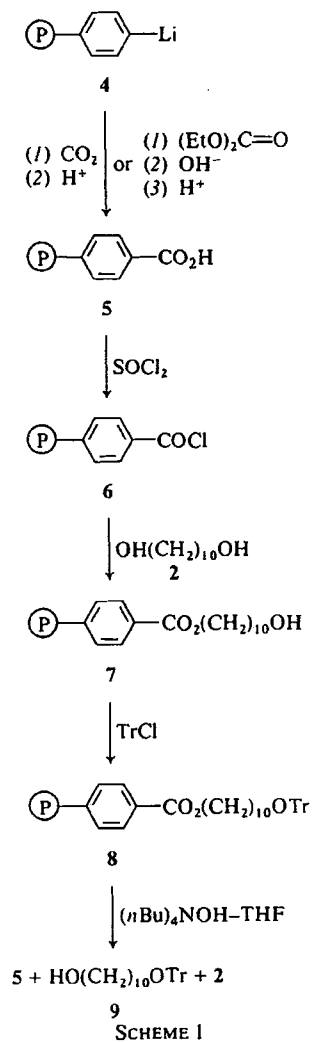
used to cleave trityl resins, (*n*Bu)<sub>4</sub>NOH is more suitable for the cleavage of benzoate resins than other bases investigated.

Attempts to oxidize polymer-bound diol 7 to a polymer-bound aldehyde using di-*tert*-butyl chromate (4,11) resulted in no observable additional bands in the ir spectrum of the product. Furthermore, attempts to elaborate this polymer-bound aldehyde to insect sex attractants by a previously described Wittig route (4) failed and yielded only starting diol 2, indicating that the initial oxidation failed.

Because of our experience with trityl resins, we initially suspected that the diol bound to 7 was bound entirely as the diester, i.e. entirely 'doubly-bound.' Conversion of 7 to the polymer-bound monotrityl ether 8 as described by Wong and Leznoff (6) followed by base cleavage gave a mixture of unreacted diol 2 and the expected monotrityl ether of 1,10-decanediol (9) as shown in Scheme 1. The yield of 9 might in fact reflect the total amount of monoprotected diol bound to 7. However, subsequent investigation (see below) showed that this was not the case. Thus this experiment showed only that 7 contained *not less than* 0.24 mmol/g of free alcohol groups of 7.

Numerous examples of a Wittig reaction in the presence of an ester have been reported (12). This, together with the complete absence of products from base catalysed decomposition of aldehydes suggested that the oxidation of 7 to a polymer-bound aldehyde had not occurred. The benzoate linkage of 7 is relatively acid insensitive and hence a large number of other (acidic) methods were tested for the oxidation of 7 to a polymer-bound aldehyde. Some reagents tested were chromium trioxide in HMPT (13), dimethylsulfoxide and dicyclohexylcarbodiimide (14), dimethylsulfoxide and trifluoroacetic anhydride (15), and even sodium dichromate in acidic HMPT (16). In no case were any products other than unreacted diol recovered upon cleavage of the polymers.

On the basis of observations made of polymers containing both trityl alcohol and benzoate groups (see below), it is likely that the failure of the oxidation of 7 to polymer-bound aldehyde is due to a combination of two factors, namely, the poor swelling properties of polymer-bound diol 7, especially in some of the solvents used for the oxidations tested, and the presence of by-products from the thionyl chloride reaction which inhibit oxidation by di-*tert*-butyl chromate (11). Indeed, a polymer-bound trityl alcohol, converted to a polymer-bound trityl chloride 1 using *thionyl chloride*, instead of *acetyl chloride*, when loaded with diol to give a



polymer-bound diol is sufficiently contaminated with this by-product to completely prevent the oxidation and subsequent 'normal' Wittig reaction. The deleterious effects of thionyl chloride on functionalized resins has been previously noted (17).

Since lithio alkynes are incompatible with the ester blocking group, the remaining 'reverse' Wittig route (4) was investigated with this system as shown in Scheme 2. Polymer-bound diol **7** was converted to the mesylate **10** in the same manner as was used with trityl resins (4). The ir spectrum of **10** showed strong absorptions at 1180 and 1360 cm<sup>-1</sup> due to the presence of mesylate groups. The free diol monomesylate could not be isolated by base cleavage due to its base lability. Conversion of **10** to the phosphonium salt **11** by treatment of **10** with molten triphenylphosphine for 48 h at 140°C succeeded as shown by the absence of the 1360 cm<sup>-1</sup>

band (unreacted mesylate groups) and the presence of the 1210 cm<sup>-1</sup> band (phosphonium salt formation) in the ir spectrum of the product polymer.

Treatment of the benzoate-bound phosphonium salt **11** with trityllithium or *tert*-butyllithium followed by treatment for 4 h with butyraldehyde gave polymer-bound alken-1-ol **12**. Base cleavage of **12** as described above produced the expected 10-tetradecen-1-ol (**13**) together with unreacted diol (Table 1). Acetylation of **13** gave **14**, the sex attractant for the oak leaf roller, *Archips semifera* Walker (18). The overall yield of attractant was comparable to previously obtained results with trityl resins (4) (Table 1). The stereoselectivity of the process was also quite high as in the previous trityl case (4), providing 85% of the *cis* isomer.

We were hoping that polymer-bound benzoic acid (**5**) prepared via diethyl carbonate would have less functional groups at adjacent sites due to quenching of adjacent phenyllithium sites with diethyl carbonate to give polymer-bound benzophenone. Although the ir spectrum of **5** indeed

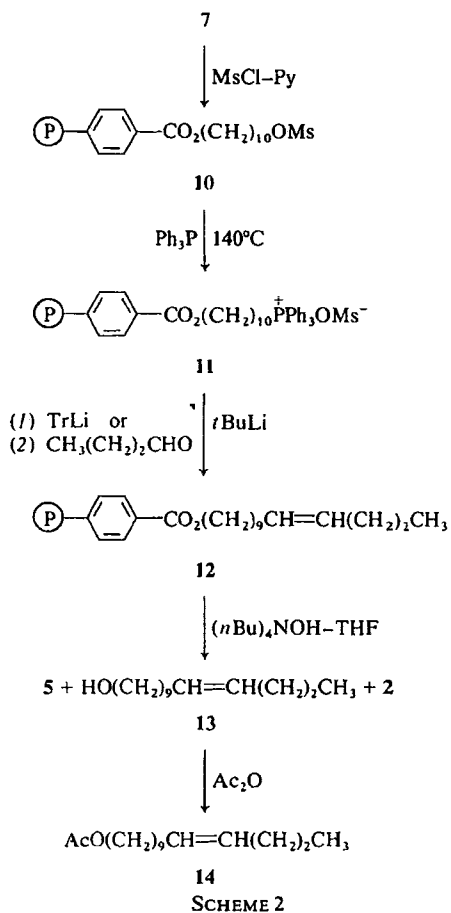


TABLE 1. Yields of monotrityl ethers (Scheme 1) and insect sex attractants (Scheme 2) prepared on benzoate polymers

Polymer	Initial quantity of diol <sup>a</sup> (mmol/g)	Quantity of monotrityl ether 9 <sup>b</sup> (recovered diol) <sup>b</sup> (mmol/g)	Overall yield <sup>c</sup> (conversion) <sup>d</sup> (%)	Quantity of alken-1-ol 13 <sup>e</sup> (recovered diol) <sup>e</sup> (mmol/g)	Cis isomer <sup>f</sup> (%)	Overall yield <sup>c</sup> (conversion) <sup>d</sup> (%)
5 <sup>g</sup>	0.60	0.24(0.36)	40(100)	0.24(0.27)	85	40(70)
5 <sup>h,i</sup>	0.41	—	—	0.15(0.19)	91	37(68)
5 <sup>i,j</sup>	0.46	0.13(0.31)	27(87)	0.17(0.24)	90	41(70)

<sup>a</sup>Recovered from cleavage of 7.

<sup>b</sup>Recovered from cleavage of 8.

<sup>c</sup>Based on quantity of diol initially bound to polymer.

<sup>d</sup>Yield if recovered diol is recycled.

<sup>e</sup>Recovered from cleavage of 12.

<sup>f</sup>As a percentage of total alken-1-ol.

<sup>g</sup>Third time used 5, ylide produced using TrLi. Freshly prepared 5 loaded 0.80 mmol of 2/g.

<sup>h</sup>Fifth time used 5.

<sup>i</sup>Ylide produced using *tert*-butyllithium.

<sup>j</sup>This entry 5 was prepared via diethyl carbonate, while the previous entries were made from CO<sub>2</sub>.

showed an additional absorption band at 1680 cm<sup>-1</sup>, the additional crosslinking of 5 and quenching of adjacent sites did not decrease the eventual amount of double-binding. Syntheses on 5 prepared via diethyl carbonate, were similar to syntheses on 5, prepared via carbon dioxide (Tables 1 and 2).

In general, benzoate polymers are not as suitable for the monoprotection of symmetrical diols as the corresponding trityl polymers for a variety of reasons. (a) Benzoate polymers swell less readily than trityl polymers and hence more forcing conditions are required to drive the desired reaction. (b) Benzoate polymers contain by-products resulting from treatment with thionyl chloride. These by-products interfere with the oxidation of alcohols to aldehydes (and possibly other reactions). (c) Benzoate polymers cannot be as efficiently recycled as trityl resins. While trityl alcohol polymers remain very little degraded after more than 20 times of reuse, the capacities of used benzoate polymers are much diminished from the initial capacities (Table 1). This problem may be related to the by-products mentioned in point b.

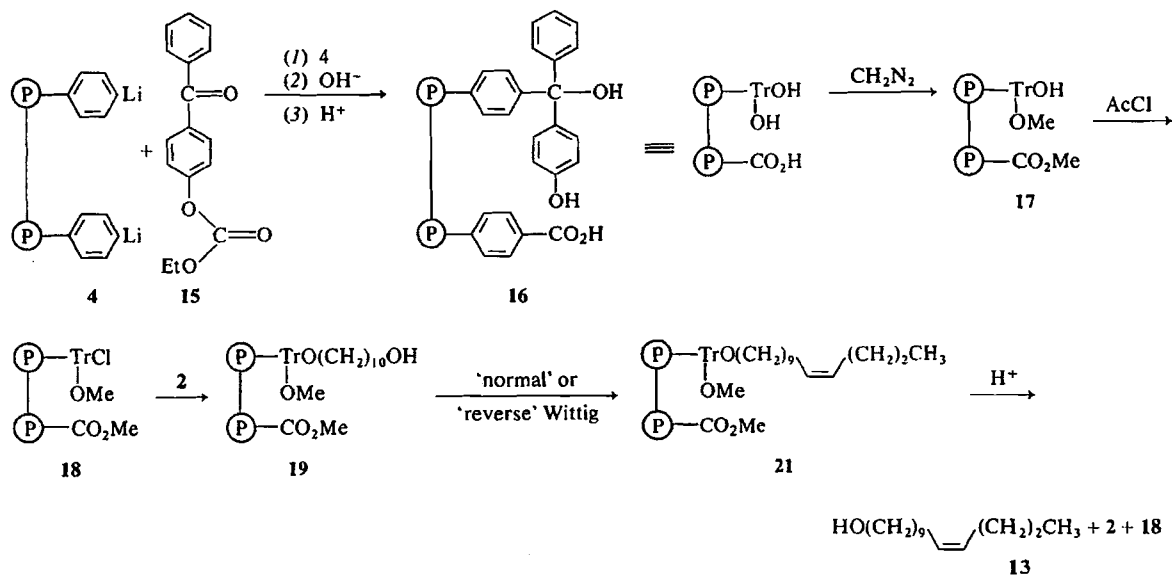
#### Bifunctional Polymers

Addition of a saturated solution of *p*-benzoylphenyl ethyl carbonate (15), prepared from 4-hydroxybenzophenone and ethyl chloroformate, in tetrahydrofuran (THF) to polymer-bound phenyllithium (4), prepared from a *sec*-butyllithium-TMEDA complex to provide a large proportion of proximally lithiated sites (19), gave a dark green mixture which was decolorized on the addition of water. The ir spectrum of this polymer showed absorptions at 1770 cm<sup>-1</sup> (carbonate, due to 15 reacted only at the benzophenone), 1740 cm<sup>-1</sup> (ester, due to mono-reaction at the carbonate of 15 with either ethoxy or phenoxy as leaving group), and 1680 cm<sup>-1</sup> (benzophenone, due to double reaction at the carbonate of 15 plus reaction at the carbonate of 15

only). Base cleavage of this polymer produced a second product whose ir spectrum contained no residual bands at 1770 and 1740 cm<sup>-1</sup> but did show a band at 1680 cm<sup>-1</sup> apparently unaltered by base treatment. Only trace quantities of 4-hydroxybenzophenone could be recovered from the base cleavage mixture and thus the amount of reaction at the carbonate functional group only is minimal. Protonation of the second polymer resulted in production of 16 whose ir spectrum showed an absorption at 1725 cm<sup>-1</sup> (free carboxylic acid) and again a band at 1680 cm<sup>-1</sup> (benzophenone). From the above sequence of changes in the ir spectra on reaction with base and acid it was likely that both trityl and benzoate groups had been produced and that the number of trityl groups probably exceeded the number of benzoate groups. This is the expected result since nucleophilic attack on benzophenone would be faster than on carbonate and some of the first formed esters would further react with adjacent lithiated sites.

Treatment of polymer 16 with diazomethane in methylene chloride at low temperature for 16 h, gave polymer 17. The phenol of 16 had been protected as the methyl ether with concomitant protection of benzoate as the methyl ester. Before proceeding with the synthesis of attractant 14 via bifunctional polymer 17, as outlined in Scheme 3, the nature of diol bound only to the trityl group of 17 was determined.

Conversion of 17 to the trityl chloride 18 using acetyl chloride in benzene as previously described (7) gave a polymer containing 0.45 mequiv. of chloride/g of resin. Treatment of 18 with 1,10-decanediol (2) gave the polymer-bound diol 19. A polymer-bound diol monoacetate was prepared in the manner previously described (7) which upon cleavage in dilute acid (7) liberated 0.27 mmol of 1,10-decanediol monoacetate (20) and no recovered



diol showing that **2** had been bound to **19** exclusively as the monoprotected trityl ether (Table 2).

Polymer-bound diol **19** could be elaborated by either the 'normal' or 'reverse' Wittig routes to give polymer-bound alken-1-ol **21**. Standard dilute acid cleavage of **21** gave 10-tetradecen-1-ol (**13**) which on acetylation gave **14** the attractant for the oak leaf roller moth (**18**). The overall yields of attractant **14** by both routes are given in Table 3. It is interesting

to note that although **19** led to complete conversion to **20**, showing that acetylation of **19** is complete, **19** leads only to partial conversion to **13** by both the 'normal' and 'reverse' Wittig routes. Diol **2** is recovered in both sequences showing that both oxidation and mesylation of **19** is incomplete. These reactions were also probably incomplete on the simple monofunctionalized resins (**4**). We then attempted to attach **2** *simultaneously* to both the

TABLE 2. Modes of binding of 1,10-decanediol and yields of monoderivatives of diol bound to bifunctionalized polymers in Schemes 3-6

Polymer	$z^a$ (mmol/g)	$x^b$ (mmol/g)	$y^c$ (mmol/g)	$q^d$ (mmol/g)	Quantity of diol monoacetate ( <b>20</b> ) (recovered diol) <sup>e</sup> (mmol/g)	Overall yield <sup>f</sup> (conversion) <sup>g</sup> (%)
<b>19</b>	0.30	0.30	—	—	0.27(0)	90(90)
<b>24</b>	0.23	0.16	0.07 <sup>h</sup>	0	0.16(0)	100
<b>19</b> <sup>i</sup>	0.17	0.17	—	—	0.15(0)	89(89)
<b>24</b> <sup>i</sup>	0.22	0.15	0.05 <sup>j</sup>	0.02	0.15(0)	100
<b>29</b>	0.20	0.20	—	—	0.20(0)	100
<b>30</b>	0.24	0.24	—	—	0.15(0.09)	63(100)
<b>32</b>	0.26	0.26	—	—	0.17(0.08)	65(100)
<b>34</b>	0.31	0.27	0.04 <sup>k</sup>	0	0.19(0.07)	68(95)
<b>32</b> <sup>l</sup>	0.10	0.10	—	—	0.06(0.04)	60(100)
<b>34</b> <sup>l</sup>	0.19	0.11	0.08 <sup>m</sup>	0	0.07(0.04)	64(100)

<sup>a</sup>Total quantity of diol bound to polymer, recovered by acid cleavage and where required by subsequent base cleavage.

<sup>b</sup>2 recovered by acid cleavage only.

<sup>c</sup>2 recovered by base cleavage only.

<sup>d</sup> $q = z - x - y$ , quantity of diol bound to polymer through both ester and ether linkages.

<sup>e</sup>Recovered by cleavage of polymer-bound diol monoacetate.

<sup>f</sup>Yield based on diol initially bound to polymer.

<sup>g</sup>Yield if recovered diol is recycled.

<sup>h</sup>0.05 mmol/g of **9** + 0.01 mmol/g of **2** prepared on this polymer via Scheme 1.

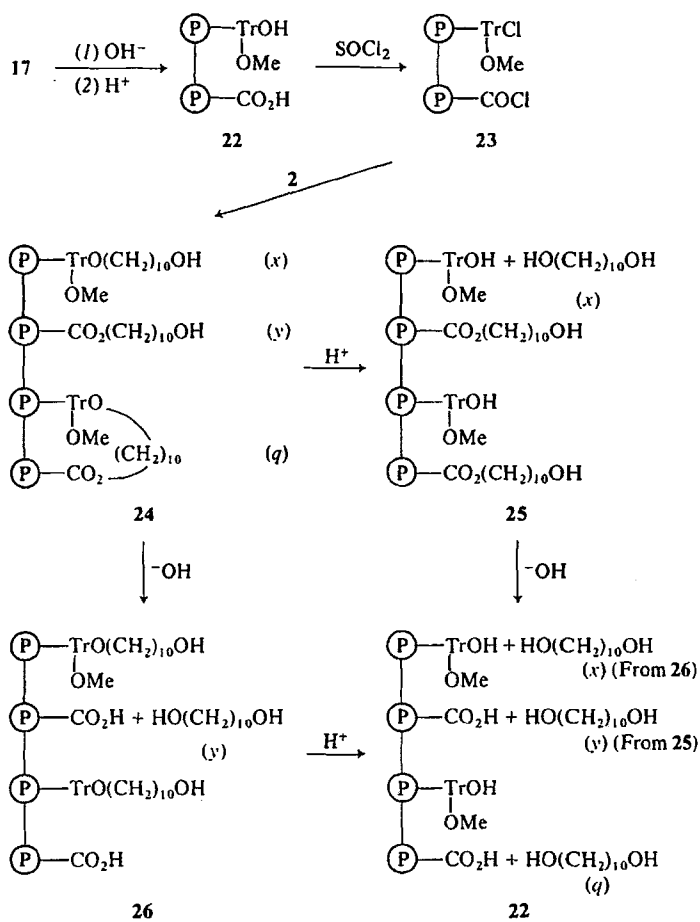
<sup>i</sup>Prepared from an 0.5 M solution of **15** in THF.

<sup>j</sup>0.04 mmol/g of **9** + 0.01 mmol/g of **2** prepared on this polymer via Scheme 1.

<sup>k</sup>0.03 mmol/g of **9** + trace of **2** prepared on this polymer.

<sup>l</sup>Prepared via a 1:10 mixture of benzophenone and diethyl carbonate.

<sup>m</sup>0.06 mmol/g of **9** + 0.02 mmol/g of **2** prepared on this polymer via Scheme 1.



SCHEME 4

trityl and carboxy groups. Base cleavage of **17** as described above followed by protonation gave polymer **22**. Thionyl chloride treatment of **22** gave the mixed trityl - acid chloride polymer **23** containing 0.55 mmol of chloride/g of **23**. Treatment of **23** with 1,10-decanediol (**2**) in pyridine gave polymer **24** containing diol bound in at least three fashions: (a) as the monotrityl ether (*x*), (b) as the monobenzoate (*y*), and (c) as the trityl ether - benzoate intraserial crosslinkage shown (*q*). The proportions of these three modes of diol binding were assessed as outlined in Scheme 4.

Successive treatment of **24** with acid (to give **25**) followed by base cleavage liberates the total quantity of diol bound to polymer **24** (*z*). The amount of diol liberated in the first acid cleavage step must be bound to **24** only via trityl groups (*x*). The amount of diol liberated in the second base cleavage step is then the sum of the amount bound only as benzoates (*y*) plus any doubly-bound diol held as the mixed trityl ether - benzoate (*q*). Alternatively, base cleav-

age of **24** gives polymer **26** and liberates only diol bound as the benzoate (*y*). Subsequent acid cleavage of **26** gives the sum of doubly-bound (as the trityl ether - benzoate) and trityl only bound diols (*q* + *x*). The maximum amount of diol bound as the mixed trityl ether - benzoate (*q*) is thus given by  $q = z - x - y$ . A check is provided by the two values of the total amount of diol bound to **24** (*z* and *z'*) obtained from the two independent cleavage sequences.

In any event, *x* was found to be 0.16 mmol/g of **24**, *y* to be 0.07 mmol/g of **24** and  $z = z' = 0.23$  mmol/g of **24**. Thus the maximum amount of diol bound by the mixed trityl ether - benzoate was found to be  $q = 0.0$  mmol/g of **24** (Table 2). Conversion of **24** to the acetate and acid cleavage as previously described (**7**) showed complete mono-protection of diol bound to the trityl groups of **24** (Table 2). Similarly conversion of **24** to the monotrityl ether (**6**) and base cleavage as described above showed at least 83% of the diol bound to the benzoate of **24** was monoprotected (Table 2). These results

TABLE 3. Yields of insect attractant **14** prepared by the "normal" and "reverse" Wittig routes on bifunctionalized polymers

Polymer	$z^a$ (mmol/g)	Quantity of <b>13</b> <sup>b</sup> (mmol/g)	Quantity of recovered diol <sup>b</sup> (mmol/g)	Overall yield of <b>13</b> <sup>c</sup> (conversion) <sup>d</sup> (%)	<i>Cis</i> isomer <sup>e</sup> (%)
<b>21</b> <sup>f</sup>	0.30	0.16	0.09	53(73)	72
<b>21</b> <sup>g</sup>	0.30	0.19	0.07	63(83)	88
<b>24</b> <sup>f,h</sup>	0.22	0	0.21	0	—
<b>24</b> <sup>g,h</sup>	0.22	0.11	0.10	50(92)	88
<b>29</b> <sup>f</sup>	0.20	0.10	0.10	50(100)	68
<b>30</b> <sup>g</sup>	0.24	0.12	0.12	50(100)	85

<sup>a</sup>Total quantity of **2** bound to polymer, recovered from acid cleavage and where required subsequent base cleavage.

<sup>b</sup>Total quantity recovered from acid cleavage and where required subsequent base cleavage.

<sup>c</sup>Based on initial quantity of diol bound to polymer.

<sup>d</sup>Yield if recovered diol is recycled.

<sup>e</sup>As a per cent of total alken-1-ol.

<sup>f</sup>'Normal' Wittig.

<sup>g</sup>'Reverse' Wittig.

<sup>h</sup>Polymer prepared from 0.5 M **15** in THF.

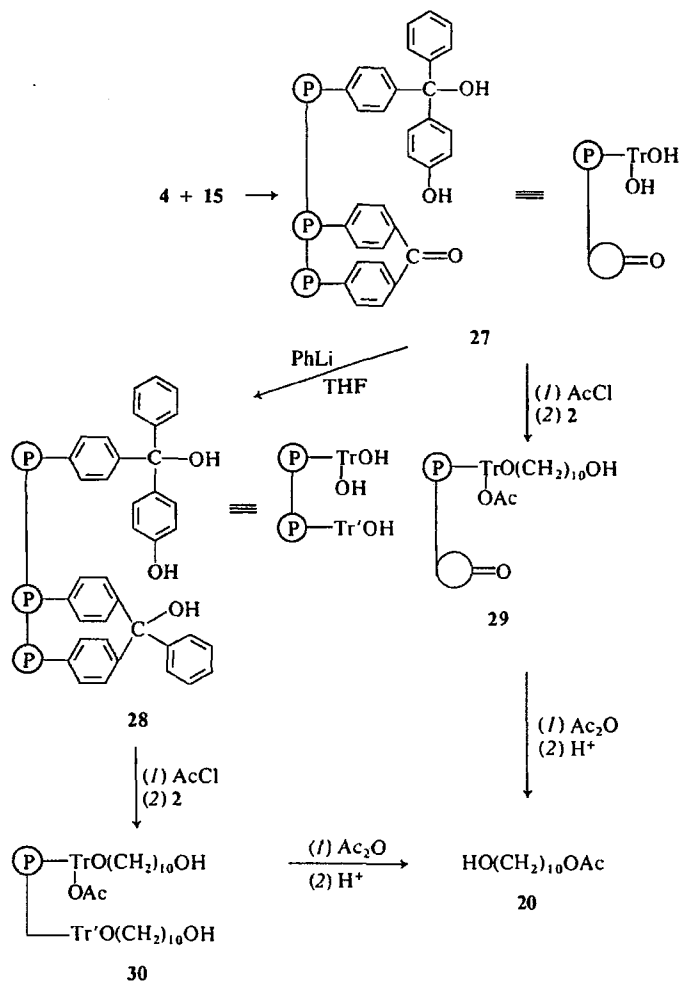
indicated that polymer **24** behaved as if it were a mixture of two separate and independently functionalized polymers. Thus the goal of obtaining a polymer-bound diol doubly-bound through a trityl group at one end and a benzoate group at the other was not achieved. However, exclusive monoprotection of diol bound to trityl groups was obtained although the loading (Table 2) was not sufficiently high nor better than a previously described trityl polymer from the controlled addition of methyl benzoate (**7**). Since **23** was prepared using  $\text{SOCl}_2$ , attempts to oxidize **24** to an aldehyde failed and the elaboration of **24** to **14** simultaneously on two functional groups by the 'normal' Wittig route failed. Polymer **24** could be elaborated to attractant **14** by the 'reverse' Wittig route (**7**), however, in modest yield (Table 3).

Attempts to produce higher levels of functionalization by varying the conditions of the quenching reaction of **4** with **15** did give us a polymer capable of double-binding diol through two different functional groups. Thus quenching **4** with a 0.5 M solution of **15** in THF did yield a sample (Scheme 4) of **24** which was found by the double cleavage sequence described above to contain 0.02 mmol of **2**/g of **24** doubly-bound as the mixed trityl ether-benzoate (Table 2) but the level of this loading was too low to be useful.

Treatment of **4** with a dilute solution of carbonate **15** resulted in complete reaction of the carbonate group to give polymer **27** as shown in Scheme 5. The ir spectrum of **27** exhibited only one carbonyl absorption at  $1680\text{ cm}^{-1}$  due to the newly-formed benzophenone group. Polymer **27** was treated with excess phenyllithium to give a new polymer **28**, containing two types of trityl alcohol groups. The two different kinds of trityl alcohol groups are

likely constrained to be near each other as they are both derived from **15**. This constraint is borne out by the following reactions. Treatment of **27** with acetyl chloride to form a polymer-bound trityl chloride, followed by the addition of excess 1,10-decanediol (**2**) gave the polymer diol **29**. Acetylation of **29** and acid cleavage yielded exclusively 1,10-decanediol monoacetate (**20**) and no unreacted **2**. Polymer **28**, however, in the same sequence, yielded a polymer diol **30**, which on acetylation and cleavage from **30**, gave **20** and unreacted **2** (Table 2). Although the quantity of diol bound to **30** is only 0.04 mmol/g of polymer more than the amount bound to **29** (Table 2), greater than half of the trityl groups of **30** are involved in double binding of diol! Diol bound to polymer **29**, however, is bound entirely as the monotrityl ether. Clearly the proximity of functional groups is an important factor in the selective monoprotection of symmetrical diols. We believe that the recovered **2** was obtained because **2** was doubly bound to **28** likely through the two different types of trityl groups. *These key experiments outlined in Scheme 5 strongly support our original hypothesis that polymer-bound phenyllithium **4** can be quenched with carbonate **15** at adjacent or conformationally proximal sites.*

For the purposes of comparison with polymer **22**, **4** was quenched with a 1:1 mixture of benzophenone and diethylcarbonate to produce a bifunctionalized polymer **31** in which the trityl groups are not constrained to be in the vicinity of the benzoate groups. Treatment of **31** with acetyl chloride and reaction with **2** gave polymer-bound diol **32**. Base cleavage of **31** and protonation yielded **33**, which reacted with  $\text{SOCl}_2$  and then **2** to give the polymer-bound diol **34** as outlined in Scheme 6. The amounts of monoprotection of diol were assessed by the methods



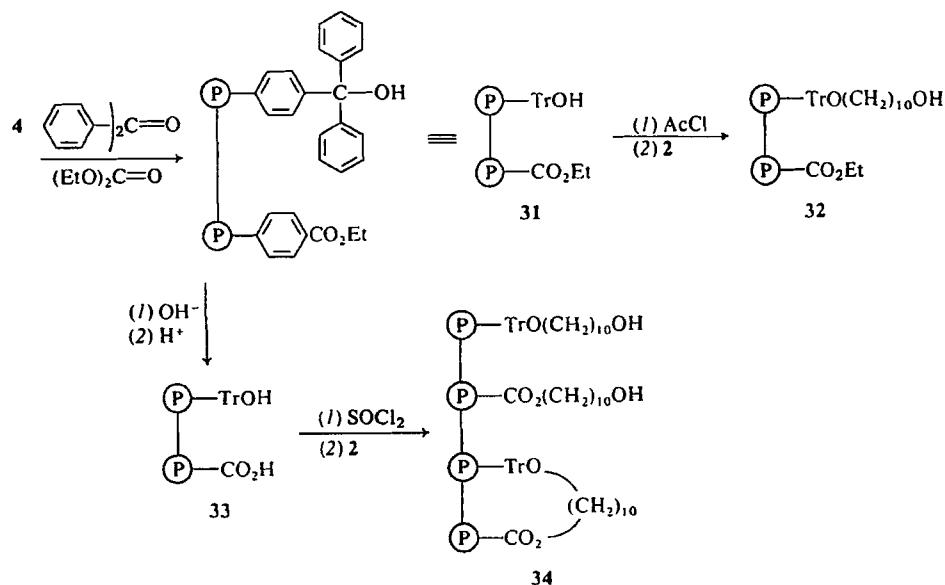
SCHEME 5

described above and gave the data in Table 2. As anticipated, trityl groups were produced in a large excess over benzoate groups due to the differences in the rates of nucleophilic attack (20) on benzophenone versus carbonate. Thus in a subsequent experiment, 4 was quenched with a 1:10 mixture of benzophenone and diethyl carbonate to give a new polymer 31 which contained relatively more carboxy groups. Identical types of experiments carried out on this 'new' 31 are recorded in Table 2. The values of  $x$ ,  $y$ ,  $z$ , and  $q$  for both 31 and 'new' 31 were determined (Table 2) by the methods described above and illustrated in Scheme 4. As a consequence the amount of diol doubly-bound to 34 (or 'new' 34) as the mixed trityl ether - benzoate was zero. What was not anticipated was the relatively high amounts of double binding of diols bound only to trityl groups even at the low level of loading observed. The possibility that double binding of diol is in part

a 'concentration' effect; the higher the degree of functionalization, the higher the double binding of diol is not necessarily the case. The total loading of diol to 32 and 34 was roughly one half the amounts obtained early in experiments on normal polymer-bound trityl chloride (7) but the proportions of double-bound diol was roughly the same.

This result is consistent with those reported previously (7) for the preparation of the monoacetates of 1,4-butanediol and 1,10-decanediol (2) and with studies done by Crowley *et al.* (21). Despite the fact that the carbon chain length of 1,4-butanediol is less than half the chain length of 2, the extent of double binding of these diols is roughly the same (7). The observation that the amount of doubly-bound diol is insensitive to both the degree of functionalization of the polymer backbone and the carbon chain length suggests that the first formed monoblocked diol is not held in an isolated site but





SCHEME 6

is relatively free to move within the polymer matrix. The unreacted end of the monoprotected diol must be sufficiently mobile to allow it to compete effectively with solution phase diol for unreacted functional groups on the polymer.

In summary, bifunctionalized resins, having spatially defined geometries, have been prepared and are expected to find wide applications in (a) studies directed towards the elucidation of intras resin interactions, (b) organic synthesis on polymer supports,<sup>4</sup> and (c) the construction of model systems capable of mimicking enzymatic systems. This study has shown how bifunctional resins can be used to restrict intras resin reactions and examined the scope of synthesizing an insect sex attractant bound to two different functional groups of a single resin.

### Experimental

Infrared spectra were recorded on a Unicam SP1000 ir spectrophotometer as neat films between NaCl discs unless otherwise specified. Nuclear magnetic resonance spectra were recorded on a Varian EM360 spectrometer using deuteriochloroform as solvent and tetramethylsilane as internal standard. Mass spectra were recorded on a Perkin-Elmer-Hitachi RMU6E mass spectrometer. Silica gel was used for all thin- and preparative-layer chromatography. Fractions were extracted with ether in a Soxhlet extractor. Filtration was done under vacuum through sintered glass Buchner funnels. Filtration under an inert atmosphere was done as previously described (7). Microanalyses were performed by G. Gygli of Toronto.

<sup>4</sup>A bifunctional resin, containing both nickel and rhodium in a *random* array has been synthesized and used as a catalyst in sequential reactions of oligomerization and hydrogenation (22).

#### Preparation of Polymer-bound 'Benzoic Acid' 5 via Diethyl Carbonate

To a suspension of 5 g of polymer-bound phenyllithium (4) in 100 ml of dry THF under an argon atmosphere was added 10 g of diethyl carbonate in 100 ml of dry THF dropwise over 0.5 h. The mixture was stirred a further 2 h, filtered, washed twice with ethanol (50 ml), and twice with water (50 ml). The polymer was suspended with 50 ml of THF and treated with 25 ml of a 0.5 M tetra-*n*-butylammonium hydroxide solution in THF. The mixture was stirred at reflux overnight, filtered, and washed twice with ethanol (50 ml). The polymer was then protonated, filtered, washed, and dried as previously described (7) in the preparation of 5 via CO<sub>2</sub>; ir: 1725 (C=O, acid), 1680 cm<sup>-1</sup> (C=O, benzophenone).

#### Preparation of Polymer-bound Acid Chloride 6

In a manner similar to that previously described (6-8), 5 g of 'benzoic acid' polymer 5 (1.0-1.5 mmol of acid/g), 10 ml of freshly distilled thionyl chloride, and 80 ml of dry benzene were stirred at reflux under argon overnight. The mixture was filtered, washed with dry benzene (50 ml), twice with dry ether (50 ml), and immediately pumped dry at high vacuum. Treatment of a standard sample of 6 with dioxane-water (1:1) liberated 0.6-1.5 mmol of chloride/g of resin.

#### Preparation of Polymer-bound Diol 7

By the method of Wong and Leznoff (6), 5 g of 6 and 5 g of 1,10-decanediol (2) gave 7; ir: 1740 cm<sup>-1</sup> (C=O).

#### Preparation of Tetra-*n*-butylammonium Hydroxide in THF Solution (23)

To a suspension of tetra-*n*-butylammonium iodide (18.5 g, 50 mmol) in 100 ml of distilled water at 90°C was added freshly prepared 'silver hydroxide' (60 mmol, from 10 g of silver nitrate and 2.4 g of sodium hydroxide). The resultant slurry was vigorously stirred at reflux for 0.5 h, cooled in ice, and filtered while cold. The filtrate was evaporated to an oil under reduced pressure, traces of water were removed as the benzene azeotrope and the oil was made to 100 ml in dry THF. Acid-base titration showed the solution to be 0.45-0.48 M in hydroxide (90-96% yield).

#### General Base Cleavage of Polymer-bound Benzoate Diols and Derivatives

In a typical procedure to liberate diol and derivatives from benzoate polymers, 1.0 g of polymer was suspended in 20 ml of THF and treated with 10 ml of a 0.5 M solution of tetra-*n*-butylammonium hydroxide. The mixture was stirred at room temperature for 48 h, filtered, and the polymer was washed twice with ethanol (10 ml), four times with water (20 ml), twice with ethanol (10 ml), twice with ether (15 ml), and air dried. The ir showed no bands above 1650  $\text{cm}^{-1}$  (C=O).

The filtrate was extracted with ether, washed with water, dilute acid, dried ( $\text{MgSO}_4$ ), and evaporated to yield the crude product.

#### Preparation of Polymer-bound Benzoate Diol Monotriptyl Ether 8

Polymer 8 was prepared from 7 and triphenylmethyl chloride as described by Wong and Leznoff (6). The ir was uninformative.

#### Isolation of 1-O-Triptyl-1,10-decanediol (9)

Standard base cleavage of 1 g of 8 and purification of the crude product by preparative tlc (eluant, ether-benzene, 2:3) gave only 1,10-decanediol 2 ( $R_f$  0.2), 63 mg, 0.36 mmol/g of 8; and 1-O-triptyl-1,10-decanediol (9) ( $R_f$  0.55), 101 mg, 0.24 mmol/g of 8; ir (neat): 3400 (OH), 2950 ( $\text{CH}_2$ ), 1604 (aromatic C-H), 1050  $\text{cm}^{-1}$  (C-O); nmr: 7.4-7.3 (br s, 15H, OTr), 3.6 (t, 8, 2H,  $\text{CH}_2\text{OH}$ ), 3.2 (t, 8, 2H,  $\text{CH}_2\text{OTr}$ ), 3 var (s, 1H, OH), 1.6-1.2 (m, 16H,  $-\text{CH}_2-$ ). The yield data for the preparation of 9 are given in Table 1.

#### Preparation of Polymer-bound Diol Monomesylate 10

Polymer-bound mesylate 10 was prepared from 7 and methanesulfonyl chloride exactly as previously described (7); ir: 1360 ( $\text{CH}_3\text{SO}_2$ ), 1180  $\text{cm}^{-1}$  ( $\text{CH}_3\text{SO}_2$ ).

#### Preparation of Polymer-bound Phosphonium Salt 11

In a manner similar to, but not identical to a previously described procedure (4), 2 g of 10 were added to 25 ml of molten triphenylphosphine and the mixture was heated to 140°C under an argon atmosphere for 48 h. The product polymer 11 was recovered as previously described; ir: 1210 (salt?), 1180  $\text{cm}^{-1}$  ( $\text{CH}_3\text{SO}_2$ ).

#### Preparation of Polymer-bound Alken-1-ol 12 ('Reverse' Wittig)

##### (a) Using Triptyllithium

To a solution of 1 g of triphenylmethane (ca. 5 mmol) in 30 ml of THF at  $-10^\circ\text{C}$  under an argon atmosphere was added 2.2 ml of methylithium (1.36 M, 3.9 mequiv.). The solution was stirred at  $0^\circ\text{C}$  overnight and 1.5 g of 11 was added. The slurry was stirred at  $0^\circ\text{C}$  for 3 h, quenched with 5 ml of butyraldehyde, and stirred a further 4 h. The polymer was filtered, washed and air dried as previously described (4).

##### (b) Using tert-Butyllithium

Polymer 11 (1.5 g) in 30 ml of dry THF was cooled to  $0^\circ\text{C}$  under an argon atmosphere and treated with 2 ml of *tert*-butyllithium (2 M, 4 mequiv.). The mixture was allowed to warm to room temperature over 1 h, quenched with 5 ml of butyraldehyde, and stirred a further 4 h. The polymer was filtered, washed and air dried as previously described (4). The ir (either method) was uninformative.

#### Isolation of 10-Tetradecen-1-ol (13)

Standard base cleavage of 12 and purification of the crude product by preparative tlc (eluant, ether-benzene, 2:3) gave 1,10-decanediol (2) ( $R_f$  0.2), 47 mg, 0.27 mmol/g of 12; and 10-tetradecen-1-ol (13) ( $R_f$  0.6), 51 mg, 0.24 mmol/g of 2. Acetylation of 13 gave 10-tetradecen-1-ol acetate (14). Compounds 13 and 14 were identical to previously prepared samples (4) and the overall yields and isomeric composition,

determined by vapour phase chromatography (vpc) and high pressure liquid chromatography (hplc) as previously described (4), of the products are given in Table 1.

#### Preparation of *p*-Benzoylphenyl Ethyl Carbonate 15

To a solution of 4-hydroxybenzophenone (25 g, 0.12 mol) and triethylamine (30 ml, ca. 0.25 mol) in 150 ml of THF was added dropwise 12 ml of ethyl chloroformate (0.15 mol) over 0.5 h. The mixture was heated to reflux for 1 h, cooled, poured into ice, and extracted with methylene chloride. The extract was washed with dilute base and water, dried ( $\text{MgSO}_4$ ) and evaporated. The crystalline mass was recrystallized from methanol (mp 118-121°C) and the recrystallized material was further purified by sublimation (115°C/0.05 Torr) to give 20.6 g of *p*-benzoylethyl ethyl carbonate (15) as white needles, mp 123-123.5°C, in 61% yield; ir (KBr): 3020 (CH), 2950 ( $\text{CH}_2$ ), 1770 ( $\text{OCO}_2$ ), 1660 (C=O), 1600 (aromatic C-H), 1470  $\text{cm}^{-1}$  ( $\text{CH}_2$ ); nmr: 8.1-7.3 (m, 9H, Ph-H), 4.5 (q, 8, 2H, O- $\text{CH}_2-$ ), 1.4 (t, 8, 3H,  $\text{CH}_3$ ); ms (70 eV *m/e* (relative intensity): C=O 270 (25) (M<sup>+</sup>), 225 (31), 197 (72), 149 (70), 121 (100), 105 (80). Anal. calcd. for  $\text{C}_{16}\text{H}_{14}\text{O}_4$ : C 71.10, H 5.22; found: C 70.93, H 5.02.

#### Preparation of Bifunctionalized Polymer 16

To a suspension of 10 g of polymer-bound phenyllithium 4 in 100 ml of dry THF under an argon atmosphere was added 5 g of 15 in approximately 100 ml of THF (saturated solution) dropwise over 15 min. The resultant mixture was stirred a further 2 h at room temperature, filtered and the polymer washed and air dried; ir: 1760 ( $\text{OCO}_2$ ), 1735 ( $\text{CO}_2\text{R}$ ), 1680  $\text{cm}^{-1}$  (C=O). Base cleavage of this product as described in the preparation of 5 followed by protonation, washing, and drying gave 16; ir: 1725 ( $\text{CO}_2\text{H}$ ), 1680  $\text{cm}^{-1}$  (C=O, benzophenone).

#### Preparation of Methylated Bifunctionalized Polymer 17

To a solution of diazomethane (7.0 mmol) in 75 ml of methylene chloride was added 10 g of polymer 17 in portions. The mixture was stirred at  $-10^\circ\text{C}$  overnight, filtered, and the polymer washed twice with methylene chloride (50 ml) and three times with ether (25 ml); ir: 1730 ( $\text{CO}_2\text{R}$ ), 1680  $\text{cm}^{-1}$  (C=O, benzophenone).

#### Preparation of Polymers 18, 19, and 21

These polymers were prepared by methods previously described (4, 7).

#### Preparation of Bifunctional Polymers 22, 23 and Polymer-bound Diol 24

Polymer 22 was prepared by the method outlined for the base cleavage/protonation sequence leading to 16; ir: 1725 ( $\text{CO}_2\text{H}$ ), 1680  $\text{cm}^{-1}$  (C=O). Polymer 23 was prepared as described for the preparation of 6; ir: 1810 and 1760 ( $\text{COCl}$ ), 1680  $\text{cm}^{-1}$  (C=O). Halide analysis (22) showed 0.55 mmol of chloride/g of 23. Treatment of 23 with 1,10-decanediol (2) in pyridine as previously described (7) gave 24; ir: 1740 (CO), 1680  $\text{cm}^{-1}$  (C=O).

#### Liberation of 1,10-Decanediol (2) from 24: Determination of *x*, *y*, *z*, and *q*

Standard acid cleavage of 1.0 g of 24 and purification of the crude product by preparative tlc (eluant, ether-benzene, 1:1) gave 1,10-decanediol (2) ( $R_f$  0.3), 28 mg, 0.16 mmol/g of 24 (*x*). The resultant polymer 25 was treated with base under the standard cleavage conditions to yield on work-up and purification on preparative tlc 1,10-decanediol (2), 12 mg, 0.07 mmol/g of 25. For this sequence  $z = 0.07 + 0.16 = 0.23$  mmol of 2/g of 24.

Standard base cleavage of a second 1.0 g sample of 24

followed by purification of the crude product on preparative tlc gave **2**, 12 mg, 0.07 mmol/g of **24** ( $\gamma$ ). The resultant polymer **26** was treated with acid under the standard conditions to yield on work-up and purification as above, **2**, 28 mg, 0.16 mmol/g of **26**. For this sequence  $z' = 0.23$  mmol of **2/g** of **24**. Therefore  $q = 0.23 - 0.16 - 0.07 = 0.0$  mmol/g of **24**.

#### Preparation of Bisfunctionalized Polymer 27

To a suspension of 10 g of polymer-bound phenyllithium **4** in 200 ml of dry THF under an argon atmosphere was added a total of 6 g of **15** in 200 ml of dry THF dropwise over 2 h. The mixture was stirred an additional 2 h, filtered, and the polymer was washed and dried as outlined in the general procedure; ir: 1680 (C=O), no bands between 1700–1900  $\text{cm}^{-1}$ .

#### Preparation of the Mixed Trityl Polymer 28

A mixture of 5 g of **27** in 100 ml of dry THF and 40 ml of phenyllithium (1.5 M in benzene, 60 mmol) was stirred at reflux under an argon atmosphere overnight. The mixture was cooled, poured into a rapidly stirring mixture of 10% acid in ice cold dioxane and the polymer was filtered, washed, and Soxhlet dried as outlined in the general procedure. The ir was uninformative with no bands between 1650 and 1800  $\text{cm}^{-1}$ .

#### Preparation of Bifunctionalized Polymer 31

To a suspension of 10 g of polymer-bound phenyllithium **4** in 100 ml of dry THF under an argon atmosphere was added a mixture of benzophenone (9.1 g, 50 mmol) and diethyl carbonate (5.9 g, 50 mmol) or a mixture of benzophenone (5 mmol) and diethyl carbonate (50 mmol) in 100 ml of dry THF dropwise over 0.5 h. The mixture was stirred a further 2 h at room temperature, filtered, and the polymer was washed and dried as described before (**4**, **7**) to give polymer **31** or new polymer **31** (1:10); ir: 1740 ( $\text{CO}_2\text{Et}$ ), 1680  $\text{cm}^{-1}$  (C=O).

#### Preparation of Bifunctionalized Polymers 32, 33, and 34

Polymers **32**, **33**, and **34** were prepared by methods identical to those for **19**, **23**, and **24**.

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