The Use of Polymer Supports in Organic Synthesis. III.[1] Selective Chemical Reactions on One Aldehyde Group of Symmetrical Dialdehydes

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An insoluble polymer support system incorporating a diol functional group was prepared. The symmetrical dialdehydes, terephthalaldehyde and isophthalaldehyde, were attached to the polymer through acetal formation, constituting a unique method of blocking one aldehyde group of symmetrical dialdehydes. The free aldehyde group was reacted with hydroxylamine to give the mono-oximes of the terephthalaldehyde and isophthalaldehyde upon acid cleavage from the polymer. Similarly, the polymer bound aldehydes were reacted with Wittig reagents to give *p*- and *m*-formylstilbenes and 1-*p*- and -*m*-formylphenyl-4-phenyl-1,3-butadienes. The crossed aldol condensation of acetophenone with the symmetrical dialdehydes gave the 3-*p*- and -*m*-formylphenyl-1-phenyl-2-propene-1-ones (formylchalcones) in high yield. The Grignard reaction of phenylmagnesium bromide on the polymer bound aldehyde gave (*p*- and *m*-formylphenyl)phenylcarbinol in quantitative yield. Reduction of the polymer bound free aldehydes with sodium bis(2-methoxyethoxy)-aluminum hydride gave *p*- and *m*-hydroxymethylbenzaldehydes. Similarly the mixed benzoin condensation of polymer bound terephthalaldehyde and isophthalaldehyde gave *p*- and *m*-formylbenzils.

Un support insoluble, à base de polymère possédant un groupe fonctionnel diol, a été préparé. Les dialdéhydes symétriques, téréphthalaldéhyde et isophthalaldéhyde, ont été fixés au polymère sous forme d'acétal constituant ainsi une méthode unique de blocage d'un seul groupe aldéhyde dans les dialdéhydes symétriques. Le groupe aldéhyde libre a été mis en réaction avec l'hydroxylamine pour conduire aux mono-oximes de téréphthalaldéhyde et isophthalaldéhyde, après clivage acide. De la même façon, les aldéhydes fixés au polymère réagissent sur les réactifs de Wittig pour conduire aux *p*- et *m*-formylstilbènes et aux *p*- et *m*-formylphényl-1 phényl-4 butadiènes-1,3. La condensation aldol croisée entre l'acétophénone et les dialdéhydes symétriques conduit aux *p*- et *m*-formylphényl-3 phényl-1 propène-2 ones-1 (formyl chalcones) avec un rendement élevé. La réaction de Grignard entre le bromure de phénylmagnésium et l'aldéhyde fixé au polymère conduit aux (*p*- et *m*-formylphényl)phénylcarbinol avec un rendement quantitatif. La réduction des groupes aldéhydes libres par l'hydrure de sodium bis(méthoxy-2 éthoxy)-aluminium conduit aux *p*- et *m*-hydroxyméthylbenzaldéhydes. De façon semblable, la condensation benzoine mixte du téréphthalaldéhyde et isophthalaldéhyde fixés au polymère conduit aux *p*- et *m*-formylbenzyles. [Traduit par le journal]

The use of insoluble polymer supports in the synthesis of polypeptides (1), polynucleotides (2), and polysaccharides (3) has been well documented. The general application of insoluble polymer supports to organic synthetic problems has only recently received scattered attention (4). We have previously shown how an insoluble polymer support, containing acid chloride groups (5) can be used as a selective blocking group for completely symmetrical diols and hence the preparation of monotrityl and monotetrahydropyranyl derivatives of symmetrical diols were facilitated (6, 7).

We now describe a procedure in which symmetrical dialdehydes are attached to a modified insoluble Merrifield polymer (**1**) through an acetal linkage of only one aldehyde group, leaving the other aldehyde group available for reaction. This procedure constitutes a unique method of blocking one aldehyde group of a symmetrical dialdehyde.

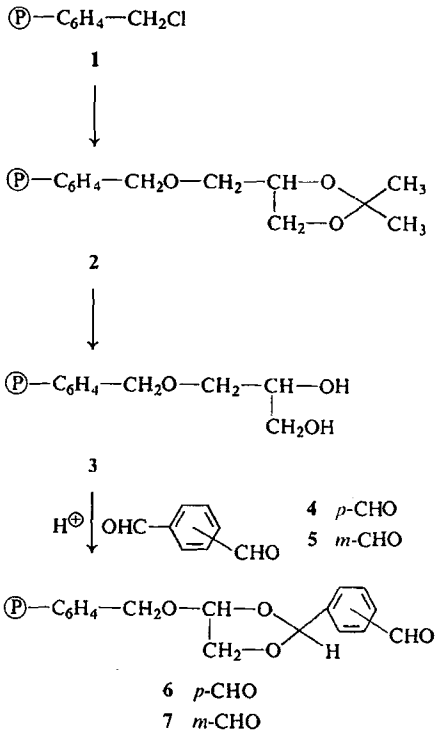
A suitable modified Merrifield polymer was prepared by reacting a commercially available Merrifield polymer (**1**) (2% cross-linked polystyrene beads with 1.7 mmol of $-CH_2Cl$ groups per gram of resin, obtained from Schwarz/Mann), with the sodium salt of 2,2-dimethyl-1,3-dioxolane-4-methanol in excess 2,2-dimethyl-1,3-dioxolane-4-methanol[2] as solvent to give resin **2**, as shown in Scheme 1. Acid hydrolysis of **2** with dilute HCl in aqueous dioxane (1:1) gave resin **3** containing a vicinal diol functional group

[1]For Part II see ref. 7.

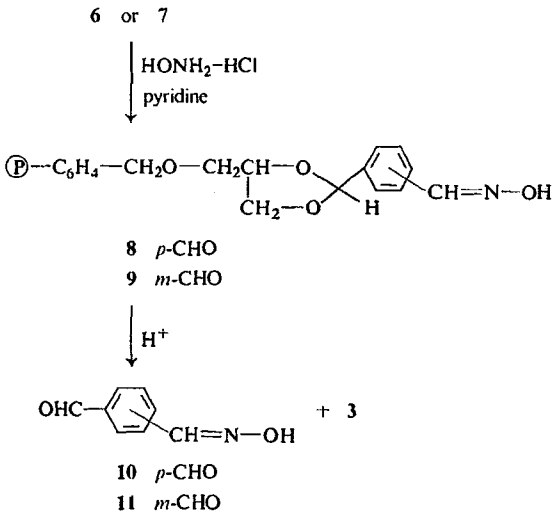
[2]Purchased from Aldrich Chemical Co.

available for acetal formation. The i.r. spectrum of **3** exhibited O—H absorption at 3415 cm^{-1} and C—O absorption at 1058 cm^{-1}.

Resin **3** reacted with excess terephthalaldehyde (**4**) or isophthalaldehyde (**5**) in anhydrous dioxane, containing *m*-benzenedisulfonic acid as a catalyst and magnesium sulfate to absorb the liberated water, to yield resins **6** or **7** containing aldehydes **4** or **5** respectively. The i.r. spectra of resins **6** and **7** exhibited typical aldehyde absorption at 1700 cm^{-1} showing that one aldehyde function did not form an acetal. The use of excess aldehyde ensured that only mono-acetal formation would predominate. The amount of aldehyde attached to the polymer was determined by acid hydrolysis of **6** and **7** in aqueous dioxane (1:1) with dilute HCl to yield **4** and **5** respectively. It was thus shown that resin **6** contained 0.34 mmol of **4** per gram and resin **7** contained 0.35 mmol of **5** per gram. Thus the capacities of resins **6** and **7** are very high compared to resins described in earlier publications (1–7).



SCHEME 1



SCHEME 2

Chemical syntheses designed to react with only one aldehyde group of symmetrical dialdehydes are quite rare and have met with success in only a few instances under special conditions (8) and even then difficulties of separation of reagents and products were apparent.

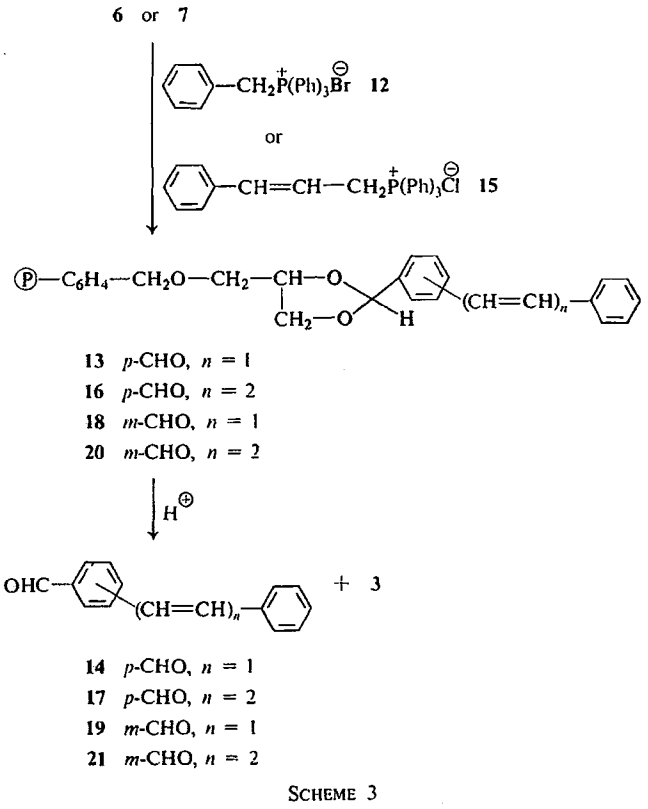
The following chemical reaction types illustrate how resin aldehydes **6** and **7** can be used to prepare largely unknown and poorly accessible compounds containing free formyl groups.

Oxime Formation

For example, the simple mono-oximes of terephthalaldehyde (**4**) and isophthalaldehyde (**5**) are unreported but these derivatives are readily synthesized using resins **6** and **7**.

In a typical reaction sequence as outlined in Scheme 2, resin **6** or **7** and an excess of hydroxylamine hydrochloride in pyridine gave after 24 h the resin oximes **8** or **9**. Acid hydrolysis of **8** or **9** as before gave terephthalaldehyde mono-oxime (**10**) and isophthalaldehyde mono-oxime (**11**) in 86 and 71% yield, respectively.[3] Elemental analysis and mass spectral data were consistent with structures **10** and **11**. Both oximes **10** and **11** exhibited strong parent ions in their mass spectra and a peak at *m/e* 120 indicating the expected loss of a formyl group by α-cleavage. The i.r. spectra

[3]All yields are based on the amount of **4** (or **5**) released from resin **6** (or **7**) upon acid hydrolysis.



SCHEME 3

of **10** and **11** showed characteristic C=O and O—H absorption.[4]

The Wittig Reaction

It was decided to examine the Wittig reaction with the monoprotected dialdehydes **6** and **7** with benzyltriphenylphosphonium bromide and cinnamyltriphenylphosphonium chloride as the products of these reactions, formylstilbenes and 1-formylphenyl-4-phenyl-1,3-butadienes were unknown compounds, difficult to prepare by other methods, and were essential in other studies in this laboratory, involving the photochemistry of diarylpolyenes (9).

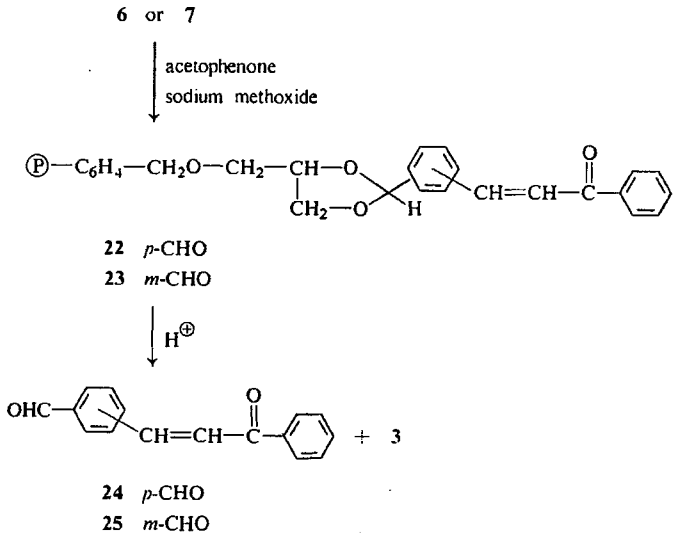
Thus reaction of the resin aldehyde **6** and benzyltriphenylphosphonium bromide (**12**) in anhydrous dimethylformamide and sodium methoxide gave resin **13**, as shown in Scheme 3. The i.r. spectrum of resin **13** showed some residual aldehyde absorption at 1692 cm^{-1}.

[4]Full spectral data are described in the Experimental section.

Acid hydrolysis of resin **13** as before gave used resin **3** and crude *p*-formylstilbene (**14**) which on further purification by t.l.c. gave pale yellow needles of **14** in 76% yield. Similarly, the resin aldehyde **6** and cinnamyltriphenylphosphonium chloride (**15**) gave resin **16** which on treatment with acid yielded 1-*p*-formylphenyl-4-phenyl-1,3-butadiene (**17**) in 59% yield.

Likewise, the Wittig reaction of resin aldehyde **7** with **12** gave resin **18** which on acid treatment yielded *m*-formylstilbene (**19**) in 50% yield. Reaction of resin **7** with **15** gave resin **20** which on acid treatment gave 1-*m*-formylphenyl-4-phenyl-1,3-butadiene (**21**) in 27% yield.

The mass spectra of **14**, **17**, **19**, and **21** exhibited parent ions and (M − 29) peaks due to the loss of the formyl group by α-cleavage. The i.r. spectra of **14**, **17**, **19**, and **21** showed absorption for the formyl and olefin moieties. The u.v. spectra of these products showed the characteristic stilbene and 1,4-diphenyl-1,3-butadiene absorption (9).



SCHEME 4

The Crossed Aldol Condensation

In experiments designed to test the feasibility of conducting mixed condensation reactions involving the mono-protected symmetrical aldehydes **4** and **5**, the cross aldol condensations of resin aldehydes **6** and **7** with acetophenone were attempted.

Resin aldehydes **6** and **7** were condensed with acetophenone and sodium methoxide in absolute ethanol to yield resin chalcones **22** and **23** respectively. Cleavage of the chalcones from resins **22** and **23** gave the chalcones 3-*p*-formylphenyl-1-phenyl-2-propen-1-one (**24**) (10) and 3-*m*-formylphenyl-1-phenyl-2-propen-1-one (**25**) in 100 and 96% yields respectively[5] as shown in Scheme 4.

The mass spectra of **24** and **25** exhibited parent ions and (M − 29) peaks due to the loss of the formyl group by α-cleavage. The i.r. spectra of **24** and **25** showed typical carbonyl and olefin absorption. The u.v. spectra were typical of chalcones.

The Benzoin Condensation

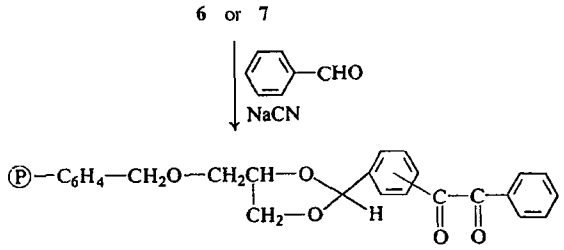
Attempts at conducting mixed benzoin condensations invariably lead to intractable mixtures of symmetrical benzoins and mixed or crossed benzoins.

It was envisoned that a polymer supported aldehyde could react with excess benzaldehyde under the conditions of the benzoin condensation. The insoluble polymer supported aromatic aldehydes could then react with benzaldehyde to give mixed or crossed benzoins exclusively. All symmetrical benzoin and excess reagents would simply be filtered from the insoluble resin containing the crossed benzoin.

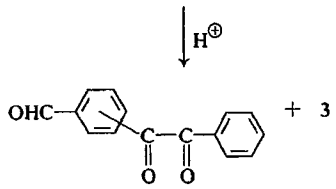
To this end resin aldehyde **6** was treated with benzaldehyde and sodium cyanide in absolute ethanol to give resin **26**, as shown in Scheme 5. Acid cleavage of **26** gave a complex mixture of products which were chromatographed on preparative t.l.c. The major fraction, obtained in only 6% yield, consisted of *p*-formylbenzil (**27**). Similarly, reaction of aldehyde resin **7** with benzaldehyde in a benzoin condensation led to resin **28** which on acid cleavage gave *m*-formylbenzil (**29**) in 4% yield.

The mass spectra of **27** and **29** were very characteristic of benzils and not benzoins and exhibited parent ions and symmetrical cleavage of the α-diketones to give fragment ions at *m/e* 105 and 134 characteristic of the benzoyl group and the formylbenzoyl groups respectively. Furthermore, the i.r. spectra of **27** and **29** exhibited strong carbonyl absorption but a noted absence of O—H absorption. Thus it appears that the crossed benzils **27** and **29** are formed by oxidation of preformed benzoins.

[5]The chalcone **24** was previously obtained in only 30% yield (10).



26 *p*-CHO
28 *m*-CHO

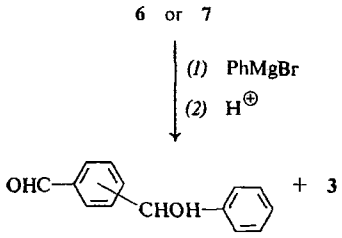


27 *p*-CHO
29 *m*-CHO

SCHEME 5

The Grignard Reaction

The reaction of Grignard reagents with symmetrical dialdehydes would inevitably lead to poorly separable mixtures containing the di-adduct, the mono-addition product, and unreacted starting material. The selective formation of the mono-addition product can be achieved using insoluble polymer supports as outlined in Scheme 6.



30 *p*-CHO
31 *m*-CHO

SCHEME 6

The resin aldehyde **6** was reacted with phenylmagnesium bromide in tetrahydrofuran to yield a resin alcohol which was not isolated, but directly treated with acid to give resin **3** and (*p*-formylphenyl)phenylcarbinol (**30**) (*p*-formylbenzhydrol) in 99% yield. Similarly resin aldehyde **7** was treated with phenylmagnesium bromide to give (*m*-formylphenyl)phenylcarbinol (**31**) (*m*-formylbenzhydrol) in 100% yield.

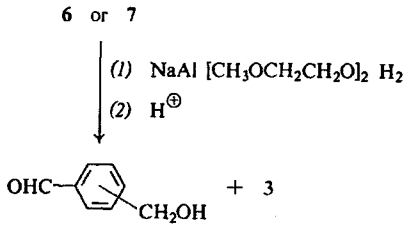
The mass spectra of **30** and **31** exhibited parent ions and peaks at 105 indicative of the formylphenyl group. The i.r. spectra of **30** and **31** showed C=O and O—H absorption.

Reductions with Metal Hydrides

As shown above, the synthesis of secondary alcohols containing free formyl groups was achieved through the use of the Grignard reaction. An attempt was made to synthesize primary alcohols containing formyl groups by metal hydride reduction of appropriate symmetrical dialdehydes mono-protected by the insoluble resin.

A suspension of resin aldehyde **6** with sodium bis(2-methoxyethoxy)-aluminum hydride in benzene gave a suspension of resin alcohol. The suspension was treated directly with dilute acid to effect cleavage from the polymer of the reaction product and gave *p*-hydroxymethylbenzaldehyde (**32**) (11) in 17% yield[6] as shown in Scheme 7.

[6]The reaction of **6** with lithium aluminum hydride in tetrahydrofuran or sodium borohydride in methanol and subsequent acid cleavage gave no **32** or **33**.



32 *p*-CHO
33 *m*-CHO

SCHEME 7

Similarly, reaction of resin aldehyde **7** with sodium bis(2-methoxyethoxy)-aluminum hydride gave *m*-hydroxymethylbenzaldehyde (**33**) in 8% yield. The poor yields of **32** and **33** are probably due to ready polymerization of these compounds. The susceptibility of these compounds to polymerization probably accounts for the fact that **33** was previously unrecorded and **32** recorded rarely (11).

The mass spectra of **32** and **33** exhibited parent ions and also showed peaks at *m/e* 107 resulting from loss of the formyl group by α-cleavage. The i.r. spectra of **32** and **33** showed C=O and O—H absorption. The n.m.r. spectra of **32** and **33** were consistent with the assigned structures.

Advantages and Limitations of Organic Synthesis Using Resin 3

The primary advantage of using resin **3** in organic synthesis was shown in the selective high yield formation of the unreported mono-oximes **10** and **11**, the formylstilbenes **14** and **19**, the formylphenyl butadienes **17** and **21**, the formylchalcones **24** and **25**, and the formylbenzhydrols **30** and **31**, from the commercially available symmetrical dialdehydes **4** and **5**. Classical preparations of some of these products from **4** and **5** would invariably lead to poorly separable mixtures of di-adducts, mono-adducts, and starting material (10, 11).[7]

It should be noted that the yields of all products obtained from isophthalaldehyde via resin **7** were slightly but consistently lower than the products from terephthalaldehyde via resin **6**. Thus it appears that steric hindrance of the less accessible meta formyl group in resin **7** plays a role in determining the yields of products derived from this resin.

In an experiment designed to test the quality of the *used* resin **3**, this resin was subjected to the reaction sequence outlined in Scheme 2 using aldehyde **4** and phosphonium salt **12**. Product **14** was obtained once again in 73% yield showing that resin **3** had not deteriorated during the reaction sequence and hence was completely regenerable. The used polymer obtained in the sequence leading to the preparation of monotrityl ethers of symmetrical diols suffered considerable deterioration (6, 7). The recovery in this instance of a completely regenerable polymer constitutes a major step in the *practical* use of polymer supports in organic synthesis.

One limitation to using an acetal linkage to attach molecules to insoluble polymer supports lies in the fact that only reactions conducted under basic conditions can be employed, as are all of the reactions described in this paper. A further limitation results from this same condition, namely that the procedures used for washing the polymer free of excess reactants and reagents cannot employ acid conditions. The Grignard reaction and the metal hydride reductions of resin aldehydes **6** and **7** result in metal salts of resin alcohols. These salts are gelatinous which creates filtering problems. The gelatinous precipitates can be solubilized by acid but of course this procedure causes cleavage of the products from the resin. Thus the Grignard products **30** and **31** were obtained by direct cleavage of the adducts obtained from the Grignard reagent with resin aldehydes **6** and **7**. For this example, this procedure was not a disadvantage as the products were still obtained in high yield but if one wanted the benzhydrol products to remain attached to the polymer for a possible sequential synthesis, the limitation against the use of acid would become serious. The limitation against using acid was more apparent in the syntheses of the hydroxymethylbenzaldehydes **32** and **33** resulting in low yields of these compounds.

The role of solvent in planning organic syntheses on insoluble polymer supports is very important but at times unpredictable. Generally, one likes to do reactions on insoluble resins in solvents that swell the polymer such as pyridine and dimethylformamide. The syntheses of the mono-oximes **10** and **11** in pyridine, and the stilbenes **14** and **19** and the butadienes **17** and **21**

[7]The mono-oxime of *o*-phthalaldehyde is known (12) and was obtained as an oil in 70% yield.

in dimethylformamide in high yields emphasize the importance of a *good* solvent. The formylbenzhydrols **30** and **31**, however, were synthesized in high yield in an only partially acceptable solvent, tetrahydrofuran, while the formylchalcones **24** and **25** were prepared in very high yield in absolute ethanol, a poor solvent for swelling the polymer. Thus, the poor yields of the hydroxymethylbenzaldehydes **32** and **33** obtained from reaction in benzene, a *good* solvent, were probably due to other reasons, although it should be noted that the metal hydride reductions of **6** and **7** in tetrahydrofuran and in methanol, poorer solvents, gave no product and thus the change in solvent (or metal hydride) allowed at least some product to be realized. The poor yields obtained in the benzoin condensation could be due to solvent effects but an attempt to accomplish the benzoin condensation in dimethylformamide, a *good* solvent, resulted in yields of benzils **27** and **29** identical to that in absolute ethanol, a *poor* solvent. Thus the role of solvent is important in organic synthesis on insoluble resins but should not be an inhibiting factor in attempting an organic synthesis.

It has thus been demonstrated that general organic syntheses can be accomplished in high yield on insoluble polymer supports, with recovery of a completely regenerable polymer. Most important of all, because of the high capacity of the insoluble polymer it becomes feasible to react only one aldehyde group of symmetrical dialdehydes with a series of organic reagents in a standard practical procedure, yielding reasonable quantities of products.

The development of further organic synthetic methods using insoluble polymer supports is in progress.

Experimental

All melting points were determined on a Kofler hot stage and are uncorrected. The i.r. spectra were recorded on a Unicam SP1000 i.r. spectrophotometer using KBr discs unless otherwise stated. The u.v. spectra were measured using a Unicam SP800A u.v. spectrometer and benzene as solvent. The n.m.r. spectra were measured on a Varian A60 spectrometer using tetramethylsilane as an internal standard ($\delta = 0$ p.p.m.) and deuterochloroform as solvent. Mass spectra were recorded on a Hitachi-Perkin-Elmer RMU-6 mass spectrometer. The number in brackets after the indicated ion shows the % of the base peak represented by that ion. Silica gel was used for thin- and thick-layer chromatography. Microanalyses were performed by Dr. C. Daesslé of Montreal. Filtering procedures were done under vacuum using a sinter-glass funnel. All the stirring described below was performed using a Fisher magnetic stirrer.

Preparation of Polymer 2

Sodium (2 g) was added to 60 ml of 2,2-dimethyl-1,3-dioxolane-4-methanol (Aldrich Chemical Co.) in a 250 ml round-bottom flask. The mixture was stirred until all the sodium had dissolved. The Merrifield resin (4.87 g) (**1**) (2% cross-linked polystyrene beads with 1.7 mmol of $-CH_2Cl$ groups per gram of resin, obtained from Schwarz/Mann) was then added. The mixture was stirred at room temperature overnight and at 80 °C for 24 h. The resin was collected by filtration and washed three times with dioxane, six times with water, three times with ethanol–water (1:1), three times with ethanol, and three times with dry ether to give 5.88 g of polymer, ν_{max} 1128–1058 cm^{-1} (C—O—C).

Preparation of Polymer 3

Polymer **2** (5.88 g) was suspended in a mixture of dioxane and 1 *M* hydrochloric acid (1:1, 60 ml). The mixture was stirred for 48 h at room temperature. The resin was filtered and washed six times with water, once with acetone, three times with ethanol, and three times with dry ether to give 5.82 g of polymer diol **3**. The i.r. spectrum showed a vicinal diol functional group at ν_{max} 3415 cm^{-1} (OH), 1058 cm^{-1} (C—O—C).

Preparation of Polymer Aldehydes 6 and 7

In a typical procedure, 4.25 g of polymer **3** was suspended in 60 ml of anhydrous dioxane. Excess terephthalaldehyde (**4**) or isophthalaldehyde (**5**) (2 g) and 0.10 g of *m*-benzenedisulfonic acid as catalyst were added. To the mixture was added 2.00 g of anhydrous sodium sulfate to absorb liberated water and the reaction was stirred at room temperature for 48 h under exclusion of moisture ($CaCl_2$, drying tube). The resin was filtered, neutralized with anhydrous pyridine (to prevent cleavage of the aldehyde from the polymer by hydrolysis of the acetal linkage), and filtered twice. Then the resin was washed twice with pyridine–water (1:1), ten times with water (to remove sodium sulfate), three times with ethanol, and at least three times with dry ether. The i.r. spectra of **6** and **7** exhibited typical aldehyde absorption at 1700 cm^{-1}; resin **6**, ν_{max} 1700 cm^{-1}; resin **7**, ν_{max} 1698 cm^{-1}.

Preparation of Mono-oximes 10 and 11

Resin **6** (3.27 g) was suspended in 50 ml of anhydrous pyridine. Excess hydroxylamine hydrochloride (2.50 g) was added. The mixture was stirred at room temperature for 48 h. The resin was filtered and washed three times with pyridine, three times with pyridine–water (1:1), three times with water, three times with ethanol, and three times with dry ether to give the resin **8** (3.43 g). A suspension of 3.43 g of resin **8** and 40 ml of a 1:1 mixture of dioxane and dilute hydrochloric acid was stirred for 48 h at room temperature. The resin was filtered and washed six times with water, once with acetone, three times with ethanol, and three times with ether. The aqueous filtrate was extracted with three aliquots of ether. The combined ether extracts were washed six times with water, dried over Na_2SO_4, and evaporated to give a slightly impure solid which was purified by preparative t.l.c. on silica gel (eluant $CHCl_3$) to give 0.1421 g (86%) of analytically pure terephthalaldehyde mono-oxime (**10**) m.p. 122–127°. No starting terephthalaldehyde **4** was

detected. I.r. spectrum, ν_{max} (Nujol) 3415 cm^{-1} (OH), 1680 cm^{-1} (C=O); mass spectrum, *m/e* 149 (19) (M^+), 120 (5) ($M^+ - CHO$), 105 (10) ($M^+ - CH{=}NOH$), 131 (100) ($M^+ - H_2O$).

Anal. Calcd. for $C_8H_7NO_2$: C, 64.43; H, 4.69; N, 9.39. Found: C, 64.45; H, 4.89; N, 9.60.

Similarly, treatment of resin 7 (3.31 g) as described above gave the resin **9**. Acid hydrolysis of **9** and identical work-up as before yielded 0.1201 g (71%) of analytically pure isophthalaldehyde mono-oxime, as an oil, (**11**) and 0.0105 g of starting aldehyde **5**. I.r. spectrum, ν_{max} (neat) 3360 cm^{-1} (OH), 1685 cm^{-1} (C=O); mass spectrum *m/e* 149 (30) (M^+), 120 (100) ($M^+ - CHO$), 105 (10) ($M^+ - CH{=}N{-}OH$).

Anal. Calcd. for $C_8H_7NO_2$: C, 64.43; H, 4.69; N, 9.39. Found: C, 64.23; H, 4.80; N, 9.25.

Preparation of p-Formylstilbene (14) and 1-p-Formylphenyl-4-phenyl-1,3-butadiene (17)

To a solution of benzyltriphenylphosphonium bromide (**12**) (4.00 g) in anhydrous dimethylformamide (60 ml) was added powdered sodium methoxide (2.50 g). After stirring for 5 min, when the solution turned orange, resin **6** (5.77 g) was added to give, after stirring 24 h at room temperature, the resin **13**. Resin **13** was separated by filtration, washed three times with DMF, three times with DMF–water (1:1), three times with water, three times with methanol, and three times with ether. Acid hydrolysis of resin **13** as before and using an identical work-up gave used resin **3** and crude *p*-formylstilbene (**14**). Further purification by preparative t.l.c. on silica gel (eluant 10% $CHCl_3$ – 90% C_6H_6) gave 0.310 g of analytically pure **14**, m.p. 101–105°, in 76% yield and 0.057 g of starting terephthalaldehyde (**4**). I.r. spectrum, ν_{max} (Nujol) 1699, 972 cm^{-1}; mass spectrum, *m/e* 208 (100) (M^+), 179 (30) ($M^+ - CHO$); u.v. spectrum, λ_{max} 335 mμ (ε 33 300).

Similarly, the addition of resin **6** (6.15 g) to the Wittig reagent, cinnamyltriphenylphosphonium chloride (**18**) as described above gave the resin **16**. Acid hydrolysis of **16** and using an identical work-up as before yielded 0.299 g (59%) of analytically pure 1-*p*-formylphenyl-4-phenyl-1,3-butadiene (**17**), m.p. 128, and also 0.088 g of starting aldehyde **4**. I.r. spectrum, ν_{max} (Nujol), 1691, 996 cm^{-1}, mass spectrum, *m/e* 234 (100) (M^+), 205 (100) ($M^+ - CHO$); u.v. spectrum, λ_{max} 347, 362, 379 mμ (ε 39 800, 49 100, 35 100).

Anal. Calcd. for $C_{17}H_{14}O$: C, 87.18; H, 5.98. Found: C, 87.13; H, 5.66.

Preparation of 1-m-Formylstilbene (19) and 1-m-Formylphenyl-4-phenyl-1,3-butadiene (21)

To a solution of benzyltriphenylphosphonium bromide (**12**) (4.00 g) in anhydrous dimethylformamide (60 ml) was added powdered sodium methoxide (2.50 g). After stirring for 5 min, when the solution turned orange, resin **7** (6.07 g) was added to give, after stirring 24 h at room temperature, the resin **18**. Resin **18** was separated by filtration and washed three times with DMF, three times with DMF–water (1:1), three times with water, three times with methanol, and three times with ether. Acid hydrolysis of resin **18** as before and using an identical work-up gave used resin 3 and crude *m*-formylstilbene (**19**). Further purification by preparative t.l.c. on silica gel (eluant 10% $CHCl_3$: 90% C_6H_6) gave 0.239 g of analytically pure **19**, m.p. 104–107°, in 50% yield and 0.100 g of starting aldehyde **5**. I.r. spectrum, ν_{max} (Nujol) 1692, 970 cm^{-1}; mass spectrum, *m/e* 208 (100) (M^+), 179 (100) ($M^+ - CHO$); u.v. spectrum, λ_{max} 300 mμ (ε 26 600).

Anal. Calcd. for $C_{15}H_{12}O$: C, 86.54; H, 5.77. Found: C, 86.86; H, 5.56.

Similarly, the addition of resin 7 (6.49 g) to the Wittig reagent, cinnamyltriphenylphosphonium chloride (**15**), as described above gave the resin **20**. Acid hydrolysis of **20** and using an identical work-up as before yielded 0.147 g (27%) of analytically pure 1-*m*-formylphenyl-4-phenyl-1,3-butadiene (**21**), m.p. 132–136°, and 0.188 g of starting aldehyde **5**. I.r. spectrum, ν_{max} (Nujol) 1690, 990 cm^{-1}; mass spectrum, *m/e* 234 (100) (M^+), 205 (100) ($M^+ - CHO$); u.v. spectrum, λ_{max} 325, 335, 354 mμ (ε 42 100, 45 000, 29 300).

Anal. Calcd. for $C_{17}H_{14}O$: C, 87.18; H, 5.98. Found: C, 87.05; H, 5.56.

Preparation of Formylchalcones 24 and 25

Resin **6** (4.31 g) was suspended in 60 ml of absolute ethanol. Excess acetophenone (4.00 g) and sodium methoxide powder (3.50 g) were added. The mixture was stirred at room temperature for 48 h with exclusion of moisture ($CaCl_2$ drying tube). The resin **22** was filtered off and washed three times with ethanol, three times with ethanol–water, three times with water, three times with methanol, and three times with dry ether. Acid hydrolysis of resin **22** as described previously and using an identical work-up gave used resin **3** and crude 3-*p*-formylphenyl-1-phenyl-2-propen-1-one (**24**). Further purification by preparative t.l.c. on silica gel (eluant $CHCl_3$) gave 0.369 g of analytically pure **24**, m.p. 121° (lit. (10) m.p. 125°), in 100% yield. I.r. spectrum, ν_{max} (Nujol) 1600, 1675, 1687 cm^{-1}; mass spectrum, *m/e* 236 (10) (M^+), 207 (8) ($M^+ - CHO$), 105 (90) (benzoyl); u.v. spectrum, λ_{max} 280 mμ (ε 3300).

Similarly, treatment of resin **7** as described above gave the resin **23**. Acid hydrolysis of resin **23** and using an identical work-up as before yielded 0.341 g (96%) of analytically pure 3-*m*-formylphenyl-1-phenyl-2-propen-1-one (**25**). I.r. spectrum, ν_{max} (neat) 1600, 1680, 1690 cm^{-1}; mass spectrum, *m/e* 236 (46) (M^+), 207 (30) ($M^+ - CHO$); u.v. spectrum, λ_{max} 292 mμ (ε 6780).

Anal. Calcd. for $C_{16}H_{12}O_2$: C, 81.36; H, 5.09. Found: C, 81.35; H, 5.38.

Preparation of Formylbenzils 27 and 29

The aldehyde resin **6** (4.33 g) was suspended in a mixture of ethyl alcohol, dioxane, and water (1:1:1, 120 ml). To this was added sodium cyanide (2.50 g) in 30 ml of water. The mixture was stirred overnight at 80 °C. Then excess benzaldehyde (4.00 g) was added and the mixture was stirred at 80 °C for another 24 h to give resin **26**. Resin **26** was collected by filtration and washed three times with dioxane–water (1:1), three times with water, three times with ethanol–water (1:1), three times with ethanol, and three times with ether. Acid cleavage of resin **26** as described previously and using an identical work-up gave used resin **3** and a complex mixture of products which were chromatographed on preparative t.l.c. (eluant 5% ether – 95% $CHCl_3$). The yield of 1-*p*-formylbenzil (**27**), as an oil, was 0.0195 g (6%). I.r. spectrum, ν_{max} (neat) 1670–1710 cm^{-1}, broad, (C=O); mass spectrum, *m/e* 238 (3) (M^+), 209 (0.3) ($M^+ - CHO$), 105 (100) (benzoyl), 134 (33) (formylbenzoyl).

Anal. Calcd. for $C_{15}H_{10}O_3$: C, 75.63; H, 4.20. Found: C, 75.71; H, 4.38.

Similarly, reaction of aldehyde resin **7** (5.33 g) with benzaldehyde in a benzoin condensation described above led to resin **28** which on acid cleavage and using an identical work-up gave used resin **3** and a complex mixture of products. Purification by preparative t.l.c. on silica gel (eluant 5% ether – 95% $CHCl_3$) yielded 0.0165 g (4%) of *m*-formylbenzil (**29**), as an oil. I.r. spectrum, ν_{max} (neat) 1670–1705 cm^{-1} (broad) (C=O); mass spectrum, *m/e* 238 (0.6) (M^+), 209 (0.3) ($M^+ - CHO$), 105 (100) (benzoyl), 134 (33) (formylbenzoyl).

Anal. Calcd. for $C_{15}H_{10}O_3$: C, 75.63; H, 4.20. Found: C, 75.57; H, 4.32.

Preparation of Formylbenzhydrols 30 and 31

Phenylmagnesium bromide was prepared as follows. To a solution of magnesium (2 g) and iodine (0.010 g) in 125 ml of anhydrous tetrahydrofuran was added dropwise with stirring bromobenzene (13.2 g) in 20 ml of tetrahydrofuran. The mixture was refluxed for 1 h until all the magnesium had dissolved.

The resin aldehyde **6** (5.57 g) was then reacted with the phenylmagnesium bromide in anhydrous tetrahydrofuran at room temperature for 48 h to give a resin alcohol which was not isolated but directly treated with acid and using an identical work-up as before yielded resin **3** and (*p*-formylphenyl)phenylcarbinol (**30**). Purification by preparative t.l.c. on silica gel (eluant $CHCl_3$) yielded 0.397 g (99%) of analytically pure **30**. I.r. spectrum, ν_{max} (neat) 1695 cm^{-1} (C=O), 3440 cm^{-1} (OH); mass spectrum, *m/e* 212 (23) (M^+), 183 (16) ($M^+ - CHO$), 105 (100) (formylphenyl); u.v. spectrum, λ_{max} (ethanol) 213, 259 mμ (ε 16 900, 16 400).

Anal. Calcd. for $C_{14}H_{12}O_2$: C, 79.24; H, 5.66. Found: C, 78.99; H, 5.47.

Similarly, reacting aldehyde resin **7** (4.63 g) with phenylmagnesium bromide in accordance with the method described above gave a resin alcohol which was directly treated with acid, and using an identical work-up as before yielded resin **3** and (*m*-formylphenyl)phenylcarbinol (**31**). Purification by preparative t.l.c. on silica gel (eluant $CHCl_3$) yielded 0.342 g (100%) of analytically pure (**31**), as an oil. I.r. spectrum, ν_{max} (neat) 1688 cm^{-1} (C=O), 3400 cm^{-1} (OH); mass spectrum, *m/e* 212 (11) (M^+), 183 (0.3) ($M^+ - CHO$), 105 (100) (formylphenyl); u.v. spectrum, λ_{max} (ethanol) 213, 251, 291 mμ (ε 25 100, 12 300; 2620).

Anal. Calcd. for $C_{14}H_{12}O_2$: C, 79.24; H, 5.66. Found: C, 79.23; H, 5.61.

Preparation of p- and m-Hydroxymethylbenzaldehydes (32) and (33)

The aldehyde resin **6** (5.08 g) was suspended in 60 ml of anhydrous benzene. Addition of 20 ml of a 70% solution of sodium bis(2-methoxyethoxy)-aluminum hydride in benzene to the above mixture gave, after stirring for 48 h at room temperature with exclusion of moisture ($CaCl_2$ drying tube), a suspension of a resin alcohol. The suspension was treated directly with dilute acid in a manner described previously to effect cleavage from the polymer of the reaction product. Similar work-up as before and purification by preparative t.l.c. on silica gel (eluant 5% ether – 95% $CHCl_3$) yielded 0.039 g (17%) of analytically pure *p*-hydroxymethylbenzaldehyde (**32**) (11). I.r. spectrum ν_{max} (neat) 1690 (C=O), 3400 cm^{-1} (OH); mass spectrum, *m/e* 136 (4) (M^+), 134 (100) ($M^+ - 2H$), 105 (10) ($M^+ - CH_2OH$); n.m.r. spectrum, 2.42 p.p.m. (1H, OH proton), 4.81 p.p.m. (2H, CH_2 singlet), 8.18–7.35 p.p.m. (4H, four aromatic protons, AB pattern), 10.10 p.p.m. (1H, aldehyde proton, singlet).

Similarly, treatment of aldehyde resin **7** (7.07 g) with sodium bis(2-methoxyethoxy)-aluminum hydride in anhydrous benzene, in a manner identical to that of aldehyde resin **6** as described above, gave a suspension of a resin alcohol. This suspension was treated directly with dilute acid followed by work-up as before. Purification by preparative t.l.c. on silica gel (eluant 5% ether – 95% $CHCl_3$) yielded 0.026 g (8%) of analytically pure *m*-hydroxymethylbenzaldehyde (**33**). I.r. spectrum, ν_{max} (neat) 1695 (C=O), 3440 cm^{-1} (OH); mass spectrum, *m/e* 136 (3) (M^+), 134 (3) ($M^+ - 2H$), 105 (10) ($M^+ - CH_2OH$); n.m.r. spectrum, 3.08 p.p.m. (1H, OH proton), 4.80 p.p.m. (2H, CH_2 protons), 7.88–7.19 p.p.m. (4H, aromatic protons), 10.05 p.p.m. (1H, aldehyde proton, singlet).

Anal. Calcd. for $C_8H_8O_2$: C, 70.59; H, 5.88. Found: C, 70.61; H, 5.90.

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