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# Polymer-Supported Synthesis as a Tool for Improving Chemoselectivity: Pauson-Khand Reaction

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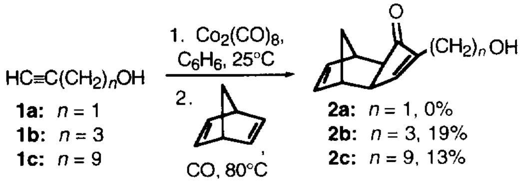
***Abstract:*** Intermolecular Pauson-Khand (PK) reactions of norbornene-derived substrates have been carried out with several $\alpha,\omega$-alkynols under both normal homogeneous conditions and with the alkynol bound to functionalized Merrifield's polymer beads. With 2% crosslinked resin chemoselectivity favoring PK product formation over alkyne trimerization and other related side reactions is enhanced over that found either in solution or on 1% crosslinked polymer. Alkynol chain length and nature of the linker also significantly affect the outcome of the polymer-supported process. © 1997 Elsevier Science Ltd.

## INTRODUCTION

The Pauson-Khand (PK) reaction, a cobalt-mediated cycloaddition of alkenes, alkynes, and carbon monoxide, has been shown to be an effective and efficient synthetic tool for the preparation of cyclopentenones.[1] In favorable cases, which usually involve reaction of acetylene or a terminal alkyne with a strained cyclic alkene, cycloaddition yields range from good to excellent, with several examples over 90%. Comparably impressive intramolecular examples of the process have been demonstrated as well. However, in some cases yields are reduced by the interference of any of several side reactions of the alkene, the alkyne, or both.[2] For example, although the PK process is generally very tolerant of functionality, cycloadditions of certain low molecular weight alkynes with polar groups proceed poorly, at least under thermal cycloaddition conditions (e.g., eq 1). In these cases metal-catalyzed alkyne trimerization appears to be the principal culprit in reducing the yield of the desired process. Recent advances in methodology have revealed a variety of reaction promoters that improve PK cycloadditions in a number of cases.[3] For some time our groups have been involved in the examination of the use of covalent attachment of reaction substrates to insoluble polymer supports as a means to improve chemoselectivity by suppression of side reactions. Over the past several years we have found this strategy to be effective in a number of different chemical situations of synthetic interest.[4]



(1)

The chloromethyl-functionalized polystyrene-based Merrifield resins provide an excellent starting point for an exploration of the utility and limitations of polymer-supported synthesis. A key issue in chemoselectivity control is the degree to which interactions between polymer-bound reactive moieties are inhibited. The term "site isolation" is often used to refer to this effect, although strictly speaking this "isolation" is never absolute even in more highly crosslinked polymers.[5] Polymer chains are flexible, and, therefore, useful inhibition of site-site interaction is a kinetic phenomenon dependent upon the mobility of polymer-bound substrate moieties being reduced significantly relative to that of solution-phase species. A major goal of this work was to ascertain the extent to which alkyne-polymer linkage would suppress side reactions involving multiple alkyne units and permit the desired alkyne-alkene interaction to proceed. Herein we report full details of this study in the context of the PK process, exploring the effects of polymer crosslinking, choice of the linkage unit, and substrate structure on overall yield and selectivity of the reaction.[6]

## RESULTS

The general approach we chose involved (a) suitable chemical modification of Merrifield polymer and attachment of an appropriately functionalized terminal alkyne, (b) complexation of the alkyne by reaction with octacarbonyldicobalt, $Co_2(CO)_8$, (c) cycloaddition in the presence of the alkene reaction component, and (d) cleavage of the product. For simplicity we chose to first use an ester linkage between the alkyne substrate and the polymer support, reasoning that it would provide minimal interference with spectroscopic characterization of intermediate polymer-bound species as well as convenient control of attachment and removal.

### *Substrate-Polymer Linkage using Aroyl Ester Functionality*

The literature describes conversion of chloromethyl-functionalized Merrifield polymer to the corresponding carboxylic acid. Preparation of the appropriately modified polymer involves first a Swern-type oxidation to the aldehyde,[7] FT-IR (KBr) 1701 (vs), 2721 (m, sh) $cm^{-1}$, Jones oxidation to the acid,[8] IR 1690 (s), 1722 (s), 2500-3500 (s, br) $cm^{-1}$, and conversion to an acid chloride with $SOCl_2$ and catalytic DMF,[7] IR 1773 (s) $cm^{-1}$. The latter was rapidly washed with dry benzene and ether, thoroughly dried over KOH and stored under vacuum as a precaution against hydrolysis. In fact, hydrolysis was never observed in such samples, presumably a result of the generally protective hydrophobic environment provided by the polystyrene backbone. A difficulty with this overall sequence arises in the oxidation to the acid, which requires harsh conditions ($Na_2Cr_2O_7$, HOAc, cat. $H_2SO_4$, 60°C, 48 hr) and leaves a dark brownish-yellow resin which, even after extensive washing with hot HOAc, water, ethanol, and ether, turns deep olive green upon treatment with thionyl chloride, suggesting considerable retention of Cr(III) ions. Although insertion of washes with pyridine and aqueous HCl prior to conversion to the acid chloride reduced this problem, we found that a Baeyer-Villiger-type oxidation with MCPBA in DME gave superior results, affording a bright white resin-bound carboxylic acid as a free-flowing powder,[9] IR 1691 (s), 1731 (s), 3457 (s, v br) $cm^{-1}$. Interestingly, although the latter resin is better-looking than the brittle, lumpy material obtained from dichromate oxidation, both behave comparably in subsequent chemistry. Polymeric carboxylic acid of similar quality may also be prepared directly from unfunctionalized crosslinked polystyrene via, e.g., a Friedel-Crafts/haloform reaction sequence.[10] All of the procedures described above were found to apply equally satisfactorily to both 2%- and 1%-crosslinked Merrifield's polymers.

Polymer-bound aroyl chloride was readily converted to esters **3a-c** by stirring with an excess of terminal alkynol in dry pyridine for 24 hr at 25°C, followed by an additional 24 hr at 100°C (Scheme 1). In each case the acyl halide carbonyl stretching signal in the IR was completely replaced by characteristic ester peaks around 1270 and 1720 $cm^{-1}$, suggesting that the reaction went to completion. In addition, peaks in the 2110-2160 and 3300 $cm^{-1}$ regions confirmed the attachment of terminal alkyne functionality. For the PK procedure, the complexation and cycloaddition processes were carried out separately. Alkynyl ester-functionalized polymers were pre-swollen with benzene and treated with a two-fold excess of $Co_2(CO)_8$ for 6 hr under an argon atmosphere (slow gas evolution). Thorough washing with benzene to remove excess metal carbonyl left resins **4a-c**, ranging in color from dark red to maroon, consistent with the presence of $Co_2(CO)_6$•alkyne moieties. The IR spectrum in each case displayed the expected intense carbonyl absorptions at approximately 2020, 2055, and 2095 $cm^{-1}$.[11] Signals for uncomplexed terminal alkyne groups were absent, although all other peaks (e.g., for the ester groups) remained essentially unaffected.

The next stage was to determine a practical method for carrying out the PK cycloaddition and for removing the products intact from the polymer. Both 1%- and 2%-crosslinked polymers containing different alkynyl $Co_2(CO)_6$-complexed groups were examined. Resins were preswollen with benzene under an inert atmosphere, treated with a large (ca. 5x) excess of 2,5-norbornadiene, and heated to reflux for a sufficient period of time for the IR peaks due to the $Co_2(CO)_6$•alkyne complex to disappear. In general, each run gave a polymer which exhibited a new carbonyl absorption at somewhat lower energy than that of the ester moiety, as expected for a cyclopentenone. Propargyl-functionalized resin **4a** was anomalous in its behavior: it apparently underwent extensive decomposition, turning black and no longer showing even the ester peaks in the IR. Removal of the organic products from polymers **4b** and **4c** was achieved by means of a modified phase-transfer hydrolysis method. Resin was suspended in THF and treated with concentrated aqueous KOH containing a small amount of tetra-*n*-butylammonium bromide. Cleavage was effected by heating to reflux for 48 hr. The resin was recovered in its carboxylate salt form, and cyclopentenones **2b** and **2c** were isolated after filtration and flash chromatography. Table 1 presents representative results (entries 2, 5, 6, and 9). It is to be noted that yields were consistently much worse with 1%-crosslinked polymer than with the 2% resin (cf. **4b-1** and **4b-2**), an observation that we have made in other systems as well.[9]

**Scheme 1**

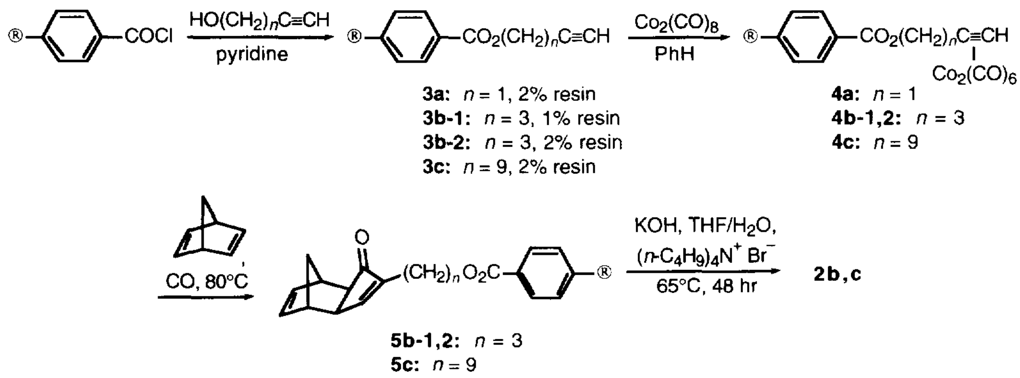
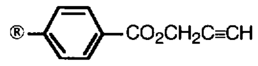
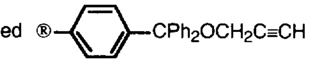
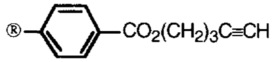
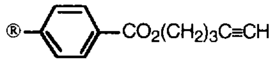
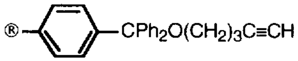
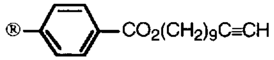
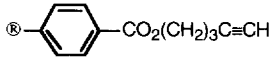
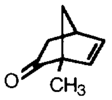
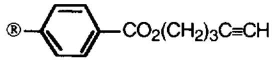


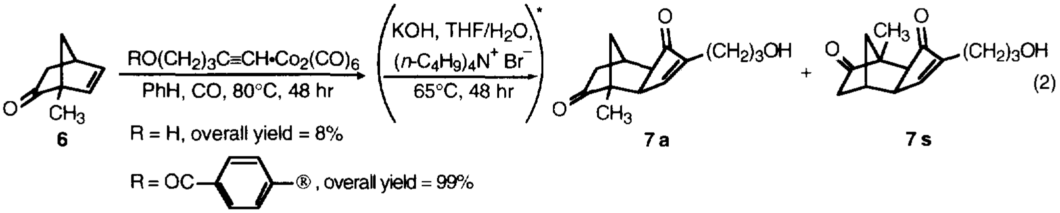
Table 1. Pauson-Khand Cycloaddition Yields for Polymer-Bound *vs.* Solution-Phase Alkyne Derivatives

| Entry | Alkyne (® = polystyrene backbone) | Alkene | Conditions | Yield[a] |
|---|---|---|---|---|
| 1. | $HOCH_2C{\equiv}CH$ |  | $Co_2(CO)_8$, 25°C, 3 h (Ar),<br>then 80°C, 6 h (CO) | 0% |
| 2. | 2%-crosslinked  | " | $Co_2(CO)_8$, 25°C, 6 h (Ar),<br>then 80°C, 7 h (CO) | 0% (dec) |
| 3. | 2%-crosslinked  | " | " | 36% |
| 4. | $HO(CH_2)_3C{\equiv}CH$ | " | $Co_2(CO)_8$, 25°C, 3 h (Ar),<br>then 80°C, 6 h (CO) | 19% |
| 5. | 1%-crosslinked  | " | $Co_2(CO)_8$, 25°C, 6 h (Ar),<br>then 80°C, 7 h (CO) | 12% |
| 6. | 2%-crosslinked  | " | " | 59% |
| 7. | 2%-crosslinked  | " | $Co_2(CO)_8$, 25°C, 4 h (Ar),<br>then 80°C, 7 h (CO) | 55% |
| 8. | $HO(CH_2)_9C{\equiv}CH$ | " | $Co_2(CO)_8$, 25°C, 3 h (Ar),<br>then 80°C, 6 h (CO) | 13% |
| 9. | 2%-crosslinked  | " | " | 56% |
| 10. | $HO(CH_2)_3C{\equiv}CH$ |  | $Co_2(CO)_8$, 25°C, 3 h (Ar),<br>then 80°C, 6 h (CO) | 29% |
| 11. | 2%-crosslinked  | " | $Co_2(CO)_8$, 25°C, 3 h (Ar),<br>then 80°C, 18 h (CO) | 8% |
| 12. | $HO(CH_2)_3C{\equiv}CH$ |  | $Co_2(CO)_8$, 25°C, 3 h (Ar),<br>then 80°C, 48 h (CO) | 8%[b] |
| 13. | 2%-crosslinked  | " | " | 99%[b] |

[a] Of simple 1:1 Pauson-Khand product (after hydrolysis of linkage to polymer, if applicable).

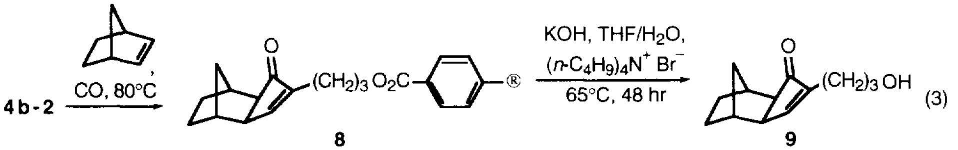
[b] Mixture of regioisomers.

Similar experiments were also carried out with norbornene and with norbornenone derivative **6** as the alkene reaction partner. The latter gave by far the most impressive result. In homogeneous solution cycloaddition with 4-pentyn-1-ol proceeded very poorly: an 8% yield of a mixture of enones (ca. 3:2 **7s**:**7a**) was obtained, whose separation from a myriad of alkyne-derived byproducts was virtually impossible (eq 2 and Table 1, entry 12). In contrast, we obtained a nearly quantitative yield of cyclopentenones using the polymer method after cleavage from the polymer (* in eq 2, and Table 1, entry 13). A more accurate determination of the regioisomeric ratio was possible under these circumstances, and the 7:3 value (**7s**:**7a**) is closely in line with those found in related systems.[12] This system most spectacularly illustrates the benefits of polymer attachment by combining optimized chemoselectivity with the need for only a trivial final purification procedure. Merely rinsing of the polymer to remove reagent-derived contaminants prior to saponification permitted the subsequent isolation of virtually analytically pure product.



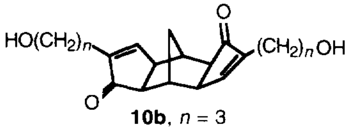
(2)

Surprisingly, norbornene performed poorly as the alkene substrate in these experiments, both on and off the polymer support (eq 3 and Table 1, entries 10 and 11). In homogeneous solution cycloaddition proceeded to give **9** in 29% yield, unusually low for this alkene.[1] Carrying out this reaction on the polymer we saw evidence of side reactions involving the alkene. Cyclopentenone **9** was obtained in only 7-8% yield. We suspect that, despite the extensive washing, small quantities of unreacted $Co_2(CO)_8$ remained trapped in or on the polymer beads and catalyzed dimerization and/or oligomerization of this unusually highly reactive alkene.[13]



(3)

The experiments using norbornadiene and 2%-crosslinked pentynyl•$Co_2(CO)_6$-functionalized polymer **4b-2** employed a large excess of the diene and afforded exclusively a monocycloaddition product **2b** in 59% yield. In contrast, reaction of only one equivalent of norbornadiene with polymer **4b-2** gave no **2b** whatsoever upon hydrolysis. Instead, the double cycloadduct **10b** was obtained as the only PK product, in 20% yield. By way of comparison, reaction of the usual five-fold excess norbornadiene with undecynyl polymer **4c** gave a 56% yield of **2c**, but in this case the product mixture was also found to contain about 10% of the corresponding double cycloaddition product **10c**.



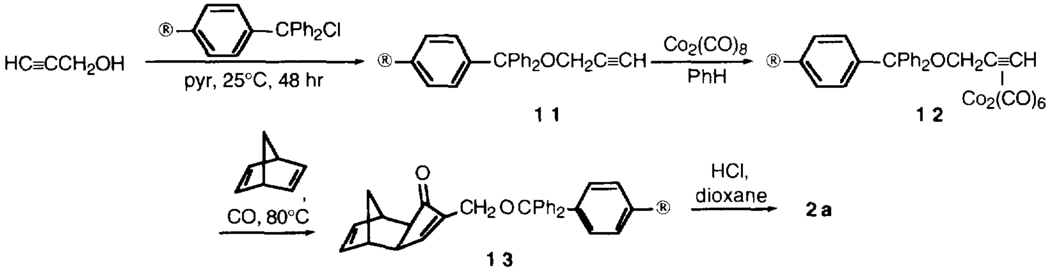
**10b**, *n* = 3
**10c**, *n* = 9

### *Substrate-Polymer Linkage using Trityl Ether Functionality*

Among the available linkers that have been used for attachment of reaction substrates to polymers, trityl-derived moieties are frequently employed, because of their relative ease of cleavage under relatively mild acidic conditions.[14] In the hope that such conditions would be compatible with the isolation of PK products in general, and the propargyl-derived products in particular, we explored this approach. Preparation of polymer-supported trityl chloride proceeded from unfunctionalized 2%-crosslinked polystyrene-divinylbenzene according to a literature sequence of lithiation, reaction with benzophenone, and conversion of the trityl alcohol (IR 1014, 3427, and 3563 cm$^{-1}$) to the chloride (IR 752 cm$^{-1}$) using excess acetyl chloride.[15] Although in the scheme we depict only the *para*-functionalized resin, the direct lithiation method actually provides a 2:1 ratio of *meta*:*para* substituted product. However, there was no reason to believe that this situation would have any material effect on the outcome of the subsequent sequences.

Viability of this linkage system was first tested with 4-pentyn-1-ol. Reaction of polymer-bound trityl chloride with the alcohol led to attachment as expected, and subsequent complexation followed by PK reaction with norbornadiene afforded a light brown polymer exhibiting IR bands at 1625 and 1700 cm$^{-1}$, consistent with cyclopentenone formation. Product cleavage was effected by exposure of the resin to 0.3 M HCl in dioxane for 48 hr at 25°C. The yield of **2b** was 55%, comparable to that obtained using the ester linkage method (Table 1, entry 7). Very similar results were obtained using 3-butyn-1-ol and 10-undecyn-1-ol. Using propargyl alcohol, attachment was achieved by stirring the trityl chloride resin in dry pyridine containing an excess of propynol at room temperature for two days. Attachment to the polymer as **11** was confirmed by the observation of IR bands at 2160 and 3290 cm$^{-1}$, somewhat shifted with respect to those observed using the ester linkage. Formation of the corresponding cobalt complex **12** also proceeded smoothly, giving a deep red resin. Finally, treatment with norbornadiene in benzene (80°C, 7 hr) gave resin **13** which, though dark brown, exhibited a strong IR band at 1699 cm$^{-1}$, characteristic of the desired product. Cleavage under similar conditions as previously described afforded 36% of enone **2a** (Scheme 2 and Table 1, entry 3).

**Scheme 2**



This product was fully characterized by IR, $^1$H- and $^{13}$C-NMR. IR analysis of the neat oil showed the alcohol hydroxyl group at 3391 cm$^{-1}$ as a very weak signal. Apparently the hydroxymethyl substituent on the cyclopentenone portion of the molecule is positioned quite favorably for intramolecular hydrogen bonding, as shown in Figure 1. Also prominent in the IR spectrum of this substance is the strong and sharp ketone C=O stretch at 1709 cm$^{-1}$, the norbornene C=C functionality at 1630 cm$^{-1}$, and the C–O stretch of the alcohol as a strong and slightly broadened peak at 1055 cm$^{-1}$.

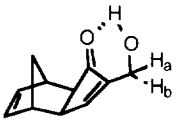


Figure 1. Intramolecular hydrogen bonding in **2a**.

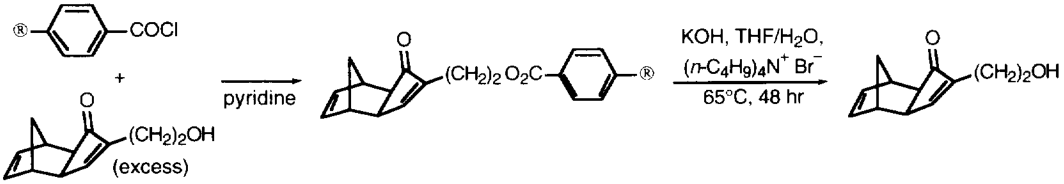
The $^1$H-NMR spectrum taken in $C_6D_6$ also showed the effect of intramolecular hydrogen bonding in this compound. The diastereotopism of the protons on the alkanol methylene group (C-11, labeled $H_a$ and $H_b$ in Figure 1) is plainly evident, giving rise to a pair of doublets of doublets with $J_{gem}$ = 14.2 Hz. The spectrum of the same sample in $CDCl_3$ shows the same alkanol peaks collapsed to a sharp two-proton singlet.

*Yield Determination: Degree of Polymer Functionalization*

We examined several methods to determine the degree of functionalization of the polymeric supports. We found that the most reproducible and internally consistent methods were an 'on/off' standardization technique and a gravimetric determination of the weight change between each step. We have used the conventionally accepted measure of milliequivalents per gram (meq/g) and assumed that complete functional group transformation occurred after each step of a sequence, based upon qualitative IR data.[9]

An example of one of the methods is illustrated in Scheme 3. A 1.00 g sample of the 2%-crosslinked acyl chloride resin was esterified using an excess of the purified alcohol from a 3-butyn-1-ol/norbornadiene cycloaddition. After attachment of the alcohol and drying of the resin, the ester was subjected to base hydrolysis, from which 0.125 g (0.657 mmol) of the alcohol was recovered. Assuming complete hydrolysis and minimal transfer losses, we can assume that resin **6** possesses 0.657 meq of accessible acyl chloride functionality per gram of this particular resin. In reality, this is a minimum value, but it is also reasonable to assume that errors in this determination will parallel errors in the actual procedures being carried out, and therefore they should approximately cancel one another.

Scheme 3



Having established this figure, it was useful to convert it into one describing the amount of acetylenic ester contained in one gram of *esterified* polymer. Thus another 1.00 g of identical resin was converted into pentynyl ester polymer **3b-2**, of which 0.74 g was recovered after filtering, washing, and drying. IR analysis indicated that all of the acyl chloride function had been converted to the ester. Assuming that no loss of the polymer-bound functional sites had occurred in the esterification process, this mass of the pentynyl ester resin possessed the same degree of functionalization as that present within the initial acyl chloride beads. Therefore, 0.657 mmol of attached alcohol per 0.74 g of the esterified resin could be normalized to 0.89 milliequivalents of functionality per gram (meq/g) of **3b-2**. It is obvious that this figure may be somewhat inflated, because it does not take into account inevitable mechanical losses in such processes. However, rather than attempt to estimate the latter, we chose to use this value for yield calculation because it would give the most conservative, i.e., the ***minimum possible*** yield estimates. The fact that one particular experiment, the polymer-supported synthesis of **4a/s**, actually gives near-quantitative yield, indicates that these losses are not significant.

In another representative degree of functionalization determination, the same 2%-crosslinked resin was esterified with 10-undecyn-1-ol and used to determine the amount of function available per gram of the undecynyl ester **3c**. After polymer attachment of the alcohol in dry pyridine, the excess alcohol and solvent were thoroughly washed away, and the resin was vacuum dried and checked by IR to ensure that the resin loading was complete. This material was then subjected to base hydrolysis to remove the attached alkynol, which was carefully weighed after removal of the solvents. It was determined that in this case there were 0.95 milliequivalents of ester functionality available per gram (0.95 meq/g) of **3c**.

A gravimetric method was also utilized. For example, 2.05 g of the pentynyl ester resin **3b-2** provided 2.56 g of the dicobalthexacarbonyl complex **4b-2** after complexation, washing, and drying. The mass gained (0.51 g) corresponded to 0.87 meq of alkynyl function available per gram of **3b-2**. We noted that if these resins were dried under high vacuum for extended periods of time, very slow decomposition of the polymer-bound alkyne/dicobalthexacarbonyl complex was observed by deposition of a dark reddish film on the wall of the desiccator and in the vacuum line traps. However, this decomposition process was very gradual, and the effect on the nearly constant weight of the resin was minimal. This supposition was supported by IR analysis, which showed essentially no loss in intensity of the metal carbonyl peaks.

## DISCUSSION

The utility of strategies involving the attachment of reaction substrates to insoluble polymer supports has been recognized for decades, many exploiting the benefits of ease of separation and purification derived therefrom. However, a number of applications to chemoselectivity control have been documented, lending an additional dimension to this strategy. At the time we embarked on this effort, however, little had been reported concerning polymer attachment of organic substrates for organometallic transformations, whose synthetic utility is often compromised by poor selectivity among several available reaction pathways.[1c] The PK reaction is an instructive system to study, because in spite of many impressive synthetic applications, the reaction still has limitations which provide an arena for the assessment of polymer-based methodologies.[Cf. ref. 5b]

Probably the most common reasons for failure of PK cycloadditions are the multitude of reaction pathways available to unsaturated organic moieties complexed to dicobalt carbonyl fragments. For example, simple substituted acyclic alkenes are such poor ligands compared to most alkynes that various coupling reactions of the latter dominate in attempted PK cycloadditions.[2,16] While norbornene-based alkenes usually afford good PK results, their cycloadditions proceed unusually poorly with simple functionalized alkynes. Alkynols containing four through eleven carbon atoms give very little PK product under thermal conditions, and propargyl alcohol gives none at all. Interestingly, 1-ethynylcyclohexanol cycloadds to norbornene derivatives in very high yield.[17] We have not looked into these systems systematically, but clearly both steric and polarity differences are tipping a fairly closely balanced competition between available modes of reaction. Upon reaction with $Co_2(CO)_8$ simple straight chain alkynols give complex mixtures of polar products containing predominantly trimerization-derived aromatics. Presumably the formation of these products is favored by association through hydrogen bonding of the alkynol-derived complexes in the otherwise non-polar reaction media. Consistent with this view is the observation that the norbornadiene-pentynol cycloaddition

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does proceed well in DMSO.[3f] Regardless, we have chosen to make use of this limitation in the PK reaction as a tool, without necessarily understanding it in full detail.

Lightly-crosslinked Merrifield's polymer may serve as vehicle for the inhibition of chemical interaction between polymer-bound functionalities if two conditions are met: deformation of the polymer backbone that would permit interaction between non-proximal polymer-bound units must be slow relative to the rate of (the desired) interaction with other chemical species, and most of these units must be farther apart than a normal interaction distance to begin with. The first condition is controlled by the degree of polymer crosslinking, the second by loading, i.e., the proportion of monomer subunits that serve as attachment points for substrate molecules. The Merrifield's resin used in this work is functionalized at approximately 12.5%, or one out of every eight of its subunits. Even if either functionalization of preformed polystyrene or copolymerization of styrene with 4-(chloromethyl)styrene (two methods for preparation of the resin) is a completely random process, the resin will still contain a small percentage of adjacent functionalized sites. In this study the loading was kept approximately constant at ca. 0.9 meq/g resin.

*Effects of Crosslinking*

While more highly crosslinked (ca. $\geq 20\%$) resins have the potential to provide greater so-called "site isolation," such "macroreticular" resins possess two drawbacks: smaller internal pores, inhibiting interaction of polymer-bound moieties with solution-phase reagents, and mechanical fragility resulting in difficulties with filtration and polymer reuse. The lightly crosslinked resins on the other hand have very large internal pores, on the order of $10^2$ Å, and are generally produced as quite robust beads, compatible with most of the usual physical operations of synthetic chemistry. The major differences that we observed between 1%- and 2%-crosslinked Merrifield's resins (E.g., Table 1, entries 5 and 6) came as somewhat of a surprise. All attempts to use the former produced final yields of PK products no better than those obtained than in homogeneous solution. Nevertheless, the existence of a large difference in both chain mobility and the mobility of substances within the pores of 1%-crosslinked resin, relative to more highly crosslinked analogs is supported by physical measurements. Regen has found that the degree of swelling of a crosslinked polymer by solvent is directly related to the mobility of both substances bound covalently to the polymer chains as well as the motion of molecules located within the solvent-swollen bead pores.[18] Both swelling of 1%-crosslinked polystyrene by benzene and rotational mobility of covalently bound nitroxyl radicals are some 40% greater than those observed for 2%-crosslinked polymer. Perhaps the proper context in which to view these results is the recognition that 2%-crosslinking is not 1% more than 1%-crosslinking, but *100% more*. Based upon our results, mutual interaction of polymer-bound sites is much more facile in the 1%-crosslinked resin on the time scale relevant to competition with reaction involving solution-phase species.

Using 2%-crosslinked resin, it was possible to "turn on" an alternative reaction pathway that was dependent upon intrachain interaction merely by adjusting the ratio of norbornadiene to polymer-bound alkyne. Reducing the quantity of diene from a five-fold excess to an equimolar amount shifts the reaction course from exclusive formation of the product of PK reaction of norbornadiene with a single alkyne to the product of PK cycloaddition at *both* of the diene's double bonds. This product can form only by the stepwise PK cycloaddition at one polymer-bound alkyne site, followed by polymer deformation to bring the polymer-bound product of single PK reaction within reacting distance of a second polymer-bound alkyne moiety—in competition against reaction of the latter with a solution-phase molecule of norbornadiene. The modest 20% yield probably reflects the decreasing polymer chain flexibility as intrachain chemistry occurs, because the latter is, in effect, increasing the overall degree of crosslinking.

### *Chain Length Effects*

Comparison of cycloaddition reactions of polymer-bound 4-pentyn-1-ol and 11-undecyn-1-ol show little difference in the yields of the respective PK cycloaddition products (Table 1, entries 6 and 9). Both proceed approximately three times better than the corresponding solution-phase processes, suggesting comparable inhibition of intrachain alkyne-alkyne interaction despite the chain length difference. However, in contrast to 4-pentyn-1-ol, whose reaction to give a "double" cycloaddition product was observed to occur only when the concentration of norbornadiene was reduced to approximately one equivalent, 10-undecyn-1-ol gives a small amount of the corresponding product even in the presence of excess norbornadiene. Thus the increased "spacer" length has compromised the kinetic inhibition of intrachain interactions to some extent.

The efforts to cyclize a propargyl alcohol derivative contend with the tendencies of both the alkyne-hexacarbonyldicobalt complex and the PK product to decompose by loss of the oxygen function from the propargylic carbon. Cobalt complexes of propargylic systems are strongly activated towards unimolecular substitution, a consequence of the stabilization by cobalt of the incipient cationic center.[19] The anomalous results with the ester-linked system, in which loss of the latter functionality was observed by IR, are consistent with such a mode of decomposition. Use of the trityl ether linker, a poorer leaving group whose cleavage chemistry is compatible with the final product, partially overcomes the problem (Table 1, entries 1-3).[20]

### *Other Alkene Substrates: Bracketing the Window*

Finally, there are the unusually poor results with norbornene, and the unusually good results with norbornenone derivative **6** (Table 1, entries 10-13). Both norbornene and norbornadiene are reactive towards low-valent transition metal systems, undergoing complexation and ultimate formation of coupled products that include, but are not limited to dimeric hydrocarbons and products of dimerization with CO insertion, viz., cyclopentanones.[21] It appears that the low norbornene PK yields in homogeneous solution and on the polymer are due to two separate effects. In solution, PK cycloaddition of norbornene competes against reactions involving multiple alkynes better than that of norbornadiene: the norbornene PK product forms in 29% yield, as opposed to 19% for the norbornadiene product.[22] In both cases, PK reaction is disfavored relative to other processes. On the polymer, suppression of interactions between multiple alkyne moieties provides a window for the *diene* to participate: interaction between solution-phase diene and polymer-bound alkyne competes successfully against interaction between either two polymer-bound alkynes or two solution-phase dienes. In contrast, given the same parameters in the case of norbornene, interaction between two solution-phase *alkenes* wins out over reaction with polymer-bound alkyne. We suspect that this observation is very likely a consequence of the well-established (but not necessarily particularly well-quantified) retardation of reaction rates associated with polymer attachment. Qualitatively one can associate the phenomenon with reduced diffusion parameters within the polymer matrix.

The outstanding results with alkene **6** present the other side of the coin: in the absence of an alkyne, the alkene in this case is essentially inert in the presence of dicobalt carbonyl complexes. Upon inhibition of alkyne-alkyne interaction, the system is essentially free of *any* process in competition with PK cycloaddition. The quantitative yield is all the more remarkable, because the alkene in this case is inherently *less* reactive towards PK chemistry than either norbornene or norbornadiene, based on the homogeneous solution-phase results. Clearly in this situation we have managed to strike an ideal balance involving sufficient inhibition of intrachain chemistry and sufficiently limited reactivity of the solution phase substrate to permit the desired reaction to completely dominate.

### *Conclusions*

Many of the practical problems that placed limitations on the scope of the PK reaction have been solved since we began examining polymer support strategies. Thus, using reaction promoters higher yields (though not necessarily similar stereoselectivities) have been obtained for the solution counterparts of several of the polymer-supported reactions described herein. A notable exception is the polymer-assisted cycloaddition of **6**, the highest-yield intermolecular PK reaction known. However, our goal was not to optimize the intermolecular PK reaction. Rather, it was to assess in a qualitative way the factors specific to a given reaction that determine whether a polymer-support strategy may be useful. Indeed, we recognize that these arguments are highly qualitative. The quantification of, for example, kinetic parameters is rendered difficult both by the multiphase character of the system as well as by the nature of the PK reaction itself, for which the mechanism is complex and, practically speaking, ill-suited for rigorous kinetic analysis. Nevertheless, we believe that this study addresses essential practical issues and may be used as a basis for a reasonable qualitative evaluation of polymer attachment as a *potential* solution for chemoselectivity problems in other chemical systems.

## EXPERIMENTAL SECTION

**General.** General procedures associated with polymer-supported synthesis have been described previously.[9] Polymer-supported aroyl and trityl chlorides were prepared from 1%- and 2%-crosslinked Merrifield's resin according to literature procedures.[8,15] In order to remove surface impurities remaining from the manufacturing process of the unfunctionalized polystyrene-divinybenzene resin, it was washed as follows. Using an overhead stirrer 100.0 g of 2%-crosslinked PS-DVB resin was successively mixed and filtered from each of the following: (1) 1 L of 1 N aq NaOH (80°C/15 min), (2) 1 L of 1 N aq HCl (70°C/15 min), (3) 800 mL of 2:1 dioxane/2 N NaOH (80°C/15 min), (4) 800 mL of 2:1 dioxane/2 N HCl (80°C/15 min), (5) 800 mL $H_2O$ (80°C), and (6) 800 mL DMF (80°C). The resin was filtered through a large sintered glass funnel, and washed at RT with (1) 2 x 250 mL 2 N HCl/MeOH, (2) 2 x 250 ml $H_2O$, (3) 2 x 250 mL MeOH, (4) 2 x 250 mL (3:1) $CH_2Cl_2$/MeOH, and (5) 2 x 250 mL (10:1) $CH_2Cl_2$/MeOH, and air and vacuum dried. All solvents and liquid reagents were purified and dried using common procedures and, where appropriate, stored over activated 3 Å molecular sieves. Dicobaltoctacarbonyl ($Co_2(CO)_8$) was supplied by Strem Corporation as a solid solution stabilized with 5-10% hexane which was stored refrigerated under an inert atmosphere

**2%-Crosslinked PS-DVB Polymer-bound 4-Pentynyl Benzoate (3b-2).** 2%-Crosslinked PS-DVB benzoyl chloride resin (2.06 g) was mixed with pyridine (30 mL) and 4-pentyn-1-ol (1.0 g, 11.9 mmol). The suspension was stirred under Ar at rt for 1 day, followed by 1 day at 100°C. After this time the mixture was filtered through a fine porosity frit, and the resin washed with 1:1 pyridine/$H_2O$ (3 x 30 mL), $H_2O$ (3 x 25 mL), 95% EtOH (3 x 25 mL), and $Et_2O$ (3 x 25 mL). After drying for 2 days in vacuo at rt, a light brown powdery resin (**3b-2**, 1.95 g) was recovered: FTIR 3303, 2119, 1718, 1701, 1272 $cm^{-1}$.

**1%-Crosslinked PS-DVB Polymer-bound 4-Pentynyl Benzoate (3b-1).** In a manner similar to that above, 1%-crosslinked PS-DVB benzoyl chloride (1.98 g) was converted to light brown pentynyl ester resin **3b-1** (1.80 g): FTIR 3305, 2121, 1717, 1273 cm$^{-1}$.

**2%-Crosslinked PS-DVB Polymer-bound Propynyl Benzoate (3a)** Similarly, 2%-crosslinked PS-DVB benzoyl chloride resin (30.4 g) was converted to the polymer-linked propynyl ester, which was recovered after drying as a dark brown, slightly lumpy powder (**3a**, 30.6 g): FTIR 3295, 2110, 1726, 1266 cm$^{-1}$.

**2%-Crosslinked PS-DVB Polymer-bound 10-Undecynyl Benzoate (3c)** Similarly, 2%-crosslinked PS-DVB benzoyl chloride (2.00 g) was converted to the polymer-linked undecynyl ester, which was recovered as a dark brown, slightly lumpy resin (**3c**, 3.10 g): FTIR 3303, 2120, 1717, 1273 cm$^{-1}$.

**(3b-2)•Hexacarbonyldicobalt complex (4b-2).** 2%-Crosslinked PS-DVB pentynyl ester resin (**3b-2**, 1.83 g) was stirred with $Co_2(CO)_8$ (1.22 g, 3.6 mmol) in $C_6H_6$ (35.0 mL) under Ar for 6 hr at rt. The reddish suspension was rapidly filtered, and the resin quickly washed with several portions of $C_6H_6$ until the filtrate became colorless, followed by several rinses with $Et_2O$. After vacuum drying overnight, a dark maroon colored resin (**4b-2**, 2.18 g) was recovered: FTIR 2092, 2051, 2015, 1718, 1270 cm$^{-1}$.

**(3b-1)•Hexacarbonyldicobalt complex (4b-1).** In a manner similar to that above, 1%-crosslinked pentynyl ester (**3b-1**, 1.80 g) was converted to a reddish brown $Co_2(CO)_6$-complexed resin (**4b-1**, 1.94 g): FTIR 2091, 2047, 2020, 1726, 1255 cm$^{-1}$.

**3a•Hexacarbonyldicobalt complex (4a).** Similarly, 2%-crosslinked propynyl ester resin (**3a**, 12.02 g) was converted to the maroon colored $Co_2(CO)_6$-complexed resin (**4a**, 12.31 g): FTIR 2097, 2058, 2024, 1719, 1262 cm$^{-1}$.

**3c•Hexacarbonyldicobalt complex (4c).** Similarly, 2%-crosslinked undecynyl ester resin (**3c**, 1.75 g) was converted in benzene to the reddish, powdery $Co_2(CO)_6$-complexed resin (**4c**, 2.00 g): FTIR 2091, 2051, 2020, 1715, 1275 cm$^{-1}$.

**2%-Crosslinked PS-DVB Polymer-bound 4-(3-Benzoyloxypropyl)tricyclo[5.2.1.0]dec-4,8-dien-3-one (5b-2).** 2%-Crosslinked PS-DVB pentynyl-$Co_2(CO)_6$-complexed resin (**4b-2**, 2.18 g) was stirred with $C_6H_6$ (35 mL) under Ar. After allowing for polymer bead swelling, 2,5-norbornadiene (1.10 g, 11.9 mmol) was added. The mixture was heated to reflux under 1 atm of CO for 7 hr, and the progress of the reaction was followed by the periodic removal of a small aliquot of resin for IR analysis. After it was apparent that the cobalt-alkyne complex had been consumed and the reaction was complete, the mixture was cooled and filtered through a fine porosity frit. The recovered resin was washed with $C_6H_6$ (4 x 30 mL), and $Et_2O$ (4 x 30 mL), and vacuum dried to yield a bluish resin (**5b-2**, 2.21 g): FTIR 1717, 1697, 1272 cm$^{-1}$.

**1%-Crosslinked PS-DVB Polymer-bound 4-(3-Benzoyloxypropyl)tricyclo[5.2.1.0]dec-4,8-dien-3-one (5b-1).** In a manner similar to that above, 1%-crosslinked pentynyl-$Co_2(CO)_6$-complexed resin (**4b-1**, 1.94 g) was reacted with freshly distilled norbornadiene (0.87 g, 9.41 mmol) in $C_6H_6$ to yield the polymer-linked cycloaddition product (**5b-1**, 1.79 g): FTIR 1701, 1274 cm$^{-1}$.

**2%-Crosslinked PS-DVB Polymer-bound 4-(9-Benzoyloxynonyl)tricyclo[5.2.1.0]dec-4,8-dien-3-one (5c)** Similarly, 2%-crosslinked nonynyl-$Co_2(CO)_6$-complexed resin (**4c**, 2.00 g) was converted to a dark brown, powdery product (**5c**, 1.96 g): FTIR 1721, 1713, 1273 cm$^{-1}$.

**2%-Crosslinked PS-DVB Polymer-bound 4-(3-Benzoyloxypropyl)tricyclo[5.2.1.0]dec-4-en-3-one (8).** The pentynyl-$Co_2(CO)_6$-complexed resin (**4b-2**, 2.17 g) was stirred with freshly distilled, dry norbornene (bicyclo[2.2.1]hept-2-ene) (1.13 g, 13.8 mmol) in $C_6H_6$ (40 mL) and heated to reflux (80°C) under 1 atm of CO. During this time, reaction progress was monitored by periodic removal and work-up of a small aliquot of the suspension, followed by IR analysis. After 18 hr, the mixture was cooled, filtered, and the resin was washed with $CHCl_3$ (4 x 20 mL), $H_2O$ (4 x 20 mL), EtOH (4 x 20 mL), and $Et_2O$ (4 x 20 mL). A grayish-violet resin (**8**, 2.09 g) was recovered after vacuum drying overnight: FTIR 1718, 1700, 1271 cm$^{-1}$.

**4-(3-Hydroxypropyl)tricyclo[5.2.1.0]deca-4,8-dien-3-one (2b).**[3f] 2%-Crosslinked PS-DVB polymer-bound pentynyl/norbornadiene cycloadduct (**5b-2**, 2.39 g) was stirred in THF (30 mL). After a few minutes to allow the resin beads adequate time to swell, 10.0 g KOH dissolved in 10.0 mL $H_2O$ was added, along with 0.1 g of *n*-$Bu_4NBr$. The suspension was heated to reflux with stirring for 2 days under Ar. After this time, the suspension was filtered and washed with $CHCl_3$ (4 x 25 mL), $H_2O$ (4 x 25 mL), and 95% EtOH (4 x 25 mL). IR analysis of the residual grayish resin after air drying showed strong IR signals at 1551 and 1318 $cm^{-1}$. The combined filtrates were transferred to a separatory funnel, the organic phase was removed, and the remaining aqueous material was extracted with $CHCl_3$ (3 x 25 mL). The combined organic extracts were washed with satd aq NaCl (2 x 30 mL), and dried ($Na_2SO_4$). A clear, colorless, sweet smelling oil (**2b**, 0.208 g) was obtained in 57% yield after filtration, solvent evaporation, and chromatotron purification ($R_f = 0.36$ on $SiO_2$ with 6:3:1 $Et_2O$/hexane/$CH_2Cl_2$ under Ar): FTIR (neat) 3415, 3060, 1695, 1624, 1055 $cm^{-1}$; $^1H$-NMR (300 MHz, $CDCl_3/D_2O$) $\delta$ 7.21 (m, 1H), 6.25 (dd, $J = 5.5$, 3.1 Hz; 1H), 6.19 (dd, $J = 5.5$, 3.1 Hz; 1H), 3.58 (t, $J = 6.3$ Hz; 2H), 2.88 (m, 1H), 2.72 (m, 1H), 2.66 (m, 1 H), 2.27 (m, 3H), 1.71 (m, 2H), 1.38 (d, $J = 9.3$ Hz; 1H), 1.19 (d, $J = 9.3$ Hz; 1H) ppm; $^{13}C$-NMR (75 MHz, $CDCl_3$) $\delta$ 210.60, 160.01, 150.09, 138.33, 136.98, 61.54, 52.52, 47.74, 43.57, 42.86, 41.13, 31.21, 20.98; HRMS (EI+): calcd for $C_{13}H_{16}O_2$ (M+) 204.1150, found 204.1129; Anal: calcd for $C_{13}H_{16}O_2$ C, 76.44%; H, 7.90%, found C, 75.83%; H, 8.03%.

In a manner similar to that above, 1%-crosslinked PS-DVB bound pentynyl/norbornadiene cycloadduct (**5b-1**, 1.75 g) was hydrolyzed to provide after chromatographic purification alcohol **2b**, 39.0 mg, corresponding to a yield of 12%.

**4-(3-Hydroxypropyl)tricyclo[5.2.1.0]dec-4,8-dien-3-one (2b). Preparation under Homogenous Solution-Phase Conditions.** 4-Pentyn-1-ol (1.67 g, 1.99 mmol) was dissolved in 120 mL $C_6H_6$. $Co_2(CO)_8$ (10.03 g, 2.94 mmol) was added, and the mixture was stirred 3 hr at rt under Ar. 2,5-Norbornadiene (6.8 g, 7.4 mmol) was added, the flask was fitted with a CO balloon and reflux condenser, and the solution was stirred for 6 hr at 80°C, during which time the progress of the reaction was monitored by thin layer chromatography. After cooling, the dark reddish solution was passed through short column of silica gel. Elution with *n*-hexane, followed by $Et_2O$ allowed for the separation of most Co-containing species. The remainder was removed by treatment of with $Fe(NO_3)_3{\bullet}9H_2O$ (59.5 g, 0.147 mol) in distilled 95% EtOH (330 mL) at 0°C for 1.5 hr. After partial evaporation of the solvent, $H_2O$ (200 mL) was added and the mixture was extracted with $Et_2O$ (3 x 200 mL). The combined extracts were washed with $H_2O$, satd aq NaCl, and dried with $MgSO_4$. Filtering and evaporation of the solvents provided a crude oil. Purification by flash chromatography ($SiO_2$, with 2% MeOH/$CHCl_3$) provided a colorless, viscous oil (**2b**, 0.764 g, 19% yield).

**4-(3-Hydroxypropyl)tricyclo[5.2.1.0]dec-4-en-3-one (9).** 2%-Crosslinked PS-DVB polymer-bound pentynyl/norbornene cycloadduct (**8**, 2.09 g) was stirred in THF (30 mL) under Ar. 9.0 g KOH in 9.0 g water was added, along with 0.10 g of *n*-$Bu_4NBr$. The suspension was refluxed with stirring for 2 days under Ar, after which time the mixture was filtered and washed repeatedly with $CHCl_3$ (4 x 20 mL), $H_2O$ (4 x 20 mL), and EtOH (4 x 20 mL). A fine, black powder (1.83 g) was recovered upon air drying. IR analysis of this material indicated a slightly broadened peak at 1380 $cm^{-1}$. The combined filtrates were added to a separatory funnel. After removal of the organic layer, the aqueous phase was extracted with $CHCl_3$ (3 x 50 mL). The combined organic material was washed with $H_2O$ (2 x 50 mL) and satd aq NaCl (2 x 50 mL), and dried over $Na_2SO_4$. Evaporation of the solvent provided a dark yellow oil, which was purified by flash chromatography ($R_f = 0.46$ on silica ($Et_2O$)); column gradient eluted with 1:1 $CH_2Cl_2/Et_2O$) to provide a colorless oil (**12**, 26.0 mg, 0.126 mmol, 7.4% yield. A second trial of this experiment provided a yield of 8.1%. A small amount of the product oil was vacuum distilled (160°C @ 0.10 torr): FTIR (neat) 3415, 1693, 1626, 1055 $cm^{-1}$; $^1H$-NMR (300 MHz, $CDCl_3/D_2O$) $\delta$ 7.16 (d, $J = 1.1$ Hz; 1H), 3.62 (t, $J = 6.0$ Hz; 2H), 2.57 (br s, 1H), 2.33 (br s, 1H), 2.27 (dt, $J = 7.3$, 1.0 Hz; 2H), 2.18 (d, $J = 5.0$ Hz; 1H), 2.14 (d, $J =$

2.9 Hz; 1H), 1.76-1.51 (m, 4H), 1.27 (m, 2H), 0.94 (br s, 2H); $^{13}$C-NMR (75 MHz, $CDCl_3$) $\delta$ 211.93, 160.06, 148.68, 61.38, 53.78, 48.22, 38.90, 37.86, 31.19, 30.95, 28.95, 28.31, 20.61; MS *m/e* = 207 (M+1), 189 ((M+1)-$H_2O$); HRMS (FAB+): calcd for $C_{13}H_{19}O_2$ (M+1) 207.1385, found 207.1365.

**4-(3-Hydroxypropyl)tricyclo[5.2.1.0]dec-4-en-3-one (9). Preparation under Homogenous Solution-Phase Conditions.** Dried 4-pentyn-1-ol (0.42 g, 5.0 mmol) was dissolved in 25 mL $C_6H_6$. $Co_2(CO)_8$ (2.65 g, 7.75 mmol) was added at once, and the mixture was stirred for 3.5 hr under Ar at rt. The solvent was removed under vacuum, and the viscous crude oil was passed through a florisil column and eluted first with *n*-hexane, followed by $Et_2O$. The product fraction was identified by TCL and, after removal of the solvents, IR analysis.(1.78 g, 96% yield): FTIR (neat) 3329, 2096, 2046, 1062 cm$^{-1}$.

The pentynyl-$Co_2(CO)_6$ complex (1.78g, 1.67 mmol) was mixed with 40 mL $C_6H_6$. Freshly distilled norbornene (2.11 g, 22.4 mmol) was added, and the solution was heated to reflux under CO (balloon) for 14 hours. After this time the mixture was cooled, and the solvent was removed under reduced pressure. The recovered viscous oil was passed through a florisil plug and gradient-eluted with hexane and then MeOH/$Et_2O$ to provide a partially purified product. Column chromatography ($SiO_2$, with 30% $CH_2Cl_2$/$Et_2O$) provided a clear, colorless oil after removal of the solvents (**9**, 0.297 g, 29%).

**4-(9-Hydroxynonyl)tricyclo[5.2.1.0]dec-4,8-dien-3-one (2c).** In a manner similar to that described for **2b** above, the 2%-crosslinked PS-DVB bound undecynyl/norbornadiene cycloadduct (**5c**, 10.45 g) was hydrolyzed from the polymer support. After workup, filtration, and evaporation of the solvents, a viscous, dark brown, sweet smelling oil (1.87 g) was recovered. Chromatotron purification (*Rf* = 0.37 on $SiO_2$ (1% MeOH/$Et_2O$)) gradient eluted with 1:1 $CHCl_3$/hexane, then pure $CHCl_3$, and finally 2% MeOH/$CHCl_3$) provided a faint yellow oil (**2c**, 1.30 g, 4.49 mmol) in 56% yield: FTIR (neat) 3441, 3060, 1699, 1623, 1600, 1057 cm$^{-1}$; $^1$H-NMR (300 MHz, $CDCl_3/D_2O$) $\delta$ 7.14 (m, 1H), 6.26 (dd, *J* = 5.6, 3.1 Hz; 1H), 6.18 (dd, *J* = 5.6, 3.1 Hz; 1H), 3.62 (t, *J* = 6.3 Hz; 2H), 2.92 (br s, 1H), 2.69 (m, 1H), 2.65 (m, 1H), 2.26 (m, 1H), 2.15 (dt, *J* = 4.5, 1.2 Hz; 2H), 1.55 (m, 2H), 1.45 (m, 2H), 1.41-1.28 (m, 11H), 1.20 (d, *J* = 9.3 Hz; 1H); $^{13}$C-NMR (75 MHz, $CDCl_3$) $\delta$ 209.98, 158.69, 150.81, 138.33, 137.00, 62.99, 52.50, 47.59, 43.58, 42.95, 41.13, 32.75, 29.40, 29.32, 29.23, 27.75, 25.68, 24.93; MS *m/e* = 289 (M+1), 271(M-$H_2O$); HRMS (FAB+): calcd for $C_{19}H_{29}O_2$ (M+1) 289.2089, found 289.2186; Anal: calcd for $C_{19}H_{28}O_2$ C, 79.12%, H, 9.78%; found: C, 77.53%; H: 9.77%.

**4-(9-Hydroxynonyl)tricyclo[5.2.1.0]dec-4,8-dien-3-one (2c). Preparation under Homogenous Solution-Phase Conditions.** In a manner similar to those described for **2b** and **9** above,, dry 10-undecyn-1-ol (0.84 g, 5.0 mmol) was converted in $C_6H_6$ to the corresponding alkyne complex by rt reaction with $Co_2(CO)_8$ under Ar. After 3 hr distilled 2,5-norbornadiene (2.53 g, 7.42 mmol) was added, and the mixture was heated to reflux for 13 hr under CO. Chromatographic purification provided a clear, colorless oil (**2c**, 0.196 g, 13% yield).

**4,10-Bis-(3-hydroxypropyl)-*exo,exo*-tetracyclo[5.5.1.0$^{2,6}$.0$^{8,12}$]trideca-4,9-diene-3,11-dione (10b).** 2%-Crosslinked PS-DVB pentynyl ester resin (**3b-2**, 0.893 g) was treated with $Co_2(CO)_8$ (0.60 g, 1.8 mmol) in $C_6H_6$ for 2 hr under $N_2$ at rt. After removal of the solvent and washing of the resin with $C_6H_6$ and $Et_2O$, fresh $C_6H_6$ (30 mL) was added, along with 2,5-norbornadiene (0.083 g, 0.90 mmol). The mixture was heated to reflux for 14 hr under CO. After this time, the resin was collected by filtration and washed with $CHCl_3$ (3 x 20 mL), $H_2O$ (3 x 20 mL), EtOH (3 x 20 mL), and $Et_2O$ (3 x 20 mL), and vacuum dried. The polymer-linked cycloadduct was stirred with dry THF (30 mL) under Ar. 5.0 g KOH in 5.0 mL $H_2O$ was added, along with 0.05 g *n*-$Bu_4NCl$. The mixture was heated to reflux for 2 days, after which time the resin was collected by filtration and washed with $CHCl_3$ (3 x 20 mL), $H_2O$ (3 x 20 mL), EtOH (3 x 20 mL). The combined extracts were added to a separatory funnel, and the aqueous material was extracted with $CHCl_3$ (3 x 25 mL). The combined organic material was washed with $H_2O$ (2 x 30 mL), satd aq NaCl (2 x 30 mL), and dried over $Na_2SO_4$. Evaporation of the solvent, followed by chromatography (florisil, 3%

MeOH/$Et_2O$) provided **10b** (25 mg, 20% yield): FTIR ($CDCl_3$) 3457, 1694 $cm^{-1}$; $^1H$-NMR (300 MHz, $CDCl_3$) $\delta$ 7.18 (s, 2H), 3.55 (t, $J$ = 6.1 Hz; 4H), 2.78 (m, 2H), 2.40-2.20 (m, 10H), 1.68 (q, $J$ = 6.9 Hz; 4H), 0.76 (d, $J$ = 4.3 Hz; 2H); HRMS (FAB+): calcd for $C_{19}H_{25}O_4$ (M+1) 317.1753, found 317.1756.

**4-(3-Hydroxypropyl)-7-methyltricyclo[5.2.1.0]dec-4-en-3,8-dione (7a) and 4-(3-hydroxypropyl)-1-methyltricyclo[5.2.1.0]dec-4-en-3,9-dione (7s).** 2%-Crosslinked PS-DVB polymer-bound pentynyl ester (**3b-2**, 1.14 g) was suspended in 20 mL $C_6H_6$. $Co_2(CO)_8$ was added at once (1.0 g, 2.9 mmol), and the mixture was stirred at rt under Ar for 3 hr. Distilled 1-methyl-5-norbornene-2-one (1.0 g, 9.1 mmol) was added, and the mixture was refluxed under CO (balloon) for 2 days. After this time the suspension was cooled and the resin was collected by filtration through a medium porosity fritted glass funnel, followed by rinsing with $CHCl_3$ (3 x 20 mL), $H_2O$ (3 x 20 mL), EtOH (3 x 20 mL), and $Et_2O$ (3 x 20 mL). Drying under vacuum provided 2.02 g of black powder: FTIR (KBr) 3025, 1747, 1698, 1265 $cm^{-1}$. This resin was next subjected to hydrolysis in a manner similar to that previously described, providing a crude oil (0.431 g) after removal of the solvent. Chromatotron purification ($SiO_2$, 3% MeOH/$Et_2O$) provided the products (**7a** and **7s**, 0.402 g, 1.72 mmol, 99% combined yield, as a 30:70 ratio of regioisomers (**7a**:**7s**).

For **7a**: IR ($CDCl_3$) 3621, 3417, 3021, 1734, 1697 $cm^{-1}$; $^1H$-NMR (300 MHz, $CDCl_3$) $\delta$ 7.14 (m, 1H), 3.52 (t, $J$ = 6.2 Hz; 2H), 2.92 (br s, 1H), 2.65 (br d, $J$ = 4.0 Hz; 1H), 2.59 (br s, 1H), 2.38 (d, $J$ = 5 Hz; 1H), 2.22 (m, 2H), 1.99 (m, 2H), 1.65 (q, $J$ = 6.4 Hz; 2H), 1.40 (d, $J$ = 11.2 Hz; 1H), 1.30 (d, $J$ = 11.2 Hz; 1H), 1.09 (s, 3H); $^{13}C$-NMR (75 MHz, $CDCl_3$) $\delta$ 216.56, 208.93, 155.22, 150.50, 61.27, 54.60, 53.16, 45.38, 43.40, 36.06, 35.28, 30.12, 21.01, 10.80; HRMS (EI+): calcd for $C_{14}H_{18}O_3$ (M+) 234.1256, found 234.1251.

For **7s**: IR ($CDCl_3$) 3584, 3475, 3020, 1745, 1701 $cm^{-1}$; $^1H$-NMR (300 MHz, $CDCl_3$) $\delta$ 7.21 (m, 1H), 3.52 (t, $J$ = 6.2 Hz; 2H), 2.90 (br s, 2H), 2.45 (br d, $J$ = 3.2 Hz; 1H), 2.22 (m, 3H), 1.99 (m, 2H), 1.65 (q, $J$ = 7.4 Hz; 2H), 1.40 (d, $J$ = 11.1 Hz; 1H), 1.26 (d, $J$ = 11.1 Hz; 1H), 1.12 (s, 3H); $^{13}C$-NMR (75 MHz, $CDCl_3$) $\delta$ 215.49, 207.04, 158.44, 150.28, 61.29, 54.53, 48.48, 48.39, 42.39, 36.21, 35.04, 30.74, 20.84, 10.02.

**4-(3-Hydroxypropyl)-7-methyltricyclo[5.2.1.0]dec-4-en-3,8-dione (7a) and 4-(3-hydroxypropyl)-1-methyltricyclo[5.2.1.0]dec-4-en-3,9-dione (7s). Preparation under Homogenous Solution-Phase Conditions.** 4-Pentyn-1-ol (0.168 g, 2.0 mmol) was mixed with $Co_2(CO)_8$ (1.30 g, 3.81 mmol) in 30 mL $C_6H_6$ at rt under $N_2$. After stirring for 3 hr, 1-methyl-5-norbornen-2-one (1.0 g, 8.2 mmol) was added, and the mixture was stirred at 80°C under CO. After this time, the solution was cooled and passed through a short column of silica gel. Hexane elution removed unreacted $Co_2(CO)_8$ and related by-products. This was followed by elution with 1% MeOH/$Et_2O$ to recover the crude mixture of products. Chromatotron separation provided an impure 40:60 (**7a**:**7s**) mixture of isomers (ca. 8% yield), as determined by $^1H$-NMR integration.

**2%-Crosslinked PS-DVB Polymer-bound Propynyl Trityl Ether (11).** 2%-Crosslinked PS-DVB trityl chloride resin (1.5 g) was suspended in dry pyridine (25 mL) under argon. Propynol (1.4 g, 25 mmol) was added, and the mixture was stirred for 2 days at rt. After filtering, the resin was washed with 3 x 25 mL $C_6H_6$ (3 x 25 mL) and $Et_2O$ (4 x 30 mL). After vacuum drying, a lumpy, light yellow resin was recovered (**11**, 1.29 g): FTIR (KBr) 3295, 2160 $cm^{-1}$.

**14•Dicobalthexacarbonyl complex (12).** 2%-Crosslinked PS-DVB propynyl trityl ether resin (**11**, 1.29 g) was stirred in $C_6H_6$ (30 mL) under Ar. $Co_2(CO)_8$ (2.80 g, 8.2 mmol) was added and the mixture was stirred for 4 hr at rt. The mixture was rapidly filtered in air, and the resin was washed with $C_6H_6$ (4 x 25 mL) and $Et_2O$ (4 x 25 mL) until the filtrate was colorless. A dark red, powdery product was obtained after vacuum drying (**12**, 1.49 g): FTIR (KBr) 2095, 2056, 2004 $cm^{-1}$.

**2%-Crosslinked PS-DVB Polymer-bound 4-(Hydroxymethyl)tricyclo[5.2.1.0]dec-4,8-dien-3-one Trityl Ether (13).** 2%-Crosslinked PS-DVB propynyl-$Co_2(CO)_6$-complexed trityl ether resin (**12**, 1.49 g) was stirred in $C_6H_6$ (40 mL) with distilled 2,5 norbornadiene (1.65 g, 18 mmol). After heating to 80°C for 7 hr under CO, the suspension was filtered and the resin was washed with $C_6H_6$ (4 x 20 mL), EtOH (2 x 20 mL) and dried at rt under high vacuum. A light brown, powdery resin was recovered (**13**, 1,49 g): FTIR (KBr) 1699, 1030 $cm^{-1}$.

**4-(Hydroxymethyl)tricyclo[5.2.1.0]dec-4,8-dien-3-one (2a).**[20] 2%-Crosslinked PS-DVB polymer-linked propynyl/norbornadiene cycloadduct (**13**, 4.39 g) was mixed with 0.3 N anhydrous HCl in 1,4-dioxane (90 mL). After stirring under Ar for 2 days, the resin was filtered and washed with EtOH (25 mL), $H_2O$ (8 x 30 mL), EtOH (2 x 30 mL), and $Et_2O$ (4 x 30 mL). The organic phase was separated and the aqueous layer extracted with $Et_2O$ (3 x 100 mL). The combined organic layers were washed with $H_2O$ (2 x 100 mL), satd aq NaCl (2 x 100 mL), and dried over $MgSO_4$. After evaporation of the solvent, a brownish oil was recovered. Chromatotron purification ($R_f$ = 0.89 ($SiO_2$, 20% $Et_2O/CH_2Cl_2$)) provided the product (**2a**, 0.1845 g, 0.83 mmol, 36% yield): FTIR (neat) 3391, 3063, 1709, 1630, 1055 $cm^{-1}$; $^1H$-NMR (300 MHz, $C_6D_6/D_2O$) $\delta$ 6.82 (d, $J$ = 1.3 Hz; 1H), 5.92 (dd, $J$ = 5.4, 3.1 Hz; 1H), 5.85 (dd, 1H), 3.93 (dd, $J$ = 14.2, 1.1 Hz; 1H), 3.85 (dd, $J$ = 14.2, 1.1 Hz; 1H), 2.77 (br s, 1H), 2.18 (br s, 2H), 2.02 (dd, $J$ = 5.1, 1.0 Hz; 1H), 1.14 (d, $J$ = 8.1 Hz; 1H), 0.98 (d, $J$ = 8.1 Hz; 1H); $^{13}C$-NMR (75 MHz, $C_6D_6$) $\delta$ 205.11, 161.33, 146.61, 138.54, 137.34, 52.85, 47.86, 44.15, 43.42, 41.46, 36.52.

**Selected Procedures for the Determination of the Polymeric Support Degree of Functionalization. Dicobalthexacarbonyl-based Gravimetric Standardization of 2%-Crosslinked PS-DVB Polymer-bound Pentynyl Trityl Ether.** 2%-Crosslinked pentynyl trityl ether resin (1.90 g) was stirred in 50 mL $C_6H_6$ under Ar. Excess $Co_2(CO)_8$ (4.00 g, 11.7 mmol) was added, and the mixture was stirred for 3 hr at rt. After this time, the suspension was carefully transferred to a pre-weighed Gooch crucible, and washed repeatedly with $C_6H_6$ until the filtrate was clear and colorless. A final rinse with $Et_2O$ was followed by vacuum drying of the resin to constant weight). For this particular batch of resin, the observed weight gain of 0.37 g corresponded to a degree of functionalization of 0.68 meq/g. IR analysis after weighing confirmed that the complexation of the available alkyne functionality was complete.

**Dicobalthexacarbonyl-based Gravimetric Standardization of 2%-Crosslinked PS-DVB Polymer-bound Pentynyl Benzoate (3b-2).** In a similar manner 2%-crosslinked PS-DVB pentynyl ester resin (**3b-2**, 2.05 g) was converted quantitatively to the pentynyl-$Co_2(CO)_6$ resin (**4b-2**, 2.56 g) after vacuum drying: FTIR (KBr) 2092, 2052, 2015 $cm^{-1}$. The degree of functionalization was determined gravimetrically to be 0.87 meq of alkyne function per gram of uncomplexed starting resin.

**'On-Off' Standardization of 2%-Crosslinked PS-DVB Polymer-bound Undecynyl Benzoate (3c).** 2%-Crosslinked benzoyl chloride resin (2.00 g) was suspended in 20 mL pyridine under $N_2$. Pure 10-undecyn-1-ol (1.50 g, 8.91 mmol) was added and the mixture was stirred for 1 day at rt, followed by 1 day at 100°C. The suspension was cooled, filtered, and the recovered polymer washed with 1:1 pyridine/$H_2O$ (3 x 20 mL), $H_2O$ (3 x 20 mL), EtOH (3 x 20 mL), and $Et_2O$ (3 x 20 mL). Drying in vacuo at rte overnight provided a light brown resin (**3c**, 2.13 g). IR of an inconsequential amount of this resin indicated that the polymer loading had occurred quantitatively. Peaks attributable to the undecynyl moiety (3301, 2115 $cm^{-1}$), as well as the ester function (1717, 1273 $cm^{-1}$) were all prominent . Likewise, peaks from the starting carboxylic acid at ca. 1720 and 1690 $cm^{-1}$ were absent.

Base hydrolysis of the resin (**3c**, 2.13 g) was carried out following the general procedure. After allowing sufficient time for a complete reaction, the resin was filtered and thoroughly rinsed with $CHCl_3$ (3 x 25 mL), $H_2O$ (3 x 25 mL), and EtOH (3 x 25 mL). The combined filtrate was washed with $H_2O$, satd aq NaCl, and dried over $Na_2SO_4$. Complete removal of the solvents (confirmed by $^1H$-NMR) provided the recovered alcohol (0.340 g, 2.02 mmol). Based on this figure, the degree of functionalization (was determined to be 0.95 mmol/g for this batch of the polymeric ester.

**'On-Off' Standardization of 2%-Crosslinked PS-DVB Polymer-bound Benzoic Acid.** In a manner similar to the previous procedure, 2%-crosslinked PS-DVB benzoyl chloride resin (1.00 g) was functionalized using an excess of purified 3-butyn-1-ol/norbornadiene cycloadduct (0.318 g, 1.67 mmol) which had been prepared in a previous and unrelated experiment. After attachment of the alcohol and work-up, the polymeric ester was subjected to base hydrolysis, which provided after work-up and removal of solvents the cycloadduct (0.125 g, 0.657 mmol). This figure corresponds to 0.657 meq per gram of acyl halide resin. Having established this figure, another sample of the same batch of the acyl chloride (1.00 g) was converted as previously described to the polymeric pentynyl ester (**3b-2**, yield 0.74 g). IR analysis indicated that all of the acyl chloride function had been converted to the ester. Thus, since this mass of the latter possessed the same degree of functionalization as that present within the initial resin, 0.657 mmol of the ester function per 0.74 g of the ester resin corresponds to 0.89 milliequivalents of function per gram of **3b-2**.

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## REFERENCES AND NOTES

1. (a) Khand, I. U.; Knox, G. R.; Pauson, P. L.; Watts, W. E.; Foreman, M. I. *J. Chem. Soc., Perkin I* **1973**, 977. (b) Pauson, P. L. In *Organometallics in Organic Synthesis*; de Meijere, A.; tom Dieck H., Eds.; Springer-Verlag: Berlin, 1988. (c) Schore, N. E. *Chem. Rev.* **1988**, *88*, 1081. (d) Schore, N. E. In *Organic Reactions*; Paquette, L.A., Ed.; John Wiley and Sons, Inc.: New York, 1991; Vol. 40. (e) Schore, N. E. In *Comprehensive Organometallic Chemistry II*; Hegedus, L. S., Ed.; Pergamon Press: Oxford, 1995; Vol. 7.

2. Schore, N. E.; La Belle, B. E.; Knudsen, M. J.; Hope, H.; Xu, X.-J. *J. Organomet. Chem.* **1984**, *272*, 435.

3. (a) Smit, W. A.; Gybin, A. S.; Simonyan, S. O.; Shashkov, A. S.; Tarasov V. A.; Ibragimov, I. I. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1985**, 2650. (b) Smit, W. A.; Simonian, S. O.; Tarasov, V. A.; Mikaelian, G. S.; Gybin, A. S.; Ibrigamov, I. I.; Caple, R.; Froen, D. E.; Kreager, A. *Synthesis* **1989**, 472. (c) Billington, D. C.; Helps, I. M.; Pauson, P. L.; Thomson, W.; Willison, D. *J. Organometal. Chem.* **1988**, *354*, 233. (d) Shambayati, S.; Crowe, W. E.; Schreiber, S. L. *Tetrahedron Lett.* **1990**, *31*, 5289. (e) Rautenstrauch, V.; Mégard, P.; Conesa, J.; Küster, W. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 1413. (f) Chung, Y. K.; Lee, B. Y.; Jeong, N.; Hudecek, M.; Pauson, P. L. *Organometallics* **1993**, *12*, 220. (g) Krafft, M. E.; Scott, I. L.; Romero, R. H.; Felbelmann, S.; Van Pelt, C. E. *J. Am. Chem. Soc.* **1993**, *115*, 7199. (h) Jeong, N.; Chung, Y. K.; Lee, B. Y.; Lee, S. H.; Yoo, S.-E. *SYNLETT* **1991**, 204. (i) Smit, W. A.; Kireev, S. L.; Nefedov, O. M.; Tarasov, V. A. *Tetrahedron Lett.* **1989**, *30*, 4021. (j) Thommer, M.; Gerber, P.; Keese, R. *Chimia* **1991**, *45*, 23 (k) van der Waals, A.; Keese, R. *J. Chem Soc., Chem. Comm.* **1992**, 570. (l) Hoye, T. R.; Suriano, J. A. *J. Org. Chem.* **1993**, *58*, 1659. (m) Lee, B. Y.; Moon, H.; Chung, Y. K.; Jeong, N. *J. Am. Chem. Soc.* **1994**, *116*, 2163. (n) Verdaguer, X.; Moyano, A.; Pericás, M.; Riera, A.; Bernardes,V.; Greene, A. E.; Alvarez-Larena, A.; Piniella, J. F. *J. Am. Chem. Soc.* **1994**, *116*, 2153. (o) Jeong, N.; Hwang, S. H.; Lee, Y.; Chung, Y. K. *J. Am. Chem. Soc.* **1994**, *116*, 3159. (p) Lee, N. Y.; Chung, Y. K. *Tetrahedron Lett.* **1996**, *37*, 3145.

4. (a) Beebe, X.; Schore, N. E.; Kurth, M. J. *J. Am. Chem. Soc.* **1992**, *114*, 10061. (b) Beebe, X.; Chiappari, C. L.; Kurth, M. J.; Schore, N. E. *J. Org. Chem.* **1993**, *58*, 7320. (c) Beebe, X.; Chiappari, C. L.; Olmstead, M. M.; Kurth, M. J.; Schore, N. E. *J. Org. Chem.* **1995**, *60*, 4204.
5. Selected early references: (a) Kraus, M. A.; Patchornik, A. *J. Am. Chem. Soc.* **1971**, *93*, 7325. (b) Crowley, J. I.; Rapoport, H. *Accts. Chem. Res.* **1976**, *9*, 135. (c) Jayalekshmy, P.; Mazur, S. *J. Am. Chem. Soc.* **1976**, *98*, 6710. (d) Scott, L. T.; Rebek, J.; Ovsyanko, L.; Sims, C. L. *J. Am. Chem. Soc.* **1977**, *99*, 625. (e) Leznoff, C. C. *Accts. Chem. Res.* **1978**, *11*, 327. (f) Farrall, M. J.; Fréchet, J. M. J. *J. Am. Chem. Soc.* **1978**, *100*, 7998. (g) Mazur, S.; Jayalekshmy, P. *J. Am. Chem. Soc.* **1979**, *101*, 677. (h) Rebek, Jr., J.; Trend, J. E. *J. Am. Chem. Soc.* **1979**, *101*, 737. (i) Fréchet, J. M. J. *Tetrahedron* **1981**, *37*, 663. (h) Regen, S. L.; Bolikal, D. *J. Am. Chem. Soc.* **1981**, *103*, 5248. (i) Fréchet, J. M. J.; Bald, E.; Švec, F. *React. Polym.* **1982**, *1*, 21. (j) Mazur, S.; Jayalekshmy, P.; Andersson, J. T.; Matusinovic, T. *ACS Symp. Ser.* **1982**, *192*, 43. (k) Kim, B.; Kirszensztejn, P.; Bolikal, D.; Regen, S. L. *J. Am. Chem. Soc.* **1983**, *105*, 1567. (l) Ford, W. T. *Chemtech*, **1987**, 246.
6. Schore, N. E.; Najdi, S. D. *J. Am. Chem. Soc.* **1990**, *112*, 441. For a recent report of a polymer-supported version of an *intramolecular* Pauson-Khand reaction, see Bolton, G. L. *Tetrahedron Lett.* **1996**, *37*, 3433.
7. Ayres, J. T.; Mann, C. K. *J. Polymer. Sci., Polymer Lett.* **1965**, *3*, 505.
8. Fréchet, J. M. J.; Haque, K. E. *Macromolecules* **1975**, *8*, 130.
9. Beebe, X.; Schore, N. E.; Kurth, M. J. *J. Org. Chem.* **1995**, *60*, 4196.
10. Letsinger, R. L.; Jerina, D. M. *J. Polym. Sci., Part A1* **1967**, *5*, 1977.
11. Sternberg, H. W.; Greenfield, H.; Friedel, R. A.; Wotiz, J.; Marby, R.; Wender, I. *J. Am. Chem. Soc.* **1954**, *76*, 1457.
12. MacWhorter, S. E.; Sampath, V.; Olmstead, M. M.; Schore, N. E. *J. Org. Chem.* **1988**, *53*, 203.
13. Cf. Schore, N. E. *Synth. Commun.* **1979**, *9*, 41.
14. Fyles, T. M.; Leznoff, C. C.; Weatherston, J. *Can. J. Chem.* **1977**, *55*, 4135.
15. Fyles, T. M.; Leznoff, C. C. *Can. J. Chem.* **1976**, *54*, 935.
16. Rautenstrauch, V.; Mégard, P.; Gamper, B.; Bourdin, B.; Walther, E. *Helvetica Chim. Acta* **1989**, *72*, 811.
17. Schore, N. E. unpublished results.
18. (a) Regen, S. L. *J. Am. Chem. Soc.* **1974**, *96*, 5275. (b) Regen, S. L. *Macromolecules* **1975**, *8*, 689.
19. Nicholas, K. M. *Accts. Chem. Res.* **1987**, *20*, 207.
20. PK Cycloaddition of norbornadiene and propargyl alcohol has been achieved by using amine oxide activation at room temperature.[3h]
21. E.g., see (a) Pettit, R. *J. Am. Chem. Soc.* **1959**, *81*, 1266. (b) Jolly, P. W.; Stone, F. G. A.; Mackenzie, K. *J. Chem. Soc.* **1965**, 6416. (c) Schrauzer, G. N.; Ho, R. K. Y.; Schlesinger, G. *Tetrahedron Lett.* **1970**, 543. (d) Weissberger, E.; Laszlo, P. *Acc. Chem. Res.* **1976**, *9*, 209. (e) Weissberger, E.; Page, G. *J. Am. Chem. Soc.* **1977**, *99*, 147 and refs. therein.
22. This difference is generally observed with other, better alkyne substrates as well.[1]

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