compact sheet characterized by O–H···O (O···O, 2.63 Å) and C–H···O (C···O, 3.36, 3.39 Å) bonds. These contacts stabilize the sheet motif and with it the β structure. The chemical consequences of this crystal structure are revealed in the thermal decomposition of solid **2**. While the reported "melting point" is 165 °C, we find that anhydride **3**, the Diels–Alder product, is formed at even 70 °C, the solid turning yellow-brown. Sublimation and decarboxylation account for some loss of material.[11]

Inspection of Figure 2 shows the orientation of the "incipient" reactive centers. The triple bond in the reference molecule is the dienophile, while the conjugated triple bond in the short axis translated neighbor is the diene. This arrangement closely parallels Haworth's original synthesis of **3**, where **2** is refluxed with Ac_2O, forming its anhydride and thereby bringing diene and dienophile to within reacting distance. In the solid state, this is successfully effected by the crystal structure itself. To give **3**, the initial 4 + 2 reaction must be followed by a secondary hydrogen shift from the allenic intermediate and also by loss of water. There is much precedent for similar processes in the solid state.[12]

We infer, as follows, that this reaction is a genuine solid state topochemical process and not a result of partial melting: (a) reaction occurs easily below 120 °C, an approximately 25% conversion to **3** occurring in 30 days at 120 °C or 50 days at 90 °C; (b) the mixture remains free-flowing without any signs of melting; (c) X-ray powder traces of the mixture may be recorded at various stages of conversion; (d) crystalline phenylpropiolic acid, C_6H_5-C≡CCO_2H, which does not have a β structure[13] is unaffected by heating yet is converted into its Diels–Alder anhydride if refluxed with Ac_2O; (e) a year-old sample of **2** stored under ambient conditions (maximum temperature 43 °C) showed definite changes in color and X-ray diffractograms.

The reaction is also quite general. The 4-chloro (short axis 3.962 Å), 3,4-dimethoxy (3.891 Å), and 3,4,5-trimethoxy (3.942 Å) derivatives all adopt β structures and all react similarly when heated, the trimethoxy compound reacting relatively rapidly.[14] Invariably the reaction temperature is 50–100 deg below the reported "melting point". With the unsubstituted compound (5.1 Å) being unreactive and the 4-methoxy (8.96 Å) compound also unreactive, an analogy to the α-, β-, and γ-cinnamic acids seems appealing.[4] However, we defer such a classification till we examine related acids for many of which variable melting points have been reported.[15] Such variations are heating-rate dependent and seem to be good pointers to solid-state reactivity. In general, any crystalline phenylpropiolic acid may be expected to form Diels–Alder products upon heating if the triple bonds are sufficiently close for topochemical reaction.

The behavior of **2** appears to be representative of a new class of solid-state reactions which may not only be deliberately engineered but also be of considerable interest in lignan biosynthesis.

Acknowledgment. We thank the DST(SERC) for financial support.

Supplementary Material Available: Tables of atomic coordinates, thermal parameters and intramolecular geometrical calculations (2 pages). Ordering information is given on any current masthead page.

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(9) Acid **2**: $P\bar{1}$, $Z = 2$, $a = 3.807$ Å; $b = 10.297$ Å, $c = 10.995$ Å, $\alpha = 84.07°$, $\beta = 96.46°$, $\gamma = 98.13°$, CAD-4 (RSIC, IIT Madras), Mo Kα, 746 3σ reflections out of 1219 with $3° \leq \theta \leq 28°$, MULTAN-80, SHELX-76, $R = 0.056$, $R_w = 0.057$, hydrogens isotropic.

(10) Baude, S.; Reychler, A. *Bull. Soc. Chim. Fr.* **1897**, *17*, 616.

(11) Typically 200 mg of **2** were heated at 120 °C for 5 weeks. TLC separation (Silica gel, 15% EtOAc–hexane) gave [3,4-(methylenedioxy)-phenyl]acetylene (63 mg), unreacted **2** (20 mg) and anhydride **3** (44 mg). The IR, NMR, and MS of **3** matched those of an authentic sample.

(12) Scheffer, J. R. *Acc. Chem. Res.* **1980**, *13*, 283. Lewis, T. W.; Duesler, E. N.; Kress, R. B.; Curtin, D. Y.; Paul, I. C. *J. Am. Chem. Soc.* **1980**, *102*, 4659. Lamartine, R.; Perrin, R.; Vicens, J.; Gamet, D.; Perrin, M.; Oehler, D.; Thozet, A. *Mol. Cryst. Liq. Cryst.* **1986**, *134*, 219.

(13) Rollett, J. S. *Acta Crystallogr.* **1955**, *8*, 487.

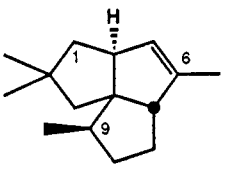
(14) Desiraju, G. R.; Kishan, K. V. R.; Murty, B. N., unpublished work.

(15) There are at least 10 such phenylpropiolic acids. 2-Nitro: Schofield, K.; Simpson, J. C. E. *J. Chem. Soc.* **1945**, 512. 4-Chloro and 4-nitro: Newman M. S.; Merrill, S. H. *J. Am. Chem. Soc.* **1955**, *77*, 5549. 3-Methyl: Benghiat, I.; Becker, E. I. *J. Org. Chem.* **1958**, *23*, 885.

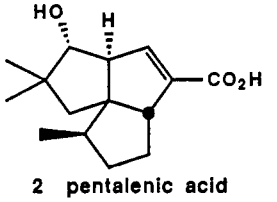
Stereocontrolled Total Synthesis of Pentalenenes via [2 + 3] and [4 + 1] Cyclopentene Annulation Methodologies

Summary: Pentalenene and epipentalenene have each been prepared from enone **5** via [2 + 3] cyclopentene annulation in eight steps. A brief investigation of unexpected diradical cleavage of several vinylcyclopropanes was undertaken. The synthesis has been compared to a previous preparation of title compounds via [4 + 1] cyclopentene annulation in 14 steps.

Sir: Pentalenene (**1**) and pentalenic acid (**2**) belong to the class of sesquiterpenes classified as nonlinearly fused triquinanes.[2] These closely related compounds have been



1 pentalenene



2 pentalenic acid

isolated from the broth of *Streptomyces griseochromogens*[3] and their role in the biogenesis of the antibiotic pentalenolactone has been actively investigated.[4] Equally active has been the effort in the area of total synthesis where the title compounds represent attractive targets.[5]

(1) Fellow of the Alfred P. Sloan Foundation, 1981–1985; Recipient of the NIH Research Career Development Award, 1984–1989.

(2) Paquette, L. A. *Top. Curr. Chem.* **1984**, *119*, 1.

(3) Isolation. (i) Pentalenene: Seto, H.; Yonehara, H. *J. Antibiot.* **1980**, *33*, 92. (ii) Pentalenic acid: Seto, H. Sasake, T.; Uzawa, J.; Takeuchi, S.; Yonehara, H. *Tetrahedron Lett.* **1978**, 4411.

(4) (a) Cane, D. E.; Tillman, A. M. *J. Am. Chem. Soc.* **1983**, *105*, 122. (b) Cane, D. E.; Rossi, T.; Tillman, A. M.; Pachlatko, J. P. *J. Am. Chem. Soc.* **1981**, *103*, 1838.

(5) Synthesis. (i) Pentalenene: (a) Ohfune, Y.; Sirahama, H. Matsumoto, T. *Tetrahedron Lett.* **1976**, 2869. (b) Misumi, S. Ohtsuka, T.; Ohfune, Y.; Sugita, K.; Shirahama, H.; Matsumoto, T. *Tetrahedron Lett.* **1979**, 31. (c) Annis, G. D.; Paquette, L. A. *J. Am. Chem. Soc.* **1982**, *104*, 4504. (d) Paquette, L. A.; Annis, G. D. *J. Am. Chem. Soc.* **1983**, *105*, 7358. (e) Piers, E.; Karunaratne, V. *J. Chem. Soc., Chem. Commun.* **1984**, 959. (f) Pattenden, G.; Teaque, S. J. *Tetrahedron Lett.* **1984**, *3021*. (g) Mehta, G.; Rao, K. S. *J. Chem. Soc., Chem. Commun.* **1985**, 1464. (h) Crimmins, M. T.; DeLoach, J. A. *J. Am. Chem. Soc.* **1986**, *108*, 800. (i) Hua, D. H. *J. Am. Chem. Soc.* **1986**, *108*, 3836. (j) Imanishi, T.; Ninbari, F.; Yamashita, M.; Iwata, C. *Chem. Pharm. Bull.* **1986**, *34*, 2268. (k) Mehta, G.; Rao, K. S. *J. Am. Chem. Soc.* **1986**, *108*, 8015. (ii) Pentalenic acid: (l) Sakai, K.; Ohtsuka, T.; Misumi, S. Shirahama, H.; Matsumoto, T. *Chem. Lett.* **1981**, 355. (m) Crimmins, M. T.; DeLoach, J. A. *J. Org. Chem.* **1984**, *49*, 2076. (n) Crimmins, M. T.; DeLoach, J. A. *J. Am. Chem. Soc.* **1986**, *108*, 800.

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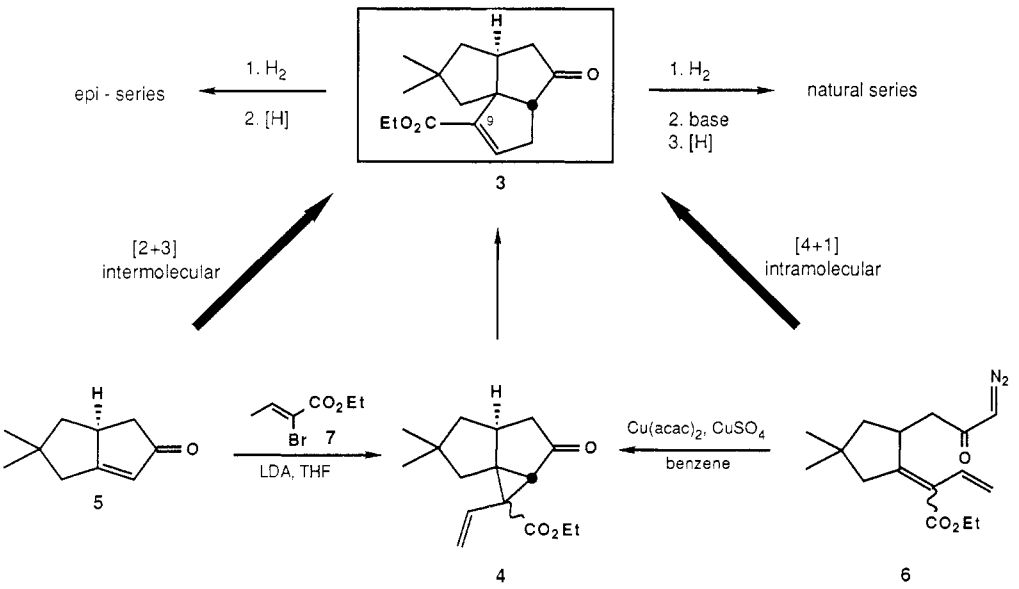
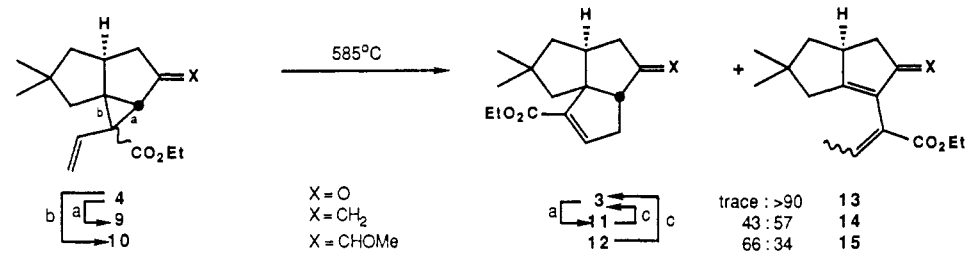
Scheme I



Scheme II[a]



[a] Reagents: (a) Ph_3PCH_3Br/t-AmOK/t-AmOH/PhH; (b) $CH_3OCH_2PPh_3Cl/t$-AmOK/t-AmOH/PhH; (c) O_3/CH_2Cl_2.

We were interested in designing a general method of synthesis not only for pentalenene and pentalenic acid but also for their C-9 epimers so that all four compounds could be available in a stereocontrolled fashion.[6,7]

The intramolecular [4 + 1] cyclopentene annulation was initially chosen as a method of choice since the stereochemistry at C-9 of the natural products could be manipulated at will by using the tricyclic acrylate of type **3** whose reductive and epimerizable operations would yield the desired stereocontrol in analogy with the synthesis of all stereoisomers of isocomenes and isocomenic acids.[8,9]

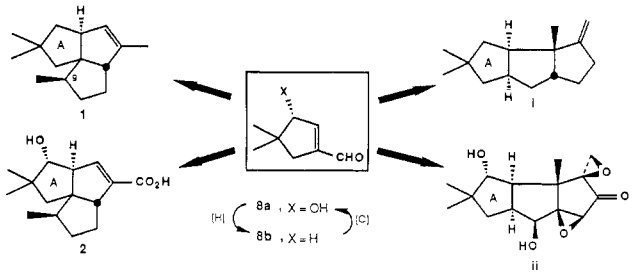
However, a new and shorter approach to triquinane **3** was envisioned by the use of [2 + 3] annulation methodology recently developed.[10] In this route, vinylcyclopropanes would become available from enones and the lithio anion of ethyl 2-bromocrotonate (**7**) (Scheme I).

Enone **5** was prepared in three steps from mesityl oxide by a known procedure.[5i,11] Activation of the β,β-disubstituted enone with BF_3 at low temperature and condensation of this complex with the lithio dienolate of ethyl 2-bromocrotonate (**7**) provided a 45% yield of vinylcyclopropane **4** (exo/endo = 1:1) in addition to 50% of recovered enone **5**, which was recycled. Vinylcyclopropane **4** was also prepared from diazo ketone **6** by cyclopropanation (exo/endo = 2:1) during the approach utilizing the [4 + 1] annulation methodology.[12] The comparison of these two approaches to **4** in terms of brevity is noteworthy: four steps from mesityl oxide vs twelve steps from dimedone, via aldehyde **8**.[7,12]

Diradical Cleavage of Vinylcyclopropanes 4. Initial thermolytic transformations of **4** gave only enone **13** resulting from the diradical cleavage of bond b in cyclo-

(6) The epimer of pentalenene at C-9 was desired in connection with a ^{13}C NMR data base on sesquiterpenes having a secondary methyl group adjacent to a ring junction. We have been compiling ^{13}C chemical shifts for compounds of this type since it appears that the stereochemistry of *three adjacent centers* may be deduced from the shift of the methyl signal above. See: Hudlicky, T.; Koszyk, F. J.; Dochwat, D. M.; Cantrell, G. L. *J. Org. Chem.* **1981**, *46*, 2911.

(7) For detailed discussion of topological selectivity in design of linear/nonlinear triquinanes, see: Hudlicky, T.; Kwart, L. D.; Tiedje, M. H.; Ranu, B. C.; Short, R. P.; Frazier, J. O.; Rigby, H. L. *Synthesis* **1986**, 716 and references therein. The design of pentalenene and pentalenic acid via [4 + 1] cyclopentene annulation methodology also took into account the preparation of coriolin. We noted that **1** and **2** possess the identical topographical relationship of ring A as do hirsutene (i) and coriolin (ii). The unified approach to all four sesquiterpenes are based on the use of common starting material, aldehyde **8**,[7] both forms of which are mutually interconvertible.[12]



(8) Hudlicky, T.; Short, R. P.; Ranu, B. C.; Revol, J. M. *J. Org. Chem.* **1983**, *48*, 4453.

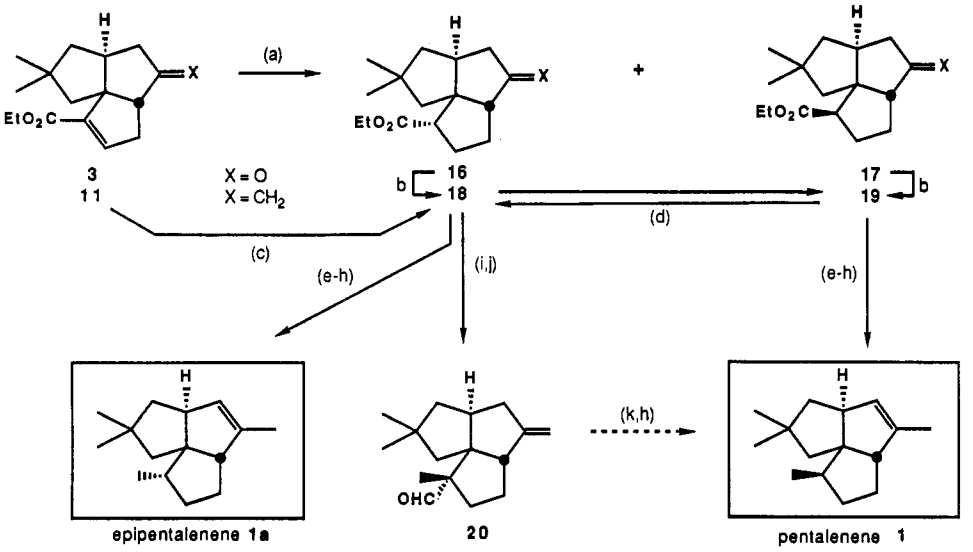
(9) Ranu, B. C.; Higgs, L. A.; Kavka, M.; Hudlicky, T. *Tetrahedron Lett.* **1984**, 2447.

(10) Hudlicky, T.; Radesca, L.; Contla, H. L.; Anderson, F. E., III. *J. Org. Chem.* **1986**, *51*, 4746.

(11) Schore, N. E.; Croudace, M. C. *J. Org. Chem.* **1981**, *46*, 5436. Magnus, P.; Principe, L. M. *Tetrahedron Lett.* **1985**, 4851.

(12) These results and experimental details of this manuscript will be reported in a full paper: *Tetrahedron Symposia in Print*, in press.

Scheme III[a]

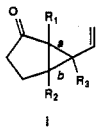


[a] Reagents: (a) H_2/PtO_2; (b) Ph_3PCH_3Br/t-AmOK/t-AmOH/PhH; (c) Mg/MeOH; (d) EtONa/EtOH/reflux; (e) $LiAlH_4$/THF; (f) $MsCl/Et_3N/CH_2Cl_2$; (g) $LiEt_3BH$/THF; (h) p-TsOH/CH_2Cl_2; (i) LDA/THF/−78 °C/MeI; (j) DIBAL/THF or $LiAlH_4$; then PCC; (k) $(Ph_3P)_4RhCl_2$/PhMe/Δ.

propanes **4**.[13] In an effort to increase the tendency of bond a to undergo scission, olefin **9** and enol ether **10** were prepared, and their behavior under pyrolytic conditions was studied. The results are summarized in Scheme II.[14] While cyclopropanes **4** gave primarily the cleavage product **13**, olefin **9** gave a good yield of triquinane **11** in addition to the cleavage product **14**, whereas enol ether **10** gave much improved yields of triquinane **12**. The best yields of triquinanes (66%) were obtained by pyrolysis of exocyclic enol ethers **10**. This indicated that, in addition to an allylic radical, increased electron content through induction was necessary for the scission of bond a in **4**. Either of the triquinanes **11** and **12** was converted to ketone **3** by selective ozonolysis. All three triquinanes **3**, **11**, and **12** could now be manipulated to the title compounds in analogy with our experience in the isocomene series,[7-9] albeit with different stereochemical outcomes.

Pentalenene and Epipentalenene. Hydrogenation of **3** gave the saturated ketones **16** and **17** with the major product **16** possessing predominantly the expected epi configuration of the ester functionality at C-9 with diastereomer **17** as a minor product (**16**/**17** = 95:5). This was expected based on the approach of hydrogen from the less concave surface of the molecule. Wittig reaction at room temperature afforded olefins **18** and **19** (Scheme III). An exciting result presented itself upon reduction of triquinane **11**, with Mg in MeOH.[15] The acrylate moiety was saturated to provide selectively the olefins **18** and **19** (**18**/**19** = 9:1) (Scheme III). In this fashion all of the triquinane intermediates could be utilized and the intermediate pool converged at the stage of ester olefins **18** and **19**, which were obtained by several different routes. We now had access to the *epi series* of the title natural products with greater than 9:1 stereoselectivity. The synthesis of epipentalenene was completed by the reduction of the ester functionality in **18** to the C-9 methyl group and isomerization of the exocyclic olefin to afford epipentalenene, whose spectral properties matched those provided to us by Prof. L. A. Paquette. The base-catalyzed isomerization performed on olefins **18**/**19** either by raising the temperature of the Wittig reaction to reflux or by subjecting the compounds obtained from the Mg/MeOH reduction to refluxing EtONa/EtOH for 2 h provided equilibrium mixtures in which the product possessing the natural pentalenene configuration predominated 55:45. This result was somewhat surprising based on the predicted behavior of the ester function in analogy with that of similar compounds successfully isomerized in the isocomene series.[7-9] Since the equilibration of the exocyclic olefin esters favored the epimer **19**, possessing the natural configuration at C-9, one recycle could improve this stereochemistry to 86:14 in favor of pentalenene precursor **19**. Reduction of the ester in **19**, followed by isomerization of the olefin, furnished pentalenene whose ^1H NMR was identical with that supplied to us by Prof. M. T. Crimmins and L. A. Paquette.[17] Additional improvement of the stereoselectivity at C-9 was available by alkylation of ester **18** with LDA/MeI. The methyl group was delivered from the less hindered face, in analogy with the results of hydrogenation and Mg reduction, to give, after reduction the aldehyde **20** with better than 9:1 stereoselectivity. Although the decarbonylation of this substance gave poor yields of β-pentalenene, we believe that this method of stereocontrol would be, in the long run, superior to epim-

(13) This result was somewhat surprising based on the number of diversely substituted vinylcyclopropanes that were successfully transformed to cyclopentenes during previous studies. For comprehensive



R_1 = H, CH_3, CO_2Et, CO_2CH_2Ph

R_2 = H, alkyl

R_3 = H, CH_3, CO_2Et, allyl

i

listing, see ref 6 and 7 above and: Hudlicky, T.; Kutchan, T. M.; Naqvi, S. M. *Org. React. (N. Y.)* **1985**, *33*, 248.

(14) For a study of these and other transformations, see also: Fleming, A.; Sinai-Zingde, G.; Natchus, M.; Hudlicky, T. *Tetrahedron Lett.* **1987**, 167.

(15) These conditions were reported in the literature for the reduction of acrylamides and acrylonitriles, respectively: Brettle, R.; Shibib, S. M. *J. Chem. Soc., Perkin Trans. 1* **1981**, 2912. Profitt, J. A.; Watt, D. S.; Corey, E. J. *J. Org. Chem.* **1975**, *40*, 127.

(16) The separation of pentalenene and its C-9 epimer could best be effected on $AgNO_3$-impregnated TLC plates or preparative GC by following the method of Piers (ref 5e) or by TLC, at the stage of esters **18** and **19**.

(17) All compounds were characterized by IR, ^1H and ^{13}C NMR, mass spectroscopy, and C,H,N analysis.

erization. Scarcity of material at this stage precluded further investigation of conditions for improved decarbonylation.[18]

Conclusion. Pentalenene sesquiterpenes have been synthesized in a stereocontrolled manner. The selectivity in the epi series was better than 95:5 as a consequence of the reduction of the cyclopentenecarboxylate from a less hindered face. The base-catalyzed epimerizations then gave equilibrium mixtures in which the isomers possessing the natural configuration at C-9 predominated and could yield, after one recycling, stereoselectivity of 86:14, in analogy with our previous experience in the isocomene series. The alkylation/decarbonylation approach gave 9:1 stereoselectivity in favor of the natural series. In addition to the controlled access to pentalenenes, pentalenic acids and desoxypentalenic acids may be prepared by starting the synthetic route with aldehyde 8 and using [4 + 1] annulation.[12] We are currently completing the synthesis of pentalenic acid (2), epipentalenic acid, and the corresponding deoxypentalenic acids.[12] Thus most members of the pentalenene family of sesquiterpenes are available by the unified design described here.

Acknowledgment. We are grateful to the National Institute of Health (AI-19749, AI-00564), the donors of the Petroleum Research Fund, administered by the American Chemical Society, the Jeffress Trust Fund, the Chemistry Department at Virginia Tech, and TDC Research, Inc., for generous support of this work. The following persons are acknowledged for their assistance with this project: Dr. B. C. Ranu, Dr. H. L. Rigby, Carol and Teresa Andre, and Penny Papadopolous. We thank Prof. Crimmins (UNC) and Prof. Paquette (OSU) for providing us with spectra of the natural products.

(18) Abstracted in part from the M.S. thesis of M. G. Natchus, VPI, 1987.

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The First Direct Formation of a Grignard Reagent on an Insoluble Polymer

Summary: Reaction of the normally mutually unreactive magnesium and solid halogenated polymers has been accomplished by using a magnesium–anthracene/THF complex to afford a high yield of the reactive Grignard polymers.

Sir: The design of specialized polymers that can be used as reagents, catalysts, or supports requires that new methods be developed for the chemical modification of cross-linked resins. In particular, it is important to be able to modify preformed polymers by grafting of reactive functionalities through C–C bonds as these are less likely to create interferences in the use of the finished polymers.[1] In spite of numerous previous attempts, the direct oxidative addition of insoluble polymeric halides to magnesium metal to form the corresponding supported Grignard reagents on insoluble polymers had not been previously achieved[2] as both the polymeric halide and the magnesium metal are insoluble solids which cannot come into intimate contact with one another (Figure 1). Even when Rieke's magnesium,[3] which is considered to be the most highly activated magnesium metal, was used, no chlorine of cross-linked (chloromethyl)polystyrene (1) was lost upon hydrolytic quenching of the reaction mixture (Table I). Although exchange of halogen for metal between organolithium reagents and organic halides has been a successful method for the preparation of cross-linked lithiopolystyrene resins,[4] the related exchange reaction for magnesium is complicated by the possible concurrent occurrence of Wurz-type coupling and the fact that, being an equibrium process, complete conversion may not be achieved.[5] The reaction of organolithium compound with 1 equiv of magnesium halide, $MgBr_2$ or MgI_2, is an alternate route to Grignard reagents that are difficult to prepare directly,[6] and indeed this indirect procedure has been used for the preparation of one insoluble Grignard from lithiopolystyrene.[7] In the case of (chloromethyl)polystyrene, this indirect route is less available as its lithiated derivative has never been prepared successfully[10] from the halogenated precursor.

Recently, some new and difficult to prepare Grignard reagents have successfully been synthesized by using a

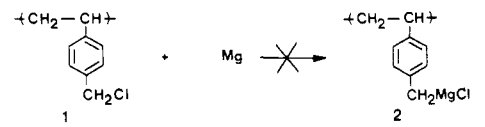
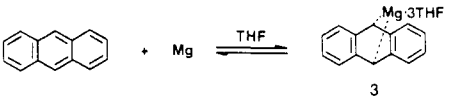


Figure 1.



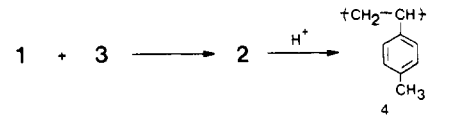


Figure 2.

Table I. Reaction of Chloromethylated Polystyrene 1 with Activated Magnesium

run	Mg transfer agent	temp, °C	time, h	loss of Cl[d] after quenching
1[a]	Mg activated by dibromoethane	r.t.[e]	75	0
2[b]	Rieke's Mg	r.t.	50	0
3[c]	Mg–anthracene/THF	−30	1	40
4[c]	Mg–anthracene/THF	r.t.	0.7	93
5[c]	Mg–anthracene/THF	r.t.	3.5	100
6[c]	Mag–anthracene/THF	60	4	100

[a] [Mg]/[Cl] = 2.5:1. [b] [Mg]/[Cl] = 2:1. [c] [Mg]/[Cl] = 5:3. [d] Determined by Cl analysis. [e] r.t. = room temperature.

(1) Darling, G. D.; Frêchet, J. M. J. *J. Org. Chem.* **1986**, *51*, 2270.
(2) Darling, G. D. Ph. D. Dissertation, University of Ottawa, 1987.
(3) Rieke, R. D.; Bales, S. E. *J. Am. Chem. Soc.* **1974**, *96*, 1775.
(4) Farrall, M. J.; Frêchet, J. M. J. *J. Org. Chem.* **1976**, *41*, 3877.
(5) Zakharkin, L. I.; Okhlobystin, O. Y.; Bilevitch, K. A. *J. Organomet. Chem.* **1964**, *2*, 309. Zakharkin, L. I.; Okhlobystin, O. Y.; Bilevitch, K. A. *Tetrahedron* **1965**, *21*, 881.
(6) Agami, C.; Chauvin, M.; Levisalles, J. *Bull. Soc. Chim. Fr.* **1970**, 2712.
(7) Weinshenker, N. M.; Crosby, G. A.; Wong, J. Y. *J. Org. Chem.* **1975**, *40*, 1966.

0022-3263/87/1952-4644$01.50/0