by chromatography on silica with 9:1 $CHCl_3$–CH_3OH) to cytochalasin B has been described previously.[13]

Acknowledgment. We thank the National Institutes of Health and the National Science Foundation for their support of this work.

References and Notes

(1) For recent reviews of (a) the chemistry and (b) the biological activity of these substances, see (a) M. Binder and Ch. Tamm, *Angew. Chem., Int. Ed. Engl.*, **12**, 370 (1973); (b) S. B. Carter, *Endeavour*, **113**, 77 (1972).
(2) The transition state involving the desired diene should be favored because in that case only a spherically symmetric methyl group, rather than a much more sterically demanding branched chain, extends from the diene plane. See also footnote 2 in G. Stork, S. Wagle, and P. C. Mukharji, *J. Am. Chem. Soc.*, **75**, 3197 (1953).
(3) J. Plesek, *Collect. Czech, Commun.*, **22**, 644 (1957).
(4) All compounds gave spectral data, in particular NMR spectra, in agreement with the postulated structures. Special features are mentioned in the text. Purifications were on silica gel unless otherwise noted, and elution was with hexane–ethyl acetate, usually 4:1. All rotations are for chloroform solution.
(5) Cf. D. H. S. Horn and Y. Y. Pretorius, *J. Chem. Soc.*, 1460 (1954).
(6) W. Rothweiler and C. Tamm, *Helv. Chim. Acta*, **53**, 696 (1970).
(7) Cf. N. C. Charturvedi, W. K. Park, R. R. Smeby, and F. M. Bumpus, *J. Med. Chem.*, **13**, 177 (1970).
(8) Cf. P. L. Southwick and R. T. Crouch, *J. Am. Chem. Soc.*, **75**, 3413 (1953).
(9) We had previously established that acetoxymaleic anhydride gives the correct orientation with model trienes corresponding to **15**.
(10) The importance of *N*-acyl groups on pyrrolone dienophiles has been established by the outstanding work of E. Vedejs and R. C. Gadwood, *J. Org. Chem.*, **43**, 376 (1978), which had been communicated to us prior to its publication.
(11) K. B. Sharpless and N. C. Michaelson, *J. Am. Chem. Soc.*, **95**, 6136 (1973).
(12) The seco acid **31** from cytochalasin B (cf. ref 13) was transformed into **29** by treatment of the methyl ester (diazomethane) with acetic anhydride–pyridine (3.5 h at room temperature). Conversion of **29** from cytochalasin B to the dihydroxy compound **30** was done as we describe for the synthetic material.
(13) S. Masamune, Y. Hayase, W. Schilling, W. K. Chan, and G. S. Bates, *J. Am. Chem. Soc.*, **99**, 6756 (1977).

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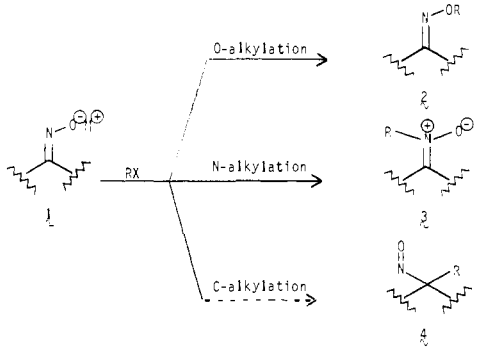
Intramolecular Carbon Alkylation of Oxime Anions. Stereospecific Generation and Rearrangement of Nitrosocyclopropanes and Nitrosocyclobutanes[1]

Sir:

Alkylation of oxime anions is well known to occur both at oxygen (to yield oxime ethers, **1** → **2**)[2] and at nitrogen (to yield nitrones, **1** → **3**).[2] The process of carbon alkylation (to yield tertiary nitroso compounds, **1** → **4**) is extremely rare.[3,4]



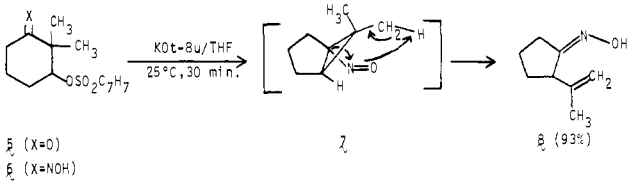
The intramolecular version of oxime alkylation should be very susceptible to kinetic control. In those cases where oxygen or nitrogen alkylation would lead to torsional strain in the imine moiety (Bredt's rule violations) it should be possible to realize carbon alkylation.[4]

Table I

base[a]	temp, °C	time, min[b]
KO-*t*-Bu[c]	25	30
NaO-*t*-Bu[c]	25	35
LiO-*t*-Bu[c]	25	300
NaH[c]	25	45
$(n\text{-}C_4H_9)_4NOH$[d]	25	5
KDPPM[d,e]	0	<1
KDPPM[d,e]	−20	50

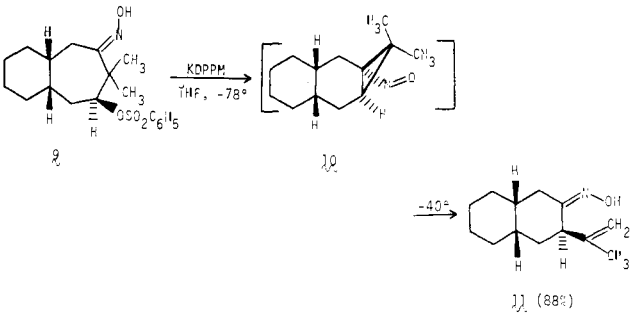
[a] 2 equiv. [b] Time for total disappearance of starting material (TLC analysis). [c] Heterogeneous reaction. [d] Homogeneous reaction. [e] 1 *or* 2 equiv.

Treatment of keto tosylate **5**[5,6] with 2.2 equiv of hydroxylamine hydrochloride in 25% pyridine–ethanol at room temperature for 12 h produced the anti-oxime tosylate **6**[6-8] (59%, mp 162–163 °C). Reaction of oxime **6** with a suspension of potassium *tert*-butoxide in tetrahydrofuran did not afford isolable cyclopropyl nitroso compound **7**. The sole kinetic reaction product was the ring-contracted syn[8] oxime **8**,[6-8] apparently via a homodienyl [1,5]-hydrogen migration on intermediate **7**.



The reaction (**6** → **8**) shows the counterion effect expected for an anionic displacement, with the more ionic potassium and tetrabutylammonium salts being fastest (Table I). The base of choice for this reaction is the *soluble* reagent, potassium diphenyl-4-pyridylmethide (KDPPM).[10,11] The five-membered-ring analogue of **6** does not undergo the ring contraction reaction.[6-8,12,13]

Thin-layer chromatographic analysis of the reaction of the cycloheptyl oxime **9**[6-8,14] with KDPPM reveals that the starting material is completely consumed within 5 min at −78 °C (syn oxime **11**[6-9] is the only product detected). The color



of the −78 °C reaction solution is a light blue, suggestive of the intermediacy of nitroso compound **10**. The blue color fades to produce a colorless solution at ca. −40 °C.[15]

Further evidence of the stereospecificity of the ring-contraction reaction was obtained in the cyclohexyl series. Partial hydrogenation (H_2, PtO_2, C_2H_5OH) of 2-ethyl-2-methyl-1,3-cyclohexanedione[6] yielded a 3:1 mixture of ketols[6] which were subsequently converted[16] to a 3:1 mixture of keto mesylates.[6] Treatment of the keto mesylate mixture with hydroxylamine hydrochloride in 25% pyridine–ethanol afforded a 3:1 mixture of oxime mesylates **12a,b**.[6] Homogeneous major oxime mesylate **12a**[6] (mp 145–146 °C) could be obtained by fractional crystallization of the **12a,b** mixture. The minor oxime mesylate **12b**[6] (mp 110–112 °C) was purified by chromatography (SiO_2) of the crystallization residues.

Reaction of the purified oxime mesylates **12a** and **12b** with

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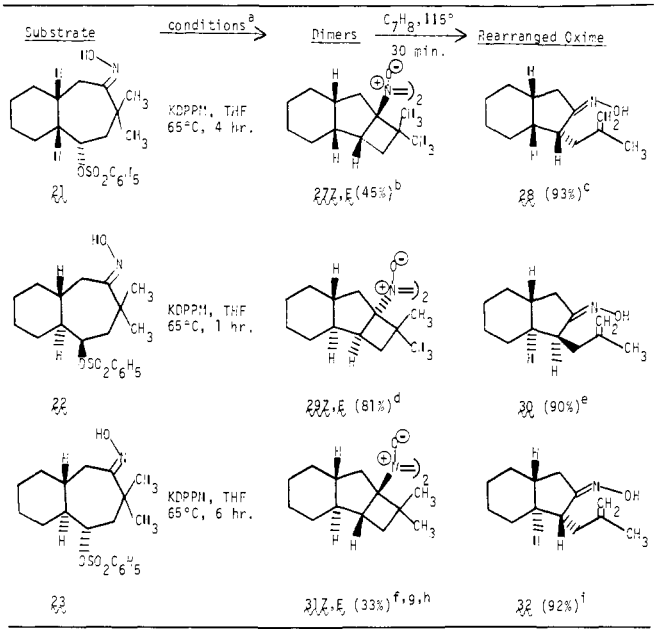
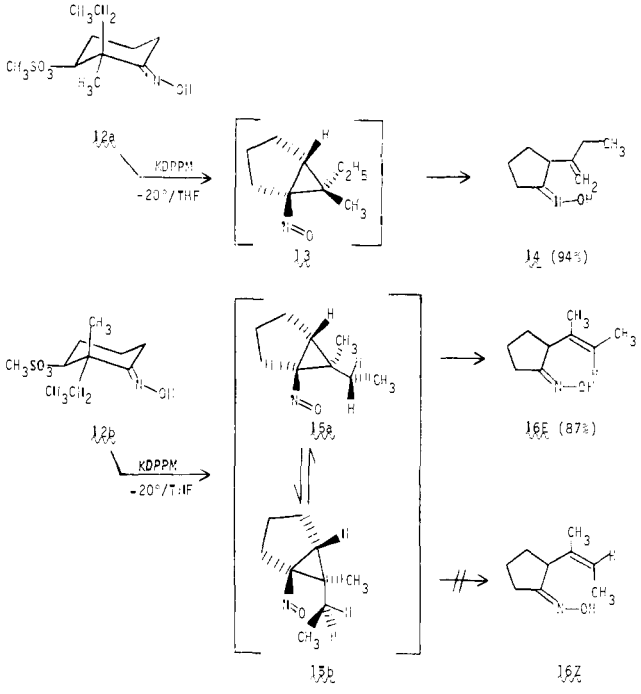
Table II[6,7]



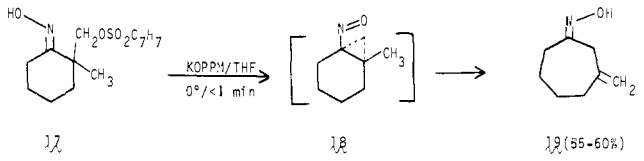
[a] All reactions are carefully run under N_2 to avoid formation of nitro compounds (cf. ref 24). [b] Cis-trans mixture by ^1H NMR, mp 175-176 °C.[26] [c] Analyzed as the isomerized[25] anti oxime, mp 115-118 °C. [d] Cis-trans mixture by ^1H NMR, mp 168-169 °C.[26] [e] Syn oxime, mp 75-76 °C; anti oxime, mp 104-105 °C after isomerization.[25] [f] Ca. 40% **32** also directly produced in the **23** → **31***E*,*Z* reaction. [g] Cis-trans mixture by ^1H NMR, mp 167-168 °C.[26] [h] This compound is *not* identical with **29***Z*,*E* which has mp 168-169 °C. Analyzed as the isomerized[25] anti oxime (oil).

KDPPM proceeded stereospecifically to afford **14** and **16***E*, respectively.[6-8] Thin-layer chromatographic analysis (1:1 ethyl acetate-ether on $AgNO_3$-coated SiO_2 plates) of the reaction mixtures gave no indication (<1%) of crossover products **12a** ↛ **16***E*; **12b** ↛ **14**.

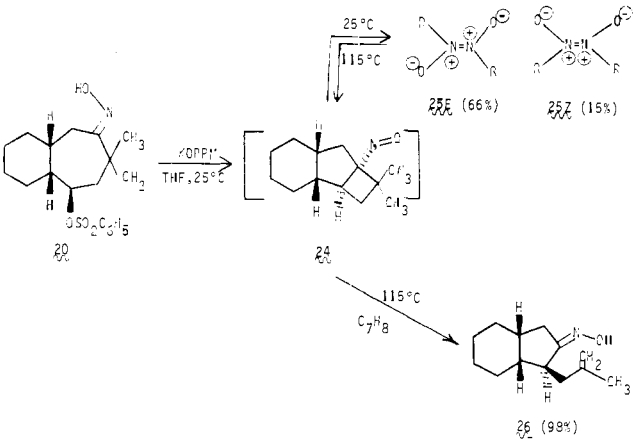
It should be noted that the reaction of **12b** appeared to produce only one geometric isomer (**16***E*) at the newly formed olefinic center (^{13}C NMR analysis[17]). This geometry is in accord with a mechanism having a chair-like transition state (**15a**) which provides excellent overlap between the nitroso moiety and the carbon-hydrogen σ bond. Formation of olefin **16***Z* would require a boat-like transition state (**15b**) which substantially increases the distance between the nitroso group and the requisite carbon-hydrogen σ bond.[18]



The intramolecular alkylation of oximes can also be utilized as a method of ring expansion. Treatment of oxime **17**[6-8,19] with KDPPM or potassium *tert*-butoxide produces oxime olefin **19**.[6-8,20]



The homologous nitrosocyclobutane rearrangement was tested with the four diastereomeric oxime benzenesulfonates (**20, 21, 22, 23**).[21,22] Reaction of **20** with KDPPM in THF for 4 h at 25 °C yielded a mixture of *trans*- and *cis*-nitroso dimers **25***E* (mp 67-68 °C) and **25***Z* (mp 160-162 °C).[6,7,23,24]



Nitroso dimers **25***E* and **25***Z* (either individually or as a mixture) were stereospecifically rearranged to syn-oxime olefin **26**[6-8,25] by heating for 30 min in toluene at reflux. Presumably, the mechanism of this reaction involves dissociation of the dimer to monomer **24** which undergoes a homodienyl hydrogen migration at the elevated temperature.[26,27]

The corresponding results from intramolecular alkylation, followed by nitroso dimer rearrangement of isomers **21, 22,** and **23,** are listed in Table II. Several points are worthy of mention: (1) comparison of dimer mixtures **25***Z*,*E* with **27***Z*,*E*, as well as **29***Z*,*E* with **31***Z*,*E*, reveals that *the intramolecular alkylations are proceeding stereospecifically* (<1% crossover, TLC analysis); (2) the intramolecular alkylation process may be used to generate relatively strained ring systems (**29, 31**); and (3) the fragmentation reaction also proceeds stereospecifically, initially producing the syn oxime under kinetic conditions.[25]

Acknowledgment. We thank Purdue University and Phillips Petroleum Co. for Fellowships (D.A.C.). We also gratefully acknowledge financial support from Pfizer Chemical Co. and the National Institutes of Health for Grant No. CA-19689, awarded by the National Cancer Institute, Department of Health, Education, and Welfare.

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(1) Synthetic Utilization of the Imine Moiety. 6. For previous papers in this series, see (a) C. E. Sacks and P. L. Fuchs, *J. Am. Chem. Soc.*, **97**, 7372 (1975); (b) C. E. Sacks and P. L. Fuchs, *Synthesis*, 456 (1976); (c) P. L. Fuchs, *J. Org. Chem.*, **41**, 2935 (1976); (d) C. A. Bunnell and P. L. Fuchs, *ibid.*, **42**, 2614 (1977); (e) C. A. Bunnell and P. L. Fuchs, *J. Am. Chem. Soc.*, **99**, 5184 (1977).

(2) (a) J. Hamer and A. Macaluso, *Chem. Rev.*, **64**, 473 (1964); (b) G. R. Delpierre and M. Lamchen, *Q. Rev. Chem. Soc.*, **19**, 329 (1965); (c) S. R. Sandler and W. Karo, "Organic Functional Group Preparations", Vol. 3, Academic Press, New York, 1972, Chapter 9, p. 301; (d) B. Unterhalt, *Method. Chim.*, 403 (1975).

(3) Oxidation reactions of oximes are known to yield α-functionalized (acetoxy, nitro, halo) tertiary nitroso compounds: (a) ref 3c, Chapter 16, p 383; (b) J. P. Freeman, *Chem. Rev.*, **73**, 283 (1973).
(4) The Eschenmoser group has provided several elegant examples of the generation of vinylogous *C*-nitroso compounds via the intramolecular C-alkylation of unsaturated oxime anions: (a) J. Schreiber, M. Pesaro, W. Leimgruber, and A. Eschenmoser, *Helv. Chim. Acta*, **41**, 2103 (1958); (b) D. Felix, P. Jakober, and A. Eschenmoser, *Chimia*, **19**, 538 (1965). See also (c) P. Wieland and G. Anner, *Helv. Chim. Acta*, **52**, 121 (1969); (d) E. R. Krajniak, E. Ritchie, and W. C. Taylor, *Aust. J. Chem.*, **26**, 1337 (1973).
(5) E. Wenkert, P. Bakuzis, R. J. Baumgarten, C. L. Leicht, and H. P. Schenk, *J. Am. Chem. Soc.*, **93**, 3208 (1971).
(6) This compound exhibited satisfactory spectral (IR, ^{13}C NMR and/or ^{1}H NMR, mass spectrometry) and analytical properties (exact mass and/or combustion analysis).
(7) Yields refer to isolated material of >95% purity.
(8) Oxime stereochemistry assigned by ^{13}C NMR (C. A. Bunnell and P. L. Fuchs, *J. Org. Chem.*, **42**, 2614 (1977)) and ^{1}H NMR (G. J. Karabatos, R. A. Taller, and F. M. Vane, *J. Am. Chem. Soc.*, **85**, 2326, 2327 (1963)).
(9) Acid-catalyzed (commercial $CDCl_3$) isomerization of the syn oxime yields the anti isomer for the purposes of spectral comparison.[8]
(10) The preparation of potassium diphenyl-4-pyridylmethide follows. Potassium hydride (55.0 mmol, 12.0 mL of 4.6 M oil suspension) was placed in a dry flask under nitrogen. Hexane (50 mL) was added, and the mixture was stirred for several minutes. The mixture was then allowed to settle and the hexane was removed via syringe. The process was repeated four times and the residual solvent removed under vacuum leaving a dry powder. Diphenyl-4-pyridylmethane (Chem Samples,[10a] 50.0 mmol, 12.3 g) dissolved in THF (50 mL) was added (slightly exothermic) and the resulting deep red solution was stirred until H_2 evolution was complete (1–2 h). The solution is conveniently titrated by adding the reagent solution (via a 1.0-mL syringe) to a known amount of benzoic acid (~80 mg) dissolved in THF (10 mL). Potassium benzoate precipitates from the colorless solution and a very sharp change (colorless to bright orange) is observed at the end point. Three such titrations gave an average of 0.97 M (0.95, 0.98, 0.99). The reagent solution is stable for at least 1 month if kept in a refrigerator. Since all triarylmethide anions react readily with oxygen,[10b] the reagent must be maintained under an inert atmosphere. (a) At the conclusion of our work we were informed that Chem Samples no longer intended to supply diphenyl-4-pyridylmethane. This material can be easily made by the procedure of Tschitschibabin (*Chem. Ber.*, **61**, 547 (1928)). Alternatively, we have found that potassium diphenyl-2-pyridylmethide (diphenyl-2-pyridylmethane is available from Aldrich) serves equally well in these reactions. (b) T. J. Kiess and L. L. Moore, *J. Heterocycl. Chem.*, **9**, 1161 (1972).
(11) Potassium triphenylmethide (J. W. Huffman, P. L. Harris, *Synth. Commun.* **7**, 137 (1977)) also serves as a base in this reaction, but the ease of removal of diphenylpyridylmethane (5% HCl) makes KDPPM a far more convenient reagent to use.
(12) The cyclopentyl oxime (mp 139–140 °C) is prepared from the known ketol (A. Hamon, B. Lacoume, G. Pasquet, and W. R. Pilgrim, *Tetrahedron Lett.*, 211 (1976)) via the standard two-step procedure.
(13) After 12 h at reflux in THF with KDPPM, 90% of the cyclopentyl oxime is recovered.
(14) Oxime **9** (mp 127–128 °C) is prepared from the ketal alcohol via successive reaction with benzenesulfonyl chloride–pyridine, 3.5% aqueous $HClO_4$ in THF, and hydroxylamine hydrochloride–25% pyridine–ethanol. Synthesis of the ketal alcohol is to be published by D. A. Clark and P. L. Fuchs; see also D. A. Clark, Ph.D. Thesis, Purdue University, 1978.
(15) This observation suggests that the rate-determining step in the **9** → **11** transformation is the nitrosocyclopropane → α-isopropylidene oxime rearrangement, while in the case of the reaction with the cyclohexyl substrate (**6** → **8**) the internal alkylation is rate limiting. Experiments are in progress to more carefully delineate these parameters.
(16) R. K. Crossland and K. L. Servis, *J. Org. Chem.*, **35**, 3195 (1970).
(17) An authentic mixture of **16***Z* and **16***E* was prepared via the reaction of (*Z*)- + (*E*)-2-butenyl cuprates (66% *Z*) with 2-chlorocyclopentanone oxime by the method of Corey, Melvin, and Haslanger (*Tetrahedron Lett.*, 3117 (1975)). Comparison of the ^{13}C NMR of this mixture with that of the product from ring contraction of **12b** allows a lower limit of 80% to be placed upon the olefinic specificity. Experiments are currently in progress to refine this number.
(18) A similar geometric preference is seen in the high-temperature thermolysis of cyclopropyl esters: D. E. McGreer and N. W. K. Chiu, *Can. J. Chem.*, **46**, 2217, 2226 (1968).
(19) Oxime **17** (mp 120–122 °C) is prepared from the known[5,19a,b] ketol via the standard two-step procedure: (a) W. C. Lumma, Jr., and O. H. Ma, *J. Org. Chem.*, **35**, 2391 (1970); (b) F. Nerdel, D. Frank, and H. Marschall, *Chem. Ber.*, **100**, 720 (1967).
(20) Oxygen alkylation is apparently prevented because of the anti geometry of oxime **17**. Nitrogen alkylation would yield a four-membered-ring nitrone and is presumably not produced in this case because of kinetic preference for cyclopropane formation. A study of substrates which *can* undergo C-, N-, and O-alkylation is currently underway.
(21) Preparation of these materials is to be published, D. A. Clark and P. L. Fuchs; see also D. A. Clark, Ph.D. Thesis, Purdue University, 1978.
(22) Melting points for oxime benzenesulfonates; **20** (mp 136–138 °C); **21** (mp 153–155 °C); **22** (mp 158–160 °C); **23** (mp 133–135 °C).
(23) (a) H. Feuer, Ed., "The Chemistry of the Nitro and Nitroso Group", Part I. Wiley-Interscience, New York, 1969; (b) P. A. S. Smith, "Open-chain Nitrogen Compounds", Vol. 2, W. A. Benjamin, New York, 1966, Chapter 13, pp 355–390; (c) A. T. Blomquist, Ed., "Organic Functional Group Preparations", Vol. II, Academic Press, New York, 1971, Chapter 16, p 383.
(24) In addition to the dimers, 2% of the tertiary tricyclic nitro compound could be isolated from this reaction.
(25) Extended thermolysis of the syn oxime or acid-catalyzed (commercial $CDCl_3$) isomerization yields the anti oxime for the purposes of spectral comparison.[8] TLC analysis (SiO_2, 30% THF–C_6H_{14}) always shows syn oximes to have smaller R_f values than anti oximes in this series.
(26) The same rearrangement occurs at the melting point of the dimer (which melts without exhibiting the typical blue color associated with the nitroso monomers).
(27) Note that these nitrosocyclobutanes rearrange at temperatures ~150 °C higher than the analogous nitrosocyclopropanes.
(28) Graduate Research Associate; David Ross Fellow, 1975–1977; Phillips Petroleum Fellow, 1977–1978.
(29) Postdoctoral Research Associate.
(30) Alfred P. Sloan Fellow, 1977–1979.

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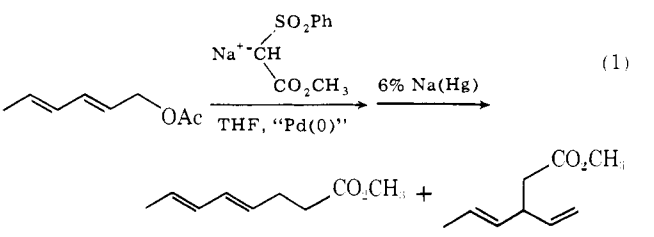
Steric Steering with Supported Palladium Catalysts

Sir:

The development of useful reactions catalyzed by soluble transition metals has led to interest in evolving "insolubilized" versions of these catalysts for ease of recovery and workup.[1] Frequently, such supported catalysts will lose some reactivity and/or selectivity. We report that supporting a palladium(0) species on both silica gel and cross-linked polystyrene not only does not lose reactivity but, because of steric steering, provides important enhanced selectivity over the solubilized forms.

Phosphinylated silica gel was prepared by treating granular silica gel (Ventron 89 346, 8–12 mesh, 300-m^2/g surface area, 1-mL/g pore volume) with 3-chloropropyltrimethoxysilane in hot toluene followed by TMS-chloride and then lithium diphenylphosphide in THF.[2] The phosphinylated silica gel[3] was refluxed with tetrakis(triphenylphosphine)palladium in deoxygenated benzene to give the deep red silica gel catalyst. Phosphinylated polystyrene[4] was prepared in the usual fashion starting with Dow polystyrene cross-linked with 2% divinylbenzene (50–100 mesh).[5] Analysis indicates that chloromethylation led to 94% ring substitution[6a] and phosphide displacement[6b] led to 94% of the chlorides displaced. Palladation of the support as above gave the bright red polystyrene catalyst containing 1.62% palladium[6c] (equiv mol wt, ~6200 per palladium).[7] Both catalysts should be stored in the *absence* of solvent. Remarkably, in the dry state, both are fairly stable toward air, retaining activity even up to 2 months' storage, in contrast to tetrakis(triphenylphosphine)palladium which rapidly decomposes in air.

In the case of carbon nucleophiles in allylic alkylation,[8,9] some increase in regioselectivity is noted. For example, sorbyl acetate showed an increased preference for alkylation at the less hindered terminus as summarized in eq 1.[10] However,



(1)

$(Ph_3P)_4Pd$	69	31
Ⓟ -Pd[11]	80	20

utilization of nitrogen nucleophiles provided dramatic illustrations of the beneficial effect of the supported catalysts.[12]

Treatment of *cis*-3-acetoxy-5-carbomethoxy-1-cyclohexene (**1**) with diethylamine and the soluble palladium catalyst led to a mixture of both the *cis*- and *trans*-3-diethylamino-5-carbomethoxy-1-cyclohexenes[10,13] (**3** and **4** (see eq 2)) with

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