Table I. Hydrogenation of Nitroaromatics (1 mmol Catalyst)

compd	mmol	pressure, psi	time, h	temp, °C	solvent, mL	product(s) (yield, %)[a]
p-nitrophenol	30	400	15	90	EtOH, 20	*p*-aminophenol (98)
m-dinitrobenzene	60	1500	1	60	EtOH, 20	*m*-nitroaniline (1) *m*-phenylenediamine (90)
β-nitrostyrene	20	400	12	90	EtOH, 20; HOAc, 1	four products (unidentified)
5-nitroquinoline	3.0	1000	18	50	EtOAc, 20	5-aminoquinoline (55)
o-nitrotoluene	15	600	4	100	EtOAc, 20	*o*-toluidine (88)
m-nitrotoluene	15	600	4	100	EtOAc, 20	*m*-toluidine (96)
p-nitrotoluene	15	600	4	100	EtOAc, 20	*p*-toluidine (80)
p-chloronitrobenzene	10	600	4	100	EtOAc	*p*-chloroaniline (56)
nitrobenzene	20	600	4	100		aniline (94)
nitrobenzene	20	60	48	25		aniline (66)

[a] Other products were present in less than 5% amounts.

almost 80% conversion to aniline. The reaction is very clean and the only intermediate seen, present in but trace amounts, was azobenzene. The activity of the catalyst dropped rapidly at first (Figure 1) and then leveled off somewhat. After 6 h of operation the catalyst was washed in the reactor at 100 °C with 95% ethanol. Upon resumption of nitrobenzene hydrogenation the initial activity was lower, but over the course of an additional 10 h of operation there was little further drop in activity. The total average turnovers equaled 900.

A point that should be emphasized from the tube reactor experiment is that XAD-4 beads are reasonably stable at fairly high temperatures. It is generally considered that polymer-bound catalysts cannot be used above 150–160 °C. Indeed this is the case for polystyrenes having a low degree of cross-linking (2%). Such temperature limitations are not observed for highly cross-linked polystyrene such as XAD-4. Thus we have hdrogenated nitrobenzene at 280 °C for 1 h without substantial alteration of bead structure or catalytic activity.

The effects of substituent groups was investigated. The three nitrotoluene isomers (Table I) were hydrogenated at room temperature and 600 psi for 4 h. All three isomers hydrogenated at approximately the same rates. The series *p*-chloronitrobenzene, nitrobenzene, and *p*-nitrotoluene provided a measure of the sensitivity of the reaction to electronic effects. Knifton found that hydrogenation rates were enhanced when electron-withdrawing groups were present.[1c] While conversion of *p*-chloronitrobenzene is somewhat lesser than that for the other nitrocompounds, it is clear the reaction is not highly dependent on electronic effects. The catalyst has an excellent shelf-life. The sample used in this investigation was evaluated over a period of 2 years. There was no measurable loss of activity upon storage at room temperature under air. All manipulations with the catalyst were accomplished without use of an inert atmosphere.

In conclusion, the catalyst is highly active for the hydrogenation of aromatic nitro compounds, has a long lifetime, and displays excellent handling properties.

Experimental Section

Materials. Amberlite XAD-4 was a gift of the Rohm and Haas Co. It was obtained as hard, insoluble 20–50-mesh spheres. The polymer was received wet and was dried in a rotary evaporator at 50 °C for 12 h before being used. Chloromethylation was performed according to the procedure of Pepper et al. In one batch the chlorine content was 1.32% (0.372 mequiv/g).

Anthranilic acid was anchored to the beads by stirring the beads with an excess of anthranilic acid in ethyl ether, acetone, or DMF. The following procedure was typical. To 520 g of the chloromethylated beads suspended in 1 L of ethanol was added 100 g of anthranilic acid. This was refluxed for 20 h, filtered, and washed with 2 L of absolute ethanol at 70 °C. Anal. N, 0.46 (0.33 mequiv/g); Cl, 0.60 (0.169 mequiv/g).

Reagent-grade chemicals were generally used without purification. Duplicate runs were made with bulk-grade benzene and no noticeable initial rate differences were observed.

$PdCl_2$–Anthranilic Acid Catalyst. The beads (200 g) were suspended in 500 mL of acetone and 4.2 g (23.4 mmol) of $PdCl_2$ and 5 mL of acetonitrile were added. The suspension was refluxed for 72 h under nitrogen, filtered, washed with acetone, and vacuum-dried. Anal. Pd, 2.05 (0.193 mequiv/g); N, 0.38 (0.271 mequiv/g); Cl, 0.71 (0.200 mequiv/g).

Instruments and Hydrogenation Procedure. Low-pressure hydrogenations were carried out in a standard, catalytic apparatus (Parr Instrument Co., Model 3911). In a typical run a 500-mL reactor was charged with unsaturated compound and catalyst and the system was sealed, purged 3 times with hydrogen, and then pressurized to 60 psig. For high-pressure hydrogenation, the reactants were added to the 300-mL reaction vessel of an Aminco Shaking Assembly (No. 44-13106). The reaction vessel was flushed 3 times with hydrogen. For room-temperature reactions the pressure was then adjusted to the desired level. For higher temperature reactions, the reactor was partially pressurized and then heated, with shaking, to the desired temperature. The pressure was then adjusted to the desired level. The reactions were not considered to have begun until the system was at the desired temperature and pressure, and all reaction times were measured from this point. Termination of several experiments at early stages revealed that a low percentage of hydrogenation had occurred.

Infrared absorption spectra were recorded on a Perkin-Elmer 457 spectrophotometer. GLC data were acquired on a Varian Aerograph 1700, using 10% Carbowax or 20% SE-30 columns. Elemental analyses were performed by Galbraith Laboratories, Knoxville, TN.

Registry No. *m*-Dinitrobenzene, 99-65-0; β-nitrostyrene, 102-96-5; 5-nitroquinoline, 607-34-1; *o*-nitrotoluene, 88-72-2; *m*-nitrotoluene, 99-08-1; *p*-nitrotoluene, 99-99-0; *p*-chloronitrobenzene, 100-00-5; nitrobenzene, 98-95-3.

Reaction of α-Terpinene with Methylphosphonous Dichloride[1]

Louis D. Quin,* Kenneth C. Caster, and S. Barney Soloway[2]

Gross Chemical Laboratory, Duke University, Durham, North Carolina 27706

Received January 18, 1984

α-Terpinene (1) is a commercially available cyclohexadiene derivative which we have considered as a possible participant in the McCormack cycloaddition reaction[3] with phosphorus(III) halides. Were this reaction to be

---

(1) Grateful acknowledgment of the partial support by the Petroleum Research Fund, administered by the American Chemical Society, is made.

(2) Shell Division Co., Modesto, CA.

(3) For a recent review, see: Quin, L. D. "The Heterocyclic Chemistry of Phosphorus"; Wiley-Interscience: New York, 1981; Chapter 2.

0022-3263/84/1949-2627$01.50/0

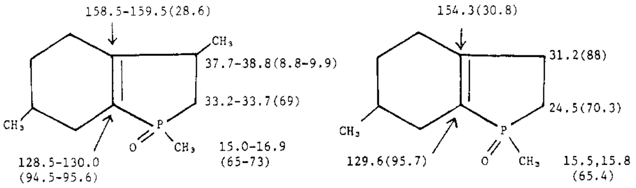
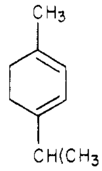
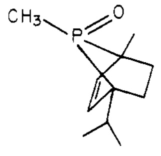


Figure 1. Comparison of ^{13}C NMR chemical shifts and J_{PC} (in parentheses, hertz) of hexahydrophosphindole oxides.

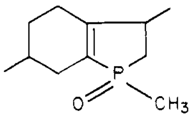
successful, it would constitute a new route to the 7-phosphanorbornene system **2**, which is proving to have special characteristics because of the combination of a highly contracted bond angle at phosphorus and the enforced proximity of orbitals capable of interaction.[4] Cyclohexadiene itself does not give McCormack cycloadducts,[5] although cycloheptadiene participates in this reaction.[6] A slow reaction has now been observed between α-terpinene and methylphosphonous dichloride, but the product obtained after hydrolysis has very different spectral characteristics from the expected 7-phosphanorbornene. We have established it to be a hexahydrophosphindole derivative of structure **3**. This or related reactions may have some practical value; hexahydrophosphindoles are approachable from cycloadditions with 1-vinylcyclohexenes,[7] which require prior synthesis, whereas α-terpinene, a natural product, is available commercially as a byproduct in the manufacture of synthetic pine oil from α-pinene.[8]



1



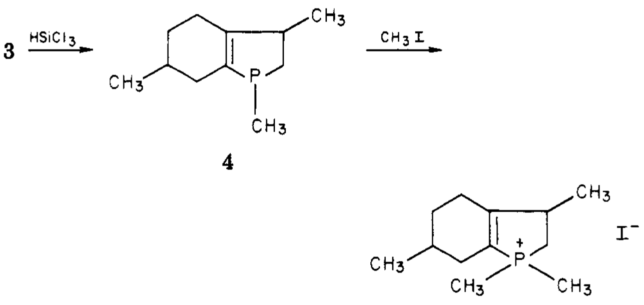
2



3

The reaction of **1** with CH_3PCl_2 was conducted by heating a 1:1 mixture (without solvent) at about 85 °C. After a few days, a dense oil began to separate, which after 3 weeks accounted for half of the liquid volume. Other conditions could well expedite the process; we have indeed observed that traces of HCl, released from CH_3PCl_2 by adding a few microliters of water to the reaction mixture, caused a more rapid deposition of the oil. That the oil constituted a diene–CH_3PCl_2 cycloadduct was obvious from its highly characteristic ^{31}P NMR chemical shift of 101.4 (e.g., δ 105 for the closely related 2-phospholene cycloadduct of 4-methyl-1-vinylcyclohexene[7a]). Only minor amounts of other phosphorus products were present. Hydrolysis followed by chloroform extraction led to a 36% yield of yellow oil, which was colorless after distillation.

The ^{31}P NMR spectrum of the oil immediately revealed that the 7-phosphanorbornene system had not been formed. The oil had four close-lying signals (δ 62.3, 62.6, 63.5, 64.0) in the region uniquely occupied by phospholene oxides[3]; a significantly more downfield shift would be expected for **2** (e.g., δ 91.4 in the dimer of 1-methylphosphole oxide[9]). The ^1H NMR spectrum revealed no olefinic protons to be present and led to the proposal that a bicyclic 2-phospholene oxide (**3**) had been formed. Proof of phosphine oxide character was further obtained by performing the trichlorosilane deoxygenation reaction to form a tertiary phosphine (**4**), which in turn was converted to its quaternary salt **5** with methyl iodide. The salt gave the correct elemental analysis for its derivation from an oxide of structure **3**. Since both oxide **3** and phosphine **4** have three chiral centers (P, C-3, C-6), four diastereoisomers are possible. As noted, this number of isomers was observed by ^{31}P NMR. The phosphine prepared from it displayed only three ^{31}P NMR signals (δ –13.5, –14.9, –16.1) apparently because of signal overlap. On quaternization of the phosphine, chirality at P is lost and only two diastereoisomers of **5** are possible; indeed two ^{31}P NMR signals were observed (δ 46.6 and 46.7).

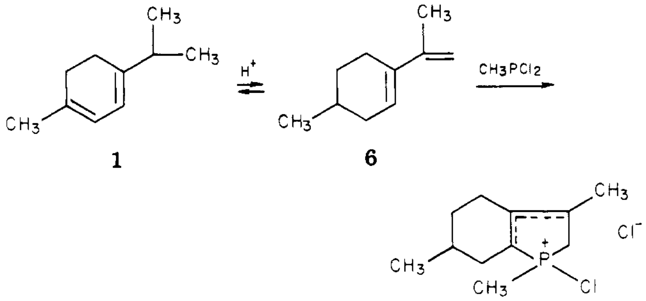


4

5

Proof of the correctness of the structure of **3** was provided by ^{13}C NMR spectral analysis. The spectrum was complex due to the presence of the diastereoisomers, but interpretation was aided by using the INEPT technique to distinguish signals from CH_3, CH_2, CH, and quaternary C. We have previously used this technique with great success on related phosphorus compounds.[7] In Figure 1 is presented a summary of pertinent ^{13}C data used for the structure proof of **3** and data for the known compound that lacks the 3-methyl.[7a] Only ranges of chemical shifts can be reported for **3** since the signals were composites for the four diastereoisomers. The differences from the model compound are easily accounted for by the deshielding α- and β-effects of the C-3 methyl of **3**.

To account for the formation of a cycloadduct (**7**) which can be hydrolyzed to **3**, it is reasonable to assume that a trace of acid causes α-terpinene to equilibrate, in part, with the rare *p*-mentha-3,8-diene (**6**), which is the actual species undergoing the McCormack reaction. This diene, which is available only from a multistep synthesis,[10] has indeed been reported as a minor component in the diene mixture resulting from H_2SO_4-catalyzed equilibration of α-terpinene.[11] That the formation of the adduct **7** is expedited



7

---

[4] Quin, L. D.; Caster, K. C.; Kisalus, J. C.; Mesch, K. A. *J. Am. Chem. Soc.*, in press.

[5] Mesch, K. A.; Quin, L. D., unpublished results.

[6] Awerbouch, O.; Kashman, Y. *Tetrahedron* **1975**, *31*, 33.

[7] (a) Quin, L. D.; MacDiarmid, J. E. *J. Org. Chem.* **1982**, *47*, 3248. (b) Quin, L. D.; Kisalus, J. C.; Mesh, K. A. *Ibid.* **1983**, *48*, 4466.

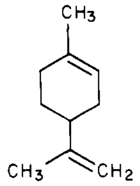
[8] Derfer, J. M.; Derfer, M. M. In Kirk-Othmer "Encyclopedia of Chemical Technology", 3rd ed.; Wiley-Interscience: New York, 1983; Vol. 22, pp 747–749.

[9] Quin, L. D.; Mesch, K. A.; Bodalski, R.; Pietrusiewicz, K. M. *Org. Magn. Reson.* **1982**, *20*, 83.

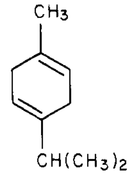
[10] Eshinazi, H. E.; Pines, H. *J. Org. Chem.* **1955**, *20*, 1666.

[11] Bates, R. B.; Caldwell, E. S.; Klein, H. P. *J. Org. Chem.* **1969**, *34*, 2615.

by added acid accords with this view. Nonconjugated isomers of α-terpinene were less readily rearranged to the structure **6** required for reaction with CH_3PCl_2 and were not useful in this process. Neither limonene (**8**) nor γ-terpinene (**9**) gave detectable amounts of phospholene oxide **3** under conditions effective for the reaction with α-terpinene. With limonene, a complex black mixture resulted, while with γ-terpinene little reaction occurred.



8



9

Exploratory experiments under similar conditions showed that PCl_3 and $C_6H_5PCl_2$ reacted less readily than CH_3PCl_2 with α-terpinene. Some phosphorus incorporation in the product was detected, but the low yields and complexity of the product mixture discouraged detailed examination.

Experimental Section[12]

1,3,6-Trimethyl-2,3,4,5,6,7-hexahydrophosphindole 1-Oxide (3). To a Teflon bottle was added 16.7 g (0.12 mol) of freshly distilled α-terpinene (Aldrich), 0.1 g of copper stearate, and 13.1 g (0.11 mol) of methylphosphonous dichloride. The solution was sealed under nitrogen and heated at 82–86 °C for 3 weeks. A dense light-brown oil, constituting approximately one-half of the original total volume of the solution, was formed. ^{31}P NMR analaysis of the oil showed it to be a mixture of CH_3PCl_2 and adduct with minor impurities: ^{31}P NMR ($CDCl_3$) δ 101.4 (adduct **7**, 66%), 190.0 (unreacted CH_3PCl_2, 21%), 87.7 and 88.1 (together 13%).

The thick oil was slowly hydrolyzed by addition to 200 g of ice in 200 mL of $CHCl_3$; care was taken to keep the temperature below 25 °C. The mixture was made pH 7 with solid $NaHCO_3$. The layers were separated, and the aqueous phase was extracted with six 40-mL portions of $CHCl_3$. The combined $CHCl_3$ layers were dried over Na_2SO_4 and $MgSO_4$. Concentration by rotoevaporation and high vacuum gave 7.9 g (36%) of a light-yellow oil which was distilled (125–127 °C (0.1 mm)) to yield a colorless oil: ^1H NMR ($CDCl_3$) δ 0.9–3.0 (complex, overlapping signals); ^{31}P NMR ($CDCl_3$) δ 64.0, 63.5, 62.6, 62.3; partial ^{13}C NMR, Figure 1. A persistent impurity (5%), preventing elemental analysis, had ^{31}P signals at δ 32.8 to 33.4.

1,3,6-Trimethyl-2,3,4,5,6,7-hexahydrophosphindole. To a solution of 1.0 g (5 mmol) of **3** in 40 mL of benzene was added dropwise under nitrogen a solution of 1.5 mL (15 mmol) of Cl_3SiH in 10 mL of benzene. A slight exotherm ensued; the mixture was refluxed for 1 h and then hydrolyzed with 80 mL of 30% NaOH in an ice–water bath. Extraction with two 20-mL portions of benzene was followed by drying over $MgSO_4$. Concentration under aspirator vacuum gave 0.9 g (98%) of **4** as a clear oil. Kugelrohr distillation gave 0.8 g (88%) of **4** (bp 30–50 °C 0.1 mm)); ^{31}P NMR ($CDCl_3$) δ −13.5, −14.9, −16.1; partial ^{13}C NMR ($CDCl_3$) CH_3 at δ 11.3 (21.5), 11.6 (20.0), 14.3 (23.1); C-2 at 30.7 (6.2), 33.2 (4.6), 34.1 (7.7); C-3a at 144–147 (coupling uncertain); C-7a at 133.5, 133.8 (apparent s).

The phosphine mixture was reacted with excess iodomethane in pentane. A white solid formed immediately, and the mixture was then allowed to stand at −18 °C. The solid was filtered and washed with pentane. Drying under high vacuum gave 1.1 g (77%), which was recrystallized from methanol–ethyl acetate to yield **3** as white flakes: mp 142–144 °C; ^{31}P NMR ($CDCl_3$) δ 46.7, 46.6. Anal. Calcd for $C_{12}H_{22}IP$: C, 44.46; H, 6.84; P, 9.55. Found: C, 44.30; H, 6.79; P, 9.59.

Registry No. 1, 99-86-5; 3 (isomer I), 90432-46-5; 3 (isomer II), 90527-95-0; 3 (isomer III), 90527-96-1; 3 (isomer IV), 90527-97-2; 4 (isomer I), 90432-47-6; 4 (isomer II), 90527-98-3; 4 (isomer III), 90527-99-4; 4 (isomer IV), 90528-00-0; 5 (isomer I), 90432-48-7; 5 (isomer II), 90432-49-8; 8, 138-86-3; 9, 99-85-4; CH_3PCl_2, 676-83-5; Cl_3SiH, 10025-78-2.

---

[12] Melting points were taken on a Mel-Temp apparatus and are corrected. Carbon-13 FT NMR spectra (including the INEPT program) were taken on a JEOL FX-90Q spectrometer at 22.5 MHz, utilizing an internal deuterium lock with proton noise-decoupling. Chemical shifts are expressed in ppm downfield from tetramethylsilane. Phosphorus-31 FT NMR spectra were obtained with the JEOL FX-90Q at 36.2 MHz; chemical shifts are expressed in ppm relative to external 85% H_3PO_4 with positive shifts downfield. Elemental analyses were performed by MHW Laboratories, Phoenix, AZ.

Method for the Preparation of Terminal and Internal Conjugated Diynes via Palladium-Catalyzed Cross-Coupling[1]

Ei-ichi Negishi,*[2] Nobuhisa Okukado, Stephen F. Lovich, and Fen-Tair Luo

Departments of Chemistry, Syracuse University, Syracuse, New York 13210, and Purdue University, West Lafayette, Indiana 47907

Received January 17, 1984

The Pd- or Ni-catalyzed cross-coupling provides one of the most general methods for the formation of a carbon–carbon single bond between two unsaturated carbon groups, i.e., aryl, alkenyl, and alkynyl. In particular, the Pd-catalyzed cross-coupling has been successfully applied to various cases covering all possible categorical combinations except the alkynyl–alkynyl coupling.[3] In fact, all our attempts to cross-couple two alkynes via the Pd-catalyzed reaction of a haloalkyne with an alkynylmetal containing Li, Mg, Zn, Al, and Sn have led to the formation of nearly the 1:2:1 mixtures of homo- and cross-coupled products, even though the combined yields were generally ca. 100%.[4] Typically, the reaction of 1-heptynylzinc chloride with 1-iodo-1-hexyne in the presence of 5 mol % of either $Pd(PPh_3)_4$ or a Pd catalyst generated in situ by treating $Cl_2Pd(PPh_3)_2$ with 2 equiv of $i\text{-}Bu_2AlH$ produced 5,7-tridecadiyne (ca. 50%), 5,7-dodecadiyne (ca. 25%), and 6,8-tetradecadiyne (ca. 25%).

In view of the above difficulty, coupled with the relative paucity of satisfactory methods for the synthesis of conjugated diynes,[5] we undertook to develop a general and

---

[1] Selective Carbon–Carbon Bond Formation via Transition-Metal Catalysis. 39. Part 38: Miller, J. A.; Negishi, E. *Isr. J. Chem.*, in press

[2] Present address: Department of Chemistry, Purdue University, West Lafayette, IN 47907.

[3] Negishi, E. *Acc. Chem. Res.* **1982**, *15*, 340 and references therein.

[4] King, A. O. Ph.D. Dissertation, Syracuse University, 1979.

[5] (a) Probably the most widely used method for preparing internal conjugated diynes is the Cadiot–Chodkiewicz reaction [Cadiot, P.; Chodkiewicz, W. In "Chemistry of Acetylenes"; Viehe, H. G., Ed.; Marcel Dekker: New York, 1969; Chapter 9]. Although various types of bromoalkynes may be used, simple alkyl-substituted alkynes have seldom been used as reagents to be coupled with bromoalkynes. Other alkynes that may not be readily used include HC≡CR where R = Me_3Si, Ph_3Sn, Ph_2P, and CHO. (b) The stoichiometric reaction of alkynylcoppers with haloalkynes generally gives mixtures of three possible coupling products except in some special cases, such as the reaction of 1-bromo-2-(trimethylsilyl)ethyne with alkynylcoppers [Miller, J. A.; Zweifel, G. *Synthesis* **1983**, 128]. (c) Treatment of dialkynylborates with iodine provides an attractive alternative to the Cu-based methodologies [Pelter, A.; Hughes, R.; Smith, K.; Tabata, M. *Tetrahedron Lett.* **1976**, 4385. Sinclair, J. A.; Brown, H. C. *J. Org. Chem.* **1976**, *41*, 1078]. (d) Treatment of 1,4-dichloro-2-butyne with 3 equiv of $NaNH_2$ followed by the addition of an alkyl halide provides a convenient method for preparing alkyl-substituted terminal diynes [Brandsma, L. "Preparative Acetylenic Chemistry"; Elsevier: Amsterdam, 1971]. The method cannot accommodate hindered alkyl and other types of carbon groups. (e) The Cadiot–Chodkiewicz reaction is applicable to the synthesis of terminal diynes by using 2-methyl-3-butyn-2-ol as an ethynyl synthon [Brandsma, L. "Preparative Acetylenic Chemistry"; Elsevier: Amsterdam, 1971]. Deprotection of the ethynyl group, however, requires treatment of the cross-coupled diynes with powdered KOH at 150–200 °C.