drogenation on the Parr shaker (1.01 equiv of H_2 absorbed in 18 h), filtration, and solvent removal gave a residue which was Kugelrohr distilled [bp 150 °C (0.05 mm)] to give 120 g of a white solid, which was heated in 1.2 L of tetralin while methanol was removed by distillation over 6 h. Cooling to room temperature while standing for 12 h gave a brown precipitate which was filtered and washed with pentane to remove tetralin. Sublimation [80 °C (0.02 mm)] gave 57 g (65%) of material containing traces of tetralin. Crystallization from benzene gave 53 g (60%) of pure material: mp 179–181 °C;[2] IR 3440 (NH), 2990, 1440 (OH), 1690 (CO) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.8–2.2 (m, 4 H), 2.6–2.8 (pentet, 1 H), 2.9–3.3 (m, 4 H), 7.8 (br s, 1 H); ^{13}C NMR (CD_3CN) δ 17.8 (t), 26.5 (d), 42.9 (t), 170.3 (s, CO).

1,2-Diazabicyclo[2.2.2]octane (7). A solution of 2.0 g (15.9 mmol) of the above hydrazide in 200 mL of THF was added to 0.92 g (24 mmol) of lithium aluminum hydride in THF. After 18 h of reflux, the cooled solution was worked up by the 1:1:3 method,[14] the filtrate was dried over magnesium sulfate, and solvent was removed by distillation. Sublimation of the residue at room temperature (0.02 mm) gives **7**[12] as a colorless, hygroscopic glass (1.5 g, 84%): mp 151–153 °C;[15] IR 3400 (NH), 2690 (CH), 1290 (CN) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.4–2.0 (m, 5 H), 2.8–3.3 (m, 6 H), 3.35 (s, 1 H); ^{13}C NMR (CD_3CN) δ 21.26 (d), 25.29 (t), 47.84, 50.42 (t).

2-Nitroso-1,2-diazabicyclo[2.2.2]octane (4). Nitrosation of **7** using the method reported for **1** on a 1.0-g scale gave 1.26 g (95% yield) of **4**,[12] mp 90–91 °C, after recrystallization from cyclohexane: IR 2920, 1440 (CH), 1620 (NNO) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.4–2.7 (m, 4 H), 2.27 (m, 1 H), 3.0–3.5 (m, 4 H), 3.50 (d, 2 H); ^{13}C NMR (CD_3CN) δ 23.6 (d), 24.5 (t), 50.0 (t, CH_2N), 51.6 (t, CH_2N).

2-Nitroso-3-methyl-1,2-diazabicyclo[2.2.2]octane (5). A solution of LDA (11 mL of 1.08 M solution, 1.08 equiv) in THF/hexane was added to 1.55 g (11 mmol) of **4** in 150 mL of THF at −78 °C, and after the solution was stirred for 1 h, 1.54 g (11 mmol) of methyl iodide was added, and the solution was stirred at room temperature for 1.5 h. After 15 mL of 20% aqueous NaCl was added and the mixture was stirred for 30 min, the aqueous layer was extracted with two 15-mL portions of chloroform. The combined organic layers were dried (magnesium sulfate) and concentrated in vacuo, and the residue was Kugelrohr distilled [bp 140 °C (0.2 mm)]. Sublimation (bath temperature 60 °C, cold finger cooled to −20 °C) gave 0.7 g (4.4 mmol, 41%) of **5**:[12] yellow solid; mp 42–44 °C; IR 2940, 1440 (CH), 1630 (NN), 1225 (CN) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.33 (d, 3 H), 1.5–2.25 (m, 5 H), 3.0–3.7 (m, 4 H), 4.2 (d of q, 1 H); ^{13}C NMR (CD_3CN) δ 14.40 (q), 18.84 (t), 25.42 (t), 28.92 (d), 49.52 (t), 51.28 (t), 56.08 (d, CHMe).

2-Nitroso-3,3-dimethyl-1,2-diazabicyclo[2.2.2]octane (6). The procedure for **5** was followed, but before quenching, the solution was recooled to −78 °C and 11 mL of 1.08 M LDA in THF/hexane added, followed by 1.54 g of methyl iodide. After 10 min at low temperature, stirring was continued at room temperature for 3 h, and workup proceeded as for **5**. Kugelrohr distillation [bp 140 °C (0.2 mm)] followed by recrystallization gave 0.73 g (5.2 mm, 47%) of **6**:[12] yellow solid; mp 173–174 °C; IR (cm^{-1}) 2935, 1430 (CH), 1540 (NNO) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.57 (s, minor isomer), 1.75 (s, major isomer), 1.2–2.5 (m, 5 H), 2.98–3.55 (m, 4 H); ^{13}C NMR (CD_3CN) δ 62.3 (s), 61.3 (s), 49.8 (t), 47.8 (t), 36.4 (d), 34.2 (d), 27.4 (q), 21.9 (q), 21.81 (t), 21.76 (t).

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Registry No. 1/1A, 21744-12-7; **2/2A/2B**, 74420-57-8; **3/3A/3B**, 74420-58-9; **4/4A**, 1632-37-7; **5/5A/5B**, 74420-59-0; **6/6A/6B**, 74420-60-3; 7, 329-94-2; isoquinuclidine, 280-38-6; methyl iodide, 74-88-4; 1-nitroso-4-(carbomethoxy)piperidine, 13458-55-4; 4-(carbomethoxy)pyridine, 2459-09-8; 1,2-diaza-3-oxobicyclo[2.2.2]octane, 1632-26-4.

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Use of Phase-Transfer Reaction Conditions for the Hydrogenation of Conjugated Dienes and α,β-Unsaturated Ketones with a Homogeneous Metal Hydride Catalyst

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The homogeneous water-soluble hydrogenation catalyst $K_3[Co(CN)_5H]$ has been shown to be very active in hydrogenation reactions with conjugated dienes and α,β-unsaturated ketones when used under phase-transfer reaction conditions. Thus, conjugated dienes are converted into monoenes, generally with overall 1,4-addition to yield *E* products, and α,β-unsaturated ketones to saturated ketones in high yield. Because of rate accelerations, stabilization of the catalyst by the phase-transfer onium reagents, and ease of isolation of products, these new reaction conditions make this readily accessible catalytic system useful for synthetic scale reactions for the first time.

Phase-transfer reaction conditions have proven to be very effective in synthetic organic chemistry.[1] The basis for this success is that these conditions allow a reaction to take place between one reactant which is soluble in water (generally a nucleophile such as OH^- or CN^-) and a second reactant which is soluble in typical organic solvents such as benzene or methylene chloride. Although simple two-phase conditions have been used successfully for this type of reaction, these reactions are generally slow, presumably because the reactants are isolated from each other. In phase-transfer catalysis, an organic onium salt such as tetrabutylammonium chloride is added to the two-phase system. The onium group will ion pair with the water-soluble anion and will transfer it to the organic phase

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(1) (a) Dockx, J. *Synthesis* **1973**, 441–456. (b) Dehmlow, E. V. *Angew. Chem., Int. Ed. Engl.* **1974**, *13*, 170. (c) Jones, R. A. *Aldrichimica Acta* **1976**, *9*, 35–52.

0022-3263/80/1945-3860$01.00/0

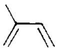
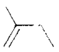
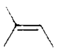
for reaction with the organic-soluble substrate. Spectacular rate accelerations have been observed for numerous organic reactions when carried out under these conditions compared with simple two-phase or conventional one-phase reactions. Another attractive feature of phase-transfer catalysis is that the product of most reactions remains in the organic phase and is easily isolated.

Although many inorganic reagents such as permanganate,[2] borohydride,[3] and dichromate[4] have been used under phase-transfer reaction conditions for organic synthesis, only recently have transition-metal organometallic reagents been used in these reactions. A number of successful phase-transfer systems have now been reported in which metal carbonyl and palladium phosphine complexes act catalytically in useful organic transformations.[5] Also, phase-transfer conditions have proven useful for the preparation of new transition-metal organometallic complexes.[6] In nearly every case, the main purpose of the phase-transfer system is to deliver base from the aqueous phase.

A different approach is to carry out phase-transfer reactions by using a water-soluble metal catalyst reacting with organic-soluble substrates. In such a system the metal catalyst needs to be transferred to the organic phase. In conjunction with our work with micellar solutions for catalytic systems,[7] we have studied the hydrogenation of a variety of dienes and α,β-unsaturated ketones and aldehydes with the water-soluble catalyst $K_3[Co(CN)_5H]$ under phase-transfer reaction conditions and report our results here.[8]

Although the $K_3[Co(CN)_5H]$ catalyst has been known for many years and has been the subject of many papers,[9] it has not generally been a useful catalyst for organic reactions. Basically, the catalyst will hydrogenate any carbon–carbon double bond in conjugation with other unsaturation but will not hydrogenate isolated carbon–carbon double bonds or reduce carbonyl functional groups. As this catalyst is easily prepared from $CoCl_2$ and KCN under hydrogen gas at 1 atm and is reactive at room temperature, the potential of the catalyst is high. This potential has generally not been realized for a number of reasons. They are as follows: (1) the catalyst is inhibited by excess substrate[9a,d] (more than 1 equiv of substrate/equiv of cobalt); (2) the lifetime of the catalyst is short and the rate of reactions relatively slow, thus leading to poor turnover numbers (generally 2 or less in reported work[9]); (3) the regioselectivity for possible ene products in the hydrogenation of dienes is not high (although some control can be obtained by adding excess cyanide[9a,d]). We show here that phase-transfer reaction conditions largely overcome these problems, making this readily accessible and inexpensive catalyst useful for a variety of hydrogenation reactions.

Table I. Catalytic Hydrogenation of 2-Methyl-1,3-butadiene (Isoprene)

	mmol[a] of 	ammonium salt[b]	% products 	% products 	% products[c] 	t, h
1	20.0[d]	$(CH_3)_4NCl$	2	98		5
2	20.0[e]	none	9	91[f]		48
3	40.0	$(CH_3)_4NCl$	2	98		11
4	50.0[g]	$(CH_3)_4NCl$	3	97		13
5	60.0	$(CH_3)_4NCl$	3	83[f]	14	24
6	30.0 (× 2)	$(CH_3)_4NCl$	2	98		18
7	20.0 (× 4)	$(CH_3)_4NCl$	4	83	13	36
8	20.0	Et_3PhCH_2NCl	100			6
9	60.0	Et_3PhCH_2NCl	3	92[f]	5	30
10	20.0	Et_4NOH	1	99		10
11	20.0	$(CH_3)_4NCl$[h]	2	73[f]	25	15
12	20.0	Et_3PhCH_2NCl[h]	100			7
13	20.0[i]	$(CH_3)_4NCl$	2	98		2
14	50.0[i]	$(CH_3)_4NCl$	3	97[f]		5
15	150.0[i]	$(CH_3)_4NCl$	3	97		15
16	20.0[j]	$(CH_3)_4NCl$	3	97		5
17	40.0[k]	$(CH_3)_4NCl$	6	82	12	18

[a] 2.2 mmol of catalyst in 40 mL of aqueous solution unless otherwise indicated. [b] 2.2 mmol in 20 mL of benzene unless otherwise indicated. [c] Recovered unreacted as estimated from GC analysis. [d] 78% isolated yield. [e] 74% isolated yield. [f] Trace amounts of 3-methyl-1-pentene also detected. [g] 87% isolated yield. [h] 20 mL of toluene used instead of benzene. [i] 6.6 mmol of catalyst. [j] After aging the catalyst for ca. 40 h. [k] A 5.0-mL mixture of 90% 2-methyl-2-butene and 10% 2-methyl-1-butene was injected initially.

Experimental Section

The organic substrates used in this work were obtained from commercial sources and checked for purity by gas chromatography. Tetramethylammonium chloride and benzyltriethylammonium chloride were purchased from Aldrich. Methyltriphenylphosphonium iodide and benzyltriphenylphosphonium chloride were made from triphenylphosphine and methyl iodide and benzyl chloride, respectively. These salts were washed with dry ether, dried in vacuo, and stored either in a Schlenk tube or under vacuum in a desiccator containing $CaCl_2$.

Benzene, toluene, chlorobenzene, dichloromethane, and ethyl ether were distilled, deaerated, and stored under a nitrogen atmosphere. Distilled water was deaerated at ca. 80 °C by being purged with nitrogen for 2 h.

Gas chromatography experiments were performed on a Hewlett-Packard 5711A dual column equipped with a Vidar 6300 digital integrator and a $^1/_8$ in. × 6 ft aluminum column with 10% HiEff-1-BP on 80/100-mesh Chromsorb P (acid washed) or a $^1/_8$ in. × 12 ft copper column with 10% UCW-982 on 80/100-mesh Chromsorb P (acid washed).

Reported yields are isolated yields which are generally lower than the actual yields as a small amount of the product remained either in the organic phase from which it was distilled or in the aqueous phase. Product identification was accomplished by comparing gas chromatography retention times with those of authentic samples when available or by ^{13}C NMR analysis. Quantitative ^{13}C NMR spectroscopy was used for the analysis of hydrogenation products of (*E*)-2,(*E*)-4-hexadiene and (*E*)-2,-(*Z*)-4-hexadiene. Spectra of these products were recorded with a 43° pulse and a pulse delay of 40.0 s, with proton decoupling and suppressed nuclear Overhauser enhancement (NOE).

Catalytic Hydrogenation of Dienes. The catalyst $K_3[Co(CN)_5H]$ was made according to a known literature procedure.[9a] All reactions were carried out under hydrogen at 1 atm of pressure and room temperature. Each reaction was carried out in a three-necked, 100-mL, round-bottomed flask. One neck was

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[2] (a) Starks, C. M. *J. Am. Chem. Soc.* **1971**, *93*, 195–199. (b) Menger, F. M.; Rhee, J. U.; Rhee, H. K. *J. Org. Chem.* **1975**, *40*, 3803–3805.

[3] Bakells, J.; Colouna, S.; Fournaier, R. *Synthesis* **1976**, 266–267.

[4] Hutchins, R. O.; Natale, N. R.; Cook, W. J. *Tetrahedron Lett.* **1977**, 4167–4170.

[5] (a) Abbayes, H.; Alper, H. *J. Am. Chem. Soc.* **1977**, *99*, 98–101. (b) Alper, H.; Abbayes, H. *J. Organomet. Chem.* **1977**, *134*, C11–C14. (c) Cassar, L.; Foa, M. *Ibid.* **1977**, *134*, C15–C16. (d) Cassar, L.; Foa, M.; Gardano, A. *Ibid.* **1976**, *121*, C55–C56.

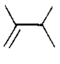
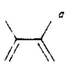
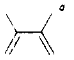
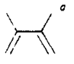
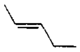
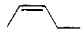
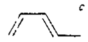
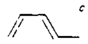
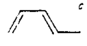
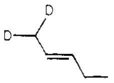
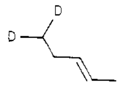
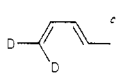
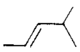
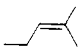
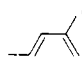
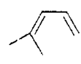
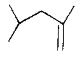
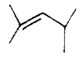
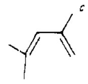
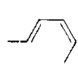
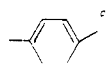
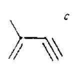
[6] (a) Alper, H.; Roches, D. *J. Organomet. Chem.* **1976**, *117*, C44–C46. (b) Alper, H.; Abbayes, H.; Roches, D. *Ibid.* **1976**, *121*, C31–C34. (c) Hui, K.; Shaw, B. L. *Ibid.* **1977**, *124*, 262–264. (d) Darensbourg, D. J.; Froelich, J. A. *J. Am. Chem. Soc.* **1978**, *100*, 338–340.

[7] (a) Reger, D. L.; Habib, M. M. *J. Mol. Catal.* **1978**, *4*, 315–324. (b) *Ibid.* **1980**, *7*, 365–372.

[8] A preliminary report of this work has appeared: Reger, D. L.; Habib, M. M.; Fauth, D. J. *Tetrahedron Lett.* **1979**, 115–116.

[9] (a) Kwiatek, J.; Seyler, J. K. "*Advances in Chemistry*"; American Chemical Society: Washington, DC, 1968; Vol. 70, p 207–232. (b) Murakami, M.; Kang, J. W. *Bull. Chem. Soc. Jpn.* **1963**, *36*, 763–769. (c) Mabrouk, A. F.; Selke, E.; Rohwedder, W. K.; Dutton, H. J. *J. Am. Oil Chem. Soc.* **1965**, *42*, 432. (d) James, B. R. "Homogeneous Hydrogenation"; Wiley: New York, 1973; pp 106–154.

Table II. Catalytic Hydrogenation of Various Conjugated Diene Substrates

	substrate (mmol)	ammonium salt	% product isomer A^n	 isomer B^n	t, h
					
1	 ^{a} (22)	none	29	71	26
2	 ^{a} (22)	$(CH_3)_4NCl^b$	20	80	8
3	 ^{a} (22)	$Et_3PhCH_2NCl^b$	20	80	6
					
4	 ^{c} (20)	none	96	4^d	19
5	 ^{c} (20)	$Et_3PhCH_2NCl^b$	100		5
6	 ^{c} (50)^e	$Et_3PhCH_2NCl^b$	100		
					
7	 ^{c} (12)^f	$Et_3PhCH_2NCl^b$	53^g	47^g	3
					
8	 ^{c} (17.5)^h	$Et_3PhCH_2NCl^j$	27	73	35
9	 ^{c} (17.5)^i	$Et_3PhCH_2NCl^j$	27	73	32
					
10	 ^{c} (15.5)^k	$Et_3PhCH_2NCl^j$	3	97	96
11	 ^{c} (17.5)^l	$Et_3PhCH_2NCl^b$	53	47	75
12	 ^{c} (17.5)^m	$Et_3PhCH_2NCl^b$	52	48	72
13	 ^{c} (20)	$Et_3PhCH_2NCl^b$	no reaction		
14	 ^{c} (14)	$Et_3PhCH_2NCl^b$	no reaction		
15	 ^{c} (22)	$Et_3PhCH_2NCl^b$	no reaction		

[a] 2.2 mmol of catalyst in 40 mL of water. [b] 2.2 mmol in 20 mL of benzene. [c] 6.6 mmol of catalyst in 40 mL of water. [d] Also a trace of 1-pentene (less than 1%). [e] 80% isolated yield. [f] Prepared as in ref 7a. [g] Percentages established by using ^{2}H NMR. [h] 83% isolated yield. [i] 79% isolated yield. [j] 2.2 mmol in 15 mL of toluene. [k] 60% isolated yield. [l] 74% isolated yield. [m] 68% isolated yield. [n] The percentages of each product are listed under the respective structures.

connected by a gas-inlet tube to a gas buret with a leveling bulb, the second was connected to a 100-mL, pressure-equalizing dropping funnel, and the third was stoppered with a septum cap (frequently a T-joint stopcock was used to isolate the septum from the system except during injections or sampling) for injection of the substrate and organic solvent. The reactions were stirred vigorously with a Teflon-coated rod magnet. A systematic set of reactions were carried out with 2-methyl-1,3-butadiene (isoprene) to establish an optimum procedure, and this was then used for the other dienes. The catalyst concentration, organic phase, phase-transfer reagent, amount of isoprene added, and concentration of phase-transfer reagent were all varied to determine the effect on the rate as well as the selectivity of the reaction. In a typical reaction, $CoCl_2{\cdot}6H_2O$ (0.52 g, 2.2 mmol), NaOH (0.090 g, 2.2 mmol), $(CH_3)_4NCl$ (TMAC; 0.24 g, 2.2 mmol), and 20 mL of degassed water were placed in the reaction flask described above. A mixture of KCN (0.740 g, 11.4 mmol) and KCl (0.36 g, 4.8 mmol) dissolved in 20 mL of degassed water was added to the dropping funnel. The system was repeatedly evacuated and refilled with hydrogen. With the hydrogen atmosphere being maintained, the cyanide solution was added rapidly, this solution was stirred efficiently, and, after about 30 min was allowed for the catalyst to form, 20 mL of degassed benzene was added followed by 2.0 mL (1.5 g, 20 mmol) of isoprene. The reaction rate was monitored by hydrogen uptake. Reaction time was ca. 5 h for complete hydrogenation of isoprene. The hydrogenation of the other dienes was accomplished according to this general procedure. Reaction times varied with each substrate (see the tables). For various reactions, the phase-transfer reagent was changed as was the organic solvent as noted in the Results section. For isolation of the products of these reactions, the organic phase was separated, small amounts were taken for GC analysis, and the remaining sample was distilled very slowly to separate the products. In many cases, repeated distillation was needed to obtain pure products.

Testing the Lifetime of the Catalyst. The catalyst (2.2 mmol) in 40 mL of solution was made as described above. Tetramethylammonium chloride (0.24 g, 2.2 mmol) was used as the phase-transfer reagent. The catalyst was tested for activity initially with 0.1 mL of isoprene which underwent hydrogenation normally. The solution was left to stir under a hydrogen atmosphere for ca. 40 h. Isoprene (2.0 mL, 20 mmol) was then injected.

Hydrogenation proceeded normally.

Product Inhibition of Catalyst. To test for product inhibition, the catalyst was made as described above. Isoprene (4.0 mL, 40 mmol) and a 5.0-mL mixture of 90% 2-methyl-2-butene and 10% 2-methyl-1-butene were injected. The reaction proceeded relatively slowly, with hydrogen absorption ceasing after ca. 18 h. GC analysis indicated the presence of ca. 12% unreacted isoprene.

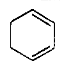
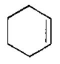
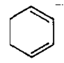
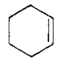
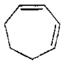
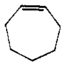
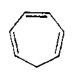
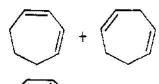
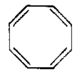
Hydrogenation of α,β-Unsaturated Carbonyl Compounds. The same experimental setup was used for ketones. Because the reactions generally were slower, a higher catalyst concentration (6.6 mmol) was used. The phase-transfer catalyst benzyltriphenylphosphonium chloride (0.3 mmol) was used. For liquid substrates, no additional organic phase was used, and solid substrates were dissolved in a minimum amount of toluene. The substrate was added in 1.0-mL increments, generally to a total amount of 5.0 mL. At completion, the reaction mixtures were extracted with an organic solvent of appropriate boiling point. Volatile products were isolated by distillation whereas higher boiling products were isolated by evaporation of the organic layer. For aldehydes, no added base was used, and a CN^-/Co ratio of exactly 5.0 was employed to minimize aldol condensation reactions.

Results

Hydrogenation of Isoprene (Table I). For the substrate 2-methyl-1,3-butadiene (isoprene), the many variables in these reactions were tested. Most importantly, comparison of entries 1–4 (Table I) shows that the addition of a phase-transfer reagent to these two-phase reactions greatly accelerates the rate of the reaction. Because entry 2 represents the upper limit in the amount of substrate that can be hydrogenated without a phase-transfer reagent present under these concentrations, these experiments demonstrate that synthetic-scale reactions can easily be carried out only under phase-transfer conditions. In addition to rate acceleration, a major effect of the phase-transfer reagent is to prevent catalyst decomposition. In entry 2, decomposition is visibly evident within a few hours (a precipitate forms), but in all of the reactions containing a phase-transfer reagent the solutions remain homogeneous for days. Subsequent entries demonstrate that there is an upper limit to the amount of isoprene that can be hydrogenated but that this limit easily can be overcome by increasing the concentration of catalysts (or, of course, the size of the reaction). The upper limit on the amount of substrate that can be hydrogenated with a given amount of catalyst is not from simple aging of the solutions. Generally, a variety of phase-transfer reagents are successful in the reaction, and toluene is an acceptable organic phase (although not with $(CH_3)_4NCl$).

Hydrogenation of Other Dienes. Tables II and III list hydrogenation data on a variety of conjugated dienes. Both 2,3-dimethylbutadiene and 1,3-pentadiene hydrogenate readily under the phase-transfer reaction conditions whereas the reactions are sluggish in a simple two-phase system. Although only one product is produced with 1,3-pentadiene, the reaction is not specific as shown by the reaction of the 1,1′-dideuterio derivative. The $^2H\{^1H\}$ NMR spectrum of the product from this reaction (entry 7, Table II) showed clearly that the product is formed from about equal overall 1,4-addition and 1,2-addition to the terminal double bond. As a higher catalyst concentration was used for this and subsequent substrates, the substitution of methyl groups at the 1- and 4-positions of the diene clearly slows the reactions, with two phenyl groups or four methyl groups inhibiting the reaction completely. Entry 15 of Table II shows that a conjugated enyne will not react. Cyclohexadiene readily reacts. Cycloheptatriene yields a mixture of the two possible dienes, and, surprisingly, the conjugated diene 1,3-cycloheptadiene reacts further only sluggishly.

Table III. Catalytic Hydrogenation of Cyclopolyene Molecules

substrate[a]	ammonium salt[b]	% products			t, h
	Et_3PhCH_2NCl				12
	none				21
					
	Et_3PhCH_2NCl	67	15.4	17.6	62
 [c]	Et_3PhCH_2NCl	45	31	24	48
	Et_3PhCH_2NCl	no reaction			

[a] 2.0 mL of substrate and 2.2 mmol of catalyst in 40 mL of water. [b] 2.2 mmol in 20 mL of benzene. [c] 70% 1,3- and 30% 1,4-cycloheptadiene.

Hydrogenation of α,β-Unsaturated Carbonyl Compounds (Table IV). These phase-transfer reaction conditions are also effective for the hydrogenation of α,β-unsaturated ketones although the reactions are substantially slower than those with dienes. Liquid substrates were used neat as the reaction rates were decreased by ca. 25% if an organic cosolvent was present.

Clearly, substitution α to the carbonyl group increases the rates of these reactions whereas β substitution slows or even stops the reactions. The reaction is successful for 2-cyclohexenone derivatives although not if there is substitution at the 3-position.

For carvone (entry 8, Table IV), hydrogenation takes place only at the conjugated double bond. The trans/cis ratio of products is 6/1 in this reaction. For (*R*)-pulegone (entry 9) the reaction is very slow, yielding a trans/cis ratio of 4/1. For β-ionone (entry 10) the reaction is specific for overall 1,4-addition to the diene system, but both the *Z* and *E* isomers are formed in a 2:3 ratio. In all three of these reactions on natural products it was difficult to hydrogenate the last few percent of substrate even though the system was still active for additional substrate.

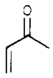
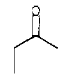
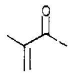
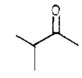
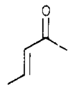
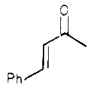
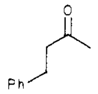
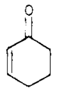
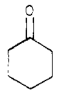
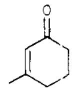
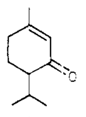
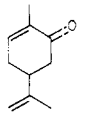
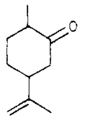
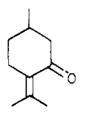
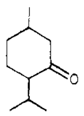
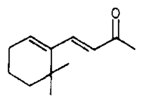
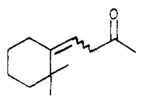
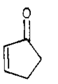
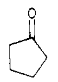
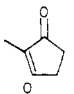
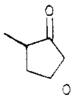
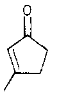
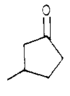
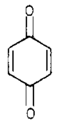
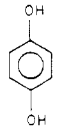
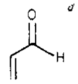
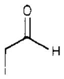
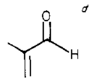
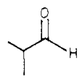
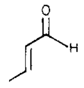
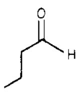
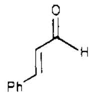
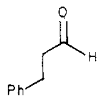
Although successful for ketones, the reaction does not proceed well with aldehydes. Yields were low, and substantial amounts of polymer formed during the reaction.

Two other results are of interest. First, the initial rates of the reactions were tested with a variety of phase-transfer reagents. Few differences were noted. In fact, the initial rate with no phase-transfer reagent present was the same although the rate fell off drastically as the reaction proceeded because of rapid catalyst decomposition, decomposition that was not evident in the presence of the phase-transfer reagents. Second, a number of organic phases were tried such as CH_2Cl_2 and toluene, and no variations were noted.

Discussion

Conjugated Dienes. The use of phase-transfer reaction conditions makes the readily prepared and inexpensive catalyst $K_3[Co(CN)_5H]$ useful for synthetic-scale reactions for the first time. In previous work[9] only small amounts of substrate were hydrogenated. In addition to improvement of reaction times, larger amounts of substrate can be hydrogenated in a single reaction. A very important influence of the phase-transfer reagent is to prevent catalyst decomposition, a definite problem with this catalyst

Table IV. Hydrogenation of α,β-Unsaturated Carbonyl Compounds[a]

	substrate	products	*t*, h/mL of substr hydrogenated[b]	isolated yield, %
1			24	60
2			8	85
3		no reaction		
4			48	60
5			30	75
6		no reaction		
7		no reaction		
8			20	93
9			720	71
10			96	75
11			16	10
12			10	78
13			70	20
14			20	35
15	 [d]		25	20
16	 [d]		12	20
17	 [d]		35	20
18	 [d]		60	10

[a] 6.6 mmol of catalyst in 40 mL of aqueous solution with 0.3 mmol of benzyltriphenylphosphonium chloride. [b] The substrate was added in 1-mL increments. [c] *Z*/*E* ratio of 2/3. [d] No base or excess cyanide added.

when used in simple aqueous or two-phase solutions. In general, the product ratios are dominated by overall 1,4-addition of hydrogen. The exceptions to this are the nonbranched dienes 1,3-pentadiene and (*Z*)- or (*E*)-2,4-hexadiene for which 1,2-addition competes evenly. In all cases, *E* products are produced as observed previously by others.[9]

A number of other catalysts also hydrogenate conjugated dienes to monoenes. Most notable are the (arene)tris(carbonyl)chromium-type catalysts, used both thermally[10] and photolytically[11] to hydrogenate dienes with 1,4-addition of H_2, yielding *Z* products. A modification of this catalyst, $(CH_3CN)_3Cr(CO)_3$, offers hydrogenation under quite mild conditions (40 psi of H_2, 40 °C).[12] The catalysts $[(\text{norbornadiene})(\text{diphos})\text{rhodium}]^{1+}$ (diphos = bidentate phosphine ligand) also converts dienes into monoenes, and some control over products can be obtained by varying the diphos ligand.[13] A system containing $CoX(PPh_3)_3$ (X = Cl, Br, I) in the presence of $BF_3{\cdot}OEt_2$ is also quite active, yielding mainly 1,2-addition products.[14] Heterogeneous[15] and homogeneous catalysts made heterogeneous by coordination to polymers[16] have also been reported. In addition, conjugated dienes can be converted into monoenes by using Birch reduction conditions[17] although coupling can be a problem if not desired. Although the choice of a reagent for a particular desired conversion of a conjugated diene to a monoene will clearly vary depending on the substrate and the desired products, the $K_3[Co(CN)_5H]$ catalyst used under phase-transfer conditions at room temperature and 1 atm of H_2 pressure is an attractive new system.

α,β-Unsaturated Carbonyl Compounds. Although the reactions are clearly slower than those with dienes, this catalytic system is a convenient method for the exclusive hydrogenation of the carbon–carbon bonds in α,β-unsaturated ketones on a synthetic scale. Others have reported synthetic-scale reactions using $K_3[Co(CN)_5H]$, but a large excess of the catalyst (3 mol/1 mol of substrate) was used.[18]

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[10] (a) Frankel, E. N.; Butterfield, R. O. *J. Org. Chem.* **1969**, *34*, 3930–3937. (b) Yagupsky, G.; Cais, M. *Inorg. Chim. Acta* **1975**, *12*, L27–L28.

[11] (a) Wrighton, M. S.; Ginley, D. S.; Schroeder, M. A.; Morse D. L. *Pure Appl. Chem.* **1975**, *41*, 671–697. (b) Platbrood, G.; Wilputte-Steinert, L. *J. Organomet. Chem.* **1974**, *70*, 407–412.

[12] Schroeder, M. A.; Wrighton, M. S. *J. Organomet. Chem.* **1974**, *74*, C29–C32.

[13] Schrock, R. R.; Osborn, J. A. *J. Am. Chem. Soc.* **1976**, *98*, 4450–4455.

[14] Kawakami, K.; Mizoroki, T.; Ozaki, A. *J. Mol. Catal.* **1979**, *5*, 175–187.

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Collman et al.[19] have recently reported the use of $NaHFe_2(CO)_8$ as a stoichiometric reagent for this reduction and have summarized various other methods. For substrates not containing a substituent β to the carbonyl group, the easily carried out reaction conditions reported here are certainly of potential utility. With carvone (entry 8, Table IV), for example, the reaction rate on a similar scale reaction is quite comparable to the $NaHFe_2(CO)_8$ system for the first equivalent of substrate, and the system is still active for more substrate because the reactions are catalytic. Also, the system is not as sensitive to air, and substrates are taken directly from reagent bottles. The nearly total inhibition with β substitution could actually be used in certain complex sytems to gain selectivity. Note that this catalyst does not generally react with other functional groups with the exception of halide substitution.[9d]

It is unlikely that phase-transfer catalysis is actually taking place in these reactions with ketones because the initial rate of the reactions is *not* accelerated by the phase-transfer reagent as was observed with the diene substrates. Presumably these ketone substrates can solubilize in the water phase sufficiently to allow reaction. The phase-transfer reagent does, however, substantially prevent catalyst decomposition, thus significantly increasing the amount of substrate that can be hydrogenated.

These reaction conditions did not prove to be useful with α,β-unsaturated aldehydes. Low yields were obtained, and a substantial amount of polymeric materials formed in the reactions.

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Registry No. 2-methyl-1,3-butadiene, 78-79-5; 2-methyl-1-butene, 563-46-2; 2-methyl-2-butene, 513-35-9; 2,3-dimethyl-1,3-butadiene, 513-81-5; 2,3-dimethyl-1-butene, 563-78-0; 2,3-dimethyl-2-butene, 563-79-1; 1,3-pentadiene, 504-60-9; (*E*)-2-pentene, 646-04-8; (*Z*)-2-pentene, 627-20-3; (*E*)-1,1-dideuterio-1,3-pentadiene, 68167-88-4; (*E*)-1,1-dideuterio-2-pentene, 74366-55-5; (*E*)-5,5-dideuterio-2-pentene, 74366-566-6; (*E*)-2-methyl-1,3-pentadiene, 926-54-5; 4-methyl-1,3-pentadiene, 926-56-7; (*E*)-4-methyl-2-pentene, 674-76-0; 2-methyl-2-pentene, 625-27-4; 2,4-dimethyl-1,3-pentadiene, 1000-86-8; 2,4-dimethyl-1-pentene, 2213-32-3; 2,4-dimethyl-2-pentene, 625-65-0; (*E,Z*)-2,4-hexadiene, 5194-50-3; (*E,E*)-2,4-hexadiene, 5194-51-4; 3-hexene, 592-47-2; 2-hexene, 592-43-8; 1,3-cyclohexadiene, 592-57-4; cyclohexene, 110-83-8; 1,3,5-cycloheptatriene, 544-25-2; 1,3-cycloheptadiene, 4054-38-0; 1,4-cycloheptadiene, 7161-35-5; cycloheptene, 628-92-2; 3-buten-2-one, 78-94-4; 2-butanone, 78-93-3; 3-methyl-3-buten-2-one, 814-78-8; 3-methyl-2-butanone, 563-80-4; (*E*)-4-phenyl-3-buten-2-one, 1896-62-4; 4-phenyl-2-butanone, 2550-26-7; 2-cyclohexen-1-one, 930-68-7; cyclohexanone, 108-94-1; carvone, 99-49-0; *cis*-2-methyl-5-(1-methylethenyl)cyclohexanone, 3792-53-8; *trans*-2-methyl-5-(1-methylethenyl)cyclohexanone, 5948-04-9; (*R*)-pulegone, 89-82-7; (2*R*-*cis*)-5-methyl-2-(1-methylethyl)cyclohexanone, 1196-31-2; (2*S*-*trans*)-5-methyl-2-(1-methylethyl)cyclohexanone, 14073-97-3; β-ionone, 14901-07-6; (*E*)-4-(2,2,6-trimethylcyclohexylidene)-2-butanone, 65790-21-8; (*Z*)-4-(2,2,6-trimethylcyclohexylidene)-2-butanone, 65790-22-9; 2-cyclopenten-1-one, 930-30-0; cyclopentanone, 120-92-3; 2-methyl-2-cyclopenten-1-one, 1120-73-6; 2-methylcyclopentanone, 1120-72-5; 3-methyl-2-cyclopenten-1-one, 2758-18-1; 3-methylcyclopentanone, 1757-42-2; *p*-benzoquinone, 106-51-4; hydroquinone, 123-31-9; acrolein, 107-02-8; propionaldehyde, 123-38-6; methacrylaldehyde, 78-85-3; isobutyraldehyde, 78-84-2; (*E*)-crotonaldehyde, 123-73-9; butyraldehyde, 123-72-8; (*E*)-cinnamaldehyde, 14371-10-9; hydrocinnamaldehyde, 104-53-0; $(CH_3)_4NCl$, 75-57-0; Et_3PhCH_2NCl, 56-37-1; Et_4NOH, 77-98-5; $K_3[Co(CN)_5H]$, 18117-30-1; cycloheptene, 628-92-2.

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Methylation of Nucleosides with Trimethylsulfonium Hydroxide. Effects of Transition Metal Ions

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The effect of transition metal acetylacetonates $[M(AA)_n]$ on the methylation of ribo- and deoxyribonucleosides with trimethylsulfonium hydroxide was studied. With ribonucleosides the metal complexes promoted O′-methylation at the 2′ and 3′ positions of the ribosyl group. A comparable effect was not observed in methylation of deoxyribonucleosides. These results are attributed to an increase in the nucleophilicity of the 2′-OH and 3′-OH groups of the ribosides through complex formation with the metal ion; such a complex cannot form with the deoxyribose derivatives. The activity of the metal ions studied for promoting this O′-methylation increased in the order $Mn^{2+} < Co^{2+} = Zn^{2+} < Ni^{2+} < Cu^{2+} < Fe^{3+}$. These $M(AA)_n$ also suppressed N-methylation of the purine and pyrimidine rings of adenosine and cytidine. It is suggested that this result may be caused by coordination of the metal ions with ring nitrogens.

Introduction

An organic molecule complexed with a metal ion often exhibits reactivity considerably different from that of the uncomplexed molecule. When the molecule bears several reactive sites, the use of the metal ion may promote or suppress reactions at the complexed sites, leading to a selective synthetic method. This rationale stimulated us to examine effects of metal ions on an alkylation reaction of nucleosides. Treatment of ribonucleosides with diazomethane in the presence of Lewis acids such as $SnCl_4$ has been shown to produce the corresponding 2′-*O*-methyl and 3′-*O*-methyl derivatives in good yields.[1-3] A bidendate complex involving ribose 2′-OH and 3′-OH has been postulated as the role of the catalysts. However, many other metal salts containing Cu^{2+}, Zn^{2+}, etc. were not active in spite of their capabilities of forming similar complexes with

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