Nitrosohydrazine Conformations. The Effect of Replacing C(1)-H of 2-Nitroso-2-azabicyclo[2.2.2]octane Derivatives by Nitrogen

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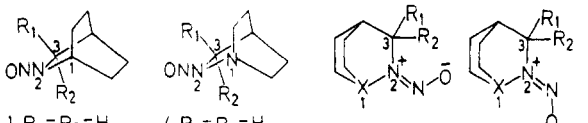
Substitution of one and two methyl groups for hydrogens at C(3) of 2-nitroso-2-azabicyclo[2.2.2]octane, **1**, which exists entirely in the A conformation (nitroso oxygen syn to C(3)), sterically destabilizes the A conformation. The monomethyl compound (**2**) exists only 85% in conformation A, and the B conformation (nitroso oxygen syn to C(1)) predominates for the dimethyl compound, **3** (13% A, 87% B). Replacement of C(1)-H by N gives the "homomorphic" nitrosohydrazines **4-6**. The monomethyl compound **5** exists 98% in conformation A and the dimethyl compound **6** 60% in conformation **A**, so the CH → N transformation favors conformation A by 1.3 to 1.4 kcal/mol for **2** → **5** and **3** → **6**. This result is the opposite to that predicted, considering steric, nitroso nitrogen lone pair-σ^*, and N(1) lone pair-nitroso nitrogen lone pair interactions.

In this paper we compare the conformations of *N*-nitrosamines **1-3** with those of the structurally related *N*-nitrosohydrazines **4-6**. Because rotation about the

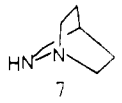


1 $R_1=R_2=H$ 4 $R_1=R_2=H$
2 $R_1=Me, R_2=H$ 5 $R_1=Me, R_2=H$
3 $R_1=R_2=Me$ 6 $R_1=R_2=Me$

N_2-NO bond is slow on the NMR time scale, it is easy to determine the ratio of the two nitroso group rotamers, A (oxygen syn to C(3)) and B (oxygen syn to position 1). Replacement of C(1)-H by N in going from nitrosamines **1-3** to nitrosohydrazines **4-6** should cause only minor steric changes; **4** is "homomorphic"[1] with **1**, and so forth. Comparison of the A/B ratios for these pairs allows direct comparison of the effect in solution of replacing a CH bond, which is held coplanar with the NNO group, by a nitrogen lone pair.

Results

We used the methodology of Seebach,[2] LDA deprotonation of the nitrosamine followed by reaction with methyl iodide, to prepare **2** and **3** from **1**. As expected from previous work,[2a] no methylation occurs at C(1), because the C(1)-H bond is protected against deprotonation by being held near to the nodal plane of the NNO group. Similar methylations allowed preparation of the nitrosohydrazines **5** and **6** from **4**. Minor improvements in the preparation of **7**, the immediate precursor of **4**, raised the



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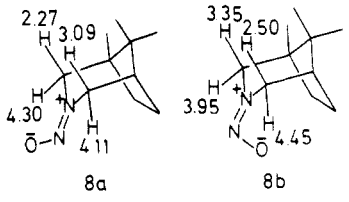
yield of **4** to 45% from 4-pyridinecarboxylic acid (see the Experimental Section). Proton and carbon NMR data which allow conformational assignments are summarized in Tables I and II. It is known from extensive ^1H NMR

Chart I. Proton NMR Shift Assignments for the Two Rotamers of *N*-Nitrosocamphidine



8a 8b

work[3] that a proton syn to oxygen which is coplanar with the NNO group is deshielded relative to one anti to oxygen, while substantially out-of-plane syn protons are shielded relative to anti protons. The differences observed are well-illustrated by the ^1H NMR shifts for **8a** and **8b**,[3d] shown next to the protons in Chart I. Similar shifts occur in the ^{13}C NMR spectra, although a steric compression upfield shift is superimposed on the anisotropic effect of the *N*-nitroso group.[5]

Solvent shifts for hydrogens α to *N*-nitroso groups are also helpful in establishing conformations, because $\Delta\delta = \delta(CCl_4) - \delta(C_6D_6)$ has been shown to be substantially more positive for α-hydrogens anti to nitroso oxygen.[3a] Traynham and co-workers[4] have already established that **1a** is the sole observed conformation of **1** on the basis of lanthanide shifts. The biggest apparent anomaly in Table I concerns comparison of the A and B isomers of **2** and **3** in the carbon spectra. For **2B**, C(1) appears 9.3 ppm downfield of C(1) in **2A**, but C(3) is 13.8 ppm upfield of C(3) in **2A**. For **3B**, C(1) appears 12.7 ppm upfield and C(3) 9.5 ppm downfield of those of the A isomer. We feel the proton-shift changes, solvent-shift changes, and isomer-ratio changes require the assignments of peaks to conformations made in Table I. The most likely cause of the anomaly is suggested to be bicyclic ring torsion in the unsymmetrical **2** system, changing the rather large steric compression and *N*-nitroso group shielding-deshielding cone terms relative to the symmetrical **3** system, which probably has little bicyclic ring torsion.

The assignments for **4-6** (Table II) are based on the behavior of the C(3) shifts in the observed isomers. The increase in the fraction of B observed as C(3) is made

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(3) (a) Karabatsos, G. J.; Taller, R. A. *J. Am. Chem. Soc.* **1964**, *86*, 4373. (b) Chow, Y. L. *Angew. Chem., Int. Ed. Engl.* **1967**, *6*, 75. (c) Chow, Y. L.; Colin, C. J. *Can. J. Chem.* **1968**, *46*, 2827. (d) Cooney, J. D.; Apsimon, J. W. *Ibid.* **1971**, *49*, 2377. (e) Forest, T. P.; Hooper, D. L.; Ray, S. *J. Am. Chem. Soc.* **1974**, *96*, 4286.

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Table I. NMR Spectral Data for 1-3

compd	H(1)[a]	H(3)[a]	$CH_3(3)$[a]	C_1[b]	C_3[b]	$CH_3(3)$[b]
1A	4.71 (+0.21)	3.39 (+0.07)	none	50.4	44.3	none
2A	4.67 (+0.25)	4.00 (+0.04)	1.18 (+0.14)	53.2	56.3[c]	16.3
2B	4.89 (−0.06)	4.34 (+0.34)	1.55 [obscured]	62.5[c]	42.5	*d*
3A	4.61 (+0.28)	none	1.44 (+0.34)	53.7	51.8	19.9
3B	5.03 (−0.09)	none	1.61 (+0.25)	41.0[c]	61.3	28.8

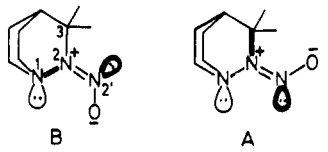
[a] Proton shifts reported are for 1 M solutions in CCl_4 vs. internal Me_4Si. The numbers in parentheses are $\Delta\delta = \delta(CCl_4) - \delta(C_6D_6)$, for 1 M solutions in deuteriobenzene. [b] Carbon shifts reported are for 1 M solutions in CD_3CN vs. internal Me_4Si. [c] Carbon assignment verified by selective decoupling of the proton attached to this carbon. [d] Obscured, but downfield of δ 16.3.

Table II. NMR Spectral Data for 4-6

compd	H(3)[a]	CH(3)[a]	H(6,7)[a]	C(3)[b]	$CH_3(3)$[b]	C(6,7)[b]
4A	3.62	none	3.42	52.5[c]	none	51.5
5A	4.17	1.35	3.4	56.5	14.9	51.8, 50.0
5B	4.55	1.52	2.8	d	*d*	*d*
6A	none	1.55	3.31	62.8	22.5	50.3
6B	none	1.73	3.03	61.8	27.9[c]	48.3

[a] Proton shifts reported are for 1 M solutions in $CDCl_3$ vs. internal Me_4Si. [b] Carbon shifts reported are for 1 M solutions in CD_3CN vs. internal Me_4Si. [c] Carbon assignment verified by selective decoupling of the proton attached to this carbon. [d] Carbon peaks for this 2% isomer were not determined due to insufficient S/N in the spectrum obtained.

Table III. Percentages of Isomers A and B from ^1H NMR Integration



B A

compd	X	R_1	R_2	% A	% B	$\Delta\Delta G°$,[a] kcal/mol
1	CH	H	H	~100	unobserved	>+2.8
2[b]	CH	Me	H	85	15	+1.0
3[c]	CH	Me	Me	13	87	−1.2
4	N	H	H	~100	unobserved	>+2.8
5[d]	N	Me	H	98	2	+2.3
6[e]	N	Me	Me	60	40	+0.24

[a] $\Delta G°(B) - \Delta G°(A)$ at 303 K. [b] Calculated from integrations of the H(3) and $CH_3(3)$ signals. [c] Calculated from integrations of the H(1) and $CH_3(3)$ signals. [d] Calculated from integrations of the H(3), $CH_3(3)$, and H(6,7) signals. [e] Calculated from integrations of the $CH_3(3)$ and H(6,7) signals.

bulkier in both the nitrosamine and nitrosohydrazine series provides a powerful check on our assignments, since this is certainly the trend required on steric grounds. The relative amounts of A and B conformations present were determined by integration of the proton spectra and appear in Table III.

Discussion

It is well-established that nitrosamine conformations are controlled by the size of the groups attached to nitrogen, the oxygen being preferentially syn to the smallest group. Traynham and co-workers[5] pointed out that **1A** is preferred over **1B** because the latter conformation has pseudoallylic $A^{1,3}$ strain[6] due to the coplanar C(1)–H and N–O bonds being cis to each other in **1B**, while the N–O bond lies between the two hydrogens at C(3) in conformation **1A**. Replacing the C(3) hydrogens by methyls increases steric interaction in the A conformation, allowing the B conformation to be detected for **2** (see Table III). Putting on the second methyl in going from **2** to **3** changes the B–A free energy difference by 2.2 kcal/mol, switching the thermodynamically favored conformation from being 85% **2A** to 87% **3B**. A factor complicating interpretation of the $\Delta(\Delta G°)$ increment upon going from **2** to **3** is that the unsymmetrically methylated **2A** conformation is likely to have significant bicyclic ring torsion to decrease the C(3)–Me, N–O steric interaction; bicyclic torsion is unlikely to decrease the energy of the either **1A** or **3A**, since the oxygen is in the most favorable position relative to the C(3) substituents when the bicyclic ring is completely eclipsed. It is unfortunate that neither **1B** nor **4B** could be detected experimentally so that all we can say is that they lie greater than 2.8 kcal/mol higher in energy than **1A** and **4A**, since we should have been able to detect 1% of either minor conformation.

Table III also shows that replacing C(1)–H by nitrogen increases the stability of conformation A relative to B, by 1.3 kcal/mol for the monomethyl systems (**5** vs. **2**) and 1.4 kcal/mol for the dimethyl systems (**6** vs. **3**). Sterically, replacement of C(1)–H by N ought to favor B relative to A, since the hydrogen involved in the pseudoallylic $A^{1,3}$ interaction destabilizing B has been removed; there is no evidence that a nitrogen lone pair is sterically large relative to a CH group. We therefore presume that the reason for nitrogen introduction at position 1 favoring conformation A is an electronic effect. One thing the nitrogen replacement at position 1 does is change the N(2′) lone pair, σ^* interactions.[7] However, since overlap is larger with the

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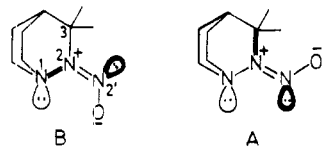
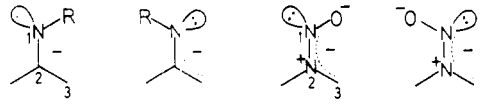
anti σ^* orbital than with the syn one and the greater electronegativity of nitrogen than carbon will cause the σ(N(2)–N(1))* orbital to be lower in energy than the σ(N-(2)–C(3))* orbital, n(N(2′)), σ^* interactions will stabilize B relative to A, the opposite of the experimental result.



B A

Electrostatic repulsive interaction between the lone pairs at N(1) and N(2′), reminiscent of Eliel's "rabbit-ear effect"[8] will also favor conformation B relative to A. Houk, Frazer, and co-workers[9] have recently concluded on the basis of MO calculations that the 1,3 electrostatic interaction between the N(1) lone pair and the negative charge at C(3) is principally responsible for the greater stability of **9**-*syn* than **9**-*anti* conformations of imine anions. Nitrosamine



9-syn 9-anti 10-syn 10-anti

anions **10** also prefer **10**-*syn* (B-like) conformations, making it obvious that the lone pair at N(1) of nitrosohydrazines **4**–**6** does not make them conformational models for nitrosamine anions.

Two factors which should favor conformation A over B for nitrosohydrazines relative to neutral nitrosamines are (a) electrostatic repulsion between the N(1) lone pair and the significantly negatively charged oxygen of **B** (a 1,4 electrostatic interaction) and (b) dipole interaction between the N(1)–N(2)$^+$ and the N(2′)–O$^-$ bond dipoles. Both of these factors are present in **10** and will tend to favor **10**-*anti* over **10**-*syn*, but the opposing 1,3 electrostatic interaction is apparently more important, because only **10**-*syn* is observed, even in calculations,[9] where chelation and kinetic effects cannot be confusing the issue. In the overall neutrally charged nitrosohydrazines, the corresponding 1,3 electrostatic interaction is decreased in size to that of the "rabbit-ear effect", and factors a and b appear to predominate in determining the conformation.

Experimental Section

Proton ^{1}H NMR spectra in $CDCl_3$, CCl_4, and C_6D_6 were obtained on a JEOL JMN-MH-100 instrument, and FT 270 MHz spectra were recorded on a Brucker WH-270. ^{13}C NMR data (decoupled and partially decoupled) were obtained on a Varian XL-100 instrument, and selective decoupling experiments employed a JEOL FX-60. All chemical shifts are reported in parts per million downfield from internal Me_4Si, and those used in conformational work (Tables I and II) were determined at 1 M substrate concentration. Mass spectra were determined by using an AEI MS-902 instrument, and IR spectra were taken on a Beckman Acculab-7 in CCl_4 solution.

The tetrahydrofuran employed was freshly distilled from benzophenone–sodium (purple solution). Tetralin was washed repeatedly with concentrated sulfuric acid, extracted with bicarbonate and water, dried over calcium chloride, and distilled from calcium hydride. All alkyllithium reactions were carried out in flame-dried apparatus. Unless noted, all reactions were carried out under a dry nitrogen atmosphere and magnetically stirred.

2-Nitrosoisoquinuclidine (1). A mixture of 2.22 g (20 mmol) of isoquinuclidine (prepared from isoquinuclidone[10] by the method of Gassman and Cryberg[11]), 10 mL of water, and 14 mL of acetic acid was cooled to 0 °C while 14 mL of an 8 N aqueous sodium nitrite solution was added over 30 min *without* stirring. After the mixture stood for 50 h, extraction with five 20-mL portions of chloroform, washing with sodium carbonate, back extraction with chloroform (2 × 20 mL), drying (magnesium sulfate), and solvent removal gave **1** as a light yellow solid, 2.7 g (96%), mp 140–141 °C, with spectral properties in agreement with those published.[4]

2-Nitroso-3-methyl-2-azabicyclo[2.2.2]octane (2). A mixture of 2.35 g (21 mmol) of diisopropylamine, 3.58 g (20 mmol) of hexamethylphosphoric triamide (freshly distilled from barium oxide) and 14 mL of *n*-butyllithium (1.5 M in hexane, 21 mmol) in 100 mL THF at 0 °C was prepared by syringe additions, and after 15 min at 0 °C, the solution was cooled to −78 °C and 2.80 g of **1** (20 mmol) in 5 mL of THF was added. After 1 h at −78 °C, 2.84 g (20 mmol) of methyl iodide was added, and the mixture was stirred for 1 h at −78 °C and 6 h at room temperature. After the solution was quenched with 1 mL of water, solvents were removed in vacuo, and HMPA was removed by distillation at 0.2 mm pressure through a 1 × 10 cm Vigreux column. The residue was chromatographed on silica gel, eluting with 1:1 chloroform–hexane, to give **2**:[12] 2.4 g (78%); mp 59–60 °C; IR 2980 (CH), 1540 (NNO) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.28 (d, 3 H), 1.5–2.3 (m, 9 H), 4.2 (d of q, 1 H), 4.7–4.9 (m, 1 H); ^{13}C NMR (CH_3CN) δ 14.0 (q), 18.3 (t), 24.4 (t), 25.8 (t), 30.9 (d), 51.5 (d, CHN), 54.3 (d, CHMeN).

3-Nitroso-3,3-dimethyl-2-azabicyclo[2.2.2]octane (3). The procedure used for **2** was followed until the solution of **2** in THF was obtained. After the solution was recooled to −78 °C, a solution of LDA in THF/hexane (1.08 M LDA, 18.5 mL, 20 mmol) was added, and after 1 h, 2.84 g (20 mmol) of methyl iodide was added. After being stirred for 2 h at −78 °C and warming to room temperature overnight, the solution was worked up as in the preparation of **2**, yielding 1.6 g (48%) of **3**[12] as a yellow solid: mp 179–180 °C; IR 2920, 1455 (CH), 1600 (NNO) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.2–2.0 (m, 9 H), 1.55 (s, 6 H), 5.06 (m, 1 H); ^{13}C NMR (CD_3CN) δ 20.5 (t), 22.9 (t), 26.8 (q), 36.3 (d), 40.4 (d, CHN), 60.4 (s).

1-Nitroso-4-(carbomethoxy)piperidine. A 1-L Parr bottle was charged with 4-(carbomethoxy)pyridine (130 g, 0.95 mol; bp 112–114 °C (lit.[13] bp 107–110 °C), prepared in 95% yield by refluxing 123 g of 4-pyridinecarboxylic acid in 1.2 L of methanol containing 60 mL of concentrated sulfuric acid for 24 h), 370 mL of acetic acid, and 1.90 g of platinum dioxide. The mixture was shaken under 5–40 psig of hydrogen until the catalyst formed clumps (1.05 equiv of H_2 absorbed), the catalyst was filtered through a pad of Filter Cel, and the filtrate was combined with 330 mL of acetic acid and 450 mL of water in a 2-L round-bottom flask. After the solution was cooled to 0 °C, 690 mL of 8 N sodium nitrite solution was added over 1 h, without stirring. After the mixture stood for 48 h, extraction with ether (5 × 20 mL), washing with saturated sodium carbonate, back extraction of the aqueous layer with ether (2 × 250 mL), drying of the organic extracts (magnesium sulfate), solvent removal, and distillation of the residue gave 152 g (0.88 m, 93%) of a yellow oil, bp 129–130 °C (0.02 mm). This material (^{1}H NMR ($CDCl_3$) δ 1.4–2.4 (m, 4 H), 2.56–2.88 (m, 1 H), 2.90–3.3 (m, 1 H), 3.72 (s, 3 H), 3.74–4.04 (m, 1 H), 4.42–4.74 (m, 2 H)) was used directly in the next step.

1,2-Diaza-3-oxobicyclo[2.2.2]octane. The above nitrosopiperidine ester (152 g, 0.88 mol), 350 mL of 50% aqueous ethanol, ferrous sulfate (2.7 g), and 10% Pd/C (2.2 g) were deaerated by passing a nitrogen stream through the mixture for 30 min. Hy-

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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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