**Registry No.**—**1**, 23081-78-9; **1** perdeuterioethyl ester, 38605-80-0; **2**, 38605-81-1; **3**, 26384-92-9; **4**, 38605-83-3; **5**, 26384-85-0; **6**, 26384-86-1; **7**, 26394-19-4; **8**, 1754-49-0; **13**, 38605-87-7; **15**, 38605-88-8; **16**, 38605-89-9; **16** diethyl ester, 38605-90-2; **17**, 38605-91-3; **17** diethyl ester, 38605-92-4; **20**, 38605-93-5; **20** anhydride, 38605-94-6; **20** diethyl ester, 38605-95-7; **20** disodium salt, 38605-96-8; **21** anhydride, 38605-97-9; **21** diethyl ester, 38605-98-0; **21** disodium salt, 38605-99-1; **22**, 38606-00-7; 3-ethyl-6-methylpyridine *N*-oxide, 768-44-5; 2,5-dimethylpyridine *N*-oxide, 4986-05-4; 3-fluoropyridine *N*-oxide, 695-37-4; phosphorus pentachloride, 10026-13-8; pyridyl-2-phosphonic dichloride, 38606-04-1; 4-benzylpyridine *N*-oxide, 7259-53-2.

**Acknowledgments.**—The author is particularly indebted to Mr. Charles W. Burkhardt for his assistance in obtaining the p*K* values and ultraviolet spectra. It is a pleasure to acknowledge valuable discussions with Professors C. D. Gutsche and C. E. Griffin, which aided in the preparation of this manuscript.

---

# Nuclear Magnetic Resonance Spectroscopy. Carbon-13 Nuclear Magnetic Resonance for Some Six-Membered Aromatic Nitrogen Heterocycles[1a]

FRANK J. WEIGERT,[1b] JANJA HUSAR, AND JOHN D. ROBERTS*

*Contribution No. 4506 from the Gates and Crellin Laboratories of Chemistry, California Institute of Technology, Pasadena, California 91109*

*Received October 10, 1972*

High-resolution, natural-abundance $^{13}$C spectra have been obtained for pyridine, pyridazine, pyrimidine, pyrazine, and *s*-triazine and some methyl derivatives. Geminal and vicinal carbon–proton coupling has been related to proton–proton coupling in substituted ethylenes.

Although one-bond carbon–proton coupling constants in aromatic systems are well characterized,[2,3] long-range carbon–proton coupling constants have not been extensively studied. Direct observation of the inner satellites in the proton spectrum is hampered by the strong resonances from molecules having no $^{13}$C. If the proton spectrum is particularly simple, these satellites can be observed,[4] but they cannot always be assigned to a particular carbon. The analysis of the outer satellites is dependent on the differences in the long-range carbon–proton coupling constants, but the magnitudes cannot be determined.[5] Homonuclear tickling of the inner satellites while observing the outer satellites gives all the transitions for a complete iterative analysis.[6] If all the proton–proton coupling constants are known (from studies of the unlabeled materials), all the carbon–proton coupling constants can be determined from the $^{13}$C spectrum.

Lauterbur[2] has measured the $^{13}$C chemical shifts of six-membered nitrogen heterocycles, but the spectra were low resolution and long-range couplings were not resolved. High-resolution $^{13}$C spectra of pyridine have been published but not interpreted in detail.[7] Long-range carbon–proton coupling constants of benzene[8] and the five-membered heterocycles[9] have been reported. This paper concerns the nmr spectra of six-membered nitrogen heterocycles.

## Experimental Section

All samples were obtained from commercial sources. Liquid samples were diluted with 5% acetone for an internal lock. Spectra of solid samples were taken as saturated acetone solutions. The spectra were obtained with the previously described Varian DFS-60 spectrometer.[8,9] Theoretical spectra were calculated by trial and error using the computer programs NMRIT, or by iteratative techniques with the LAOCOON programs.[10]

## Results

The $^{13}$C spectra of pyridine, pyridazine, and pyrazine are shown in Figures 1–6. The $^{13}$C spectra of all of the carbons of pyrimidine and *s*-triazine are first order. Only the low field half of the pyrazine spectrum is shown because the high field half is simply its mirror image. The carbon–proton coupling constants for the parent heterocycles are summarized in Table I. Long-range coupling constants are accurate to ±0.2 Hz.

TABLE I

CARBON–PROTON COUPLING CONSTANTS IN THE SIX-MEMBERED NITROGEN HETEROCYCLES

| Compound | Registry no. | Carbon | H-2 | H-3 | H-4 | H-5 | H-6 |
|---|---|---|---|---|---|---|---|
| Pyridine | 110-86-1 | 2 | 175.3 | 3.3 | 6.4 | ±1.6 | 10.9 |
| | | 3 | 8.7 | 162.5 | 1.0 | 6.4 | ±1.6 |
| | | 4 | 6.4 | 0.0 | 169.2 | 0.0 | 6.4 |
| Pyridazine | 289-80-5 | 3 | | 182.5 | 6.5 | 2.0 | −1.4 |
| | | 4 | | 6.7 | 169.9 | 0.0 | 5.2 |
| Pyrimidine | 289-95-2 | 2 | 202.7 | | 10.3 | 0.0 | 10.3 |
| | | 4 | 9.1 | | 182.8 | 1.9 | 5.3 |
| | | 5 | 1.9 | | 9.5 | 166.2 | 9.5 |
| Pyrazine | 290-37-9 | | 182.7 | 10.4 | | −1.5 | 9.8 |
| *s*-Triazine | 290-87-9 | | 207.5 | | 7.95 | | 7.95 |

---

[1] (a) Supported by the Public Health Service, Research Grant No. GM-11072 from the Division of General Medical Sciences, and by the National Science Foundation; (b) National Science Foundation Predoctoral Fellow, 1965–1968.

[2] K. Tori and T. Nakagawa, *J. Phys. Chem.*, **68**, 3163 (1964).

[3] P. C. Lauterbur, *J. Chem. Phys.*, **43**, 360 (1965).

[4] H. M. Hutton, W. F. Reynolds, and T. Schaefer, *Can. J. Chem.*, **40**, 1758 (1962).

[5] J. M. Read, Jr., R. E. Mayo, and J. H. Goldstein, *J. Mol. Spectrosc.*, **22**, 419 (1967).

[6] G. Govil, *J. Chem. Soc. A*, 1420 (1967).

[7] (a) J. M. Shoolery in "High-Resolution Nuclear Magnetic Resonance Spectroscopy," J. W. Emsley, J. Feeney, L. H. Sutcliffe, Ed., Pergamon Press, Oxford, 1960, p 994; (b) see also R. L. Lichter and J. D. Roberts, *J. Amer. Chem. Soc.*, **93**, 5218 (1971).

[8] F. J. Weigert and J. D. Roberts, *ibid.*, **89**, 2967 (1967).

[9] F. J. Weigert and J. D. Roberts, *ibid.*, **90**, 3543 (1968).

[10] C. A. Reilly and J. D. Swalen, *J. Chem. Phys.*, **32**, 1378 (1960); S. Castellano and A. A. Bothner-By, *ibid.*, **41**, 3863 (1964).

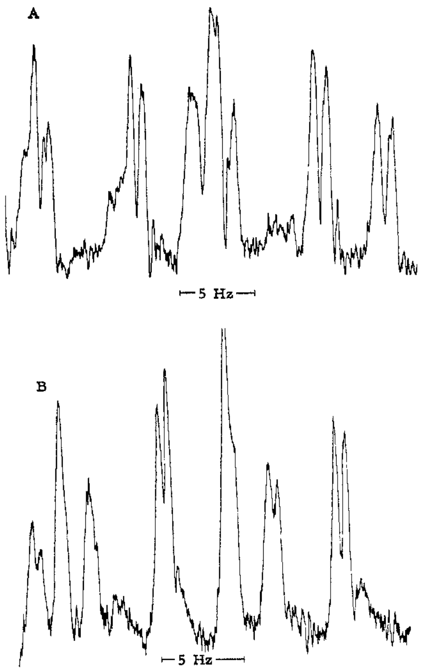


Figure 1.—Low (A) and high (B) field segments of the $\alpha$-$^{13}$C resonance of pyridine at 15.0 MHz, 500 scans at a sweep rate of 0.25 Hz/sec.

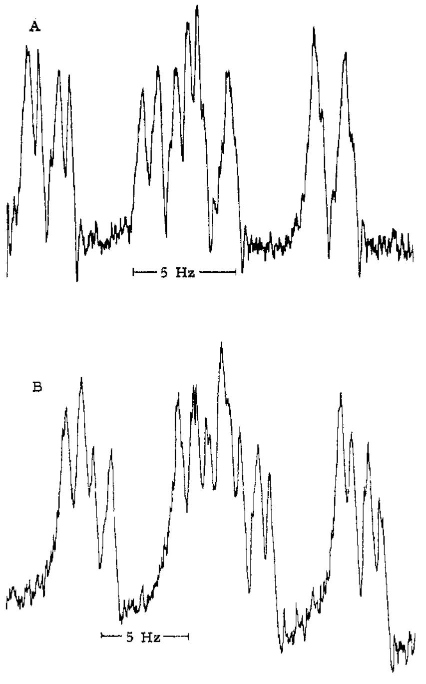


Figure 2.—Low (A) and high (B) field segments of the $\beta$-$^{13}$C resonance of pyridine at 15.09 MHz, 500 scans at a sweep rate of 0.25 Hz/sec.

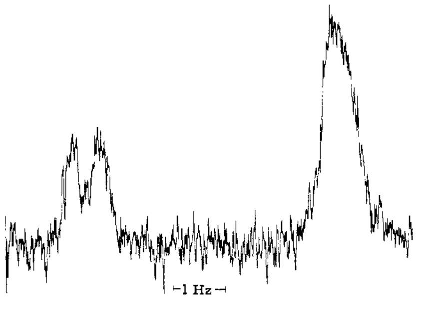


Figure 3.—Part of the $^{13}$C spectrum of the $\gamma$ carbon of pyridine at 15.09 MHz, 100 scans.

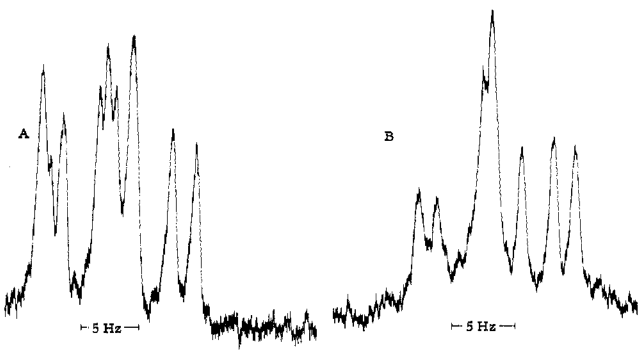


Figure 4.—Low (A) and high (B) field segments of the $\alpha$-$^{13}$C resonance of pyridazine at 15.09 MHz, taken with 400 and 300 scans, respectively.

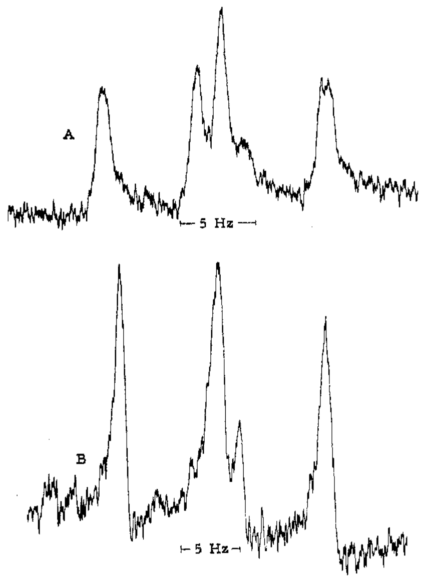


Figure 5.—Low (A) and high (B) field segments of the $\alpha$-$^{13}$C resonance of pyridazine at 15.09 MHz, taken with 400 and 300 scans, respectively.

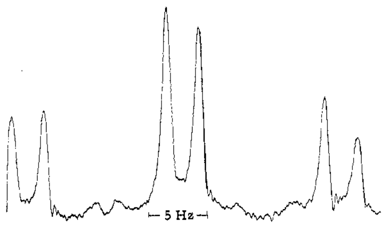


Figure 6.—Half of the $^{13}$C spectrum of pyrazine at 15.09 MHz, 300 scans. The other half is the mirror image of this one.

Because of the complexity of the spectra of some of the parent compounds, methyl derivatives were examined and their carbon–proton couplings applied to the analysis of the parent compounds. Selective decoupling of the methyl protons was necessary to observe the long-range couplings to the aromatic protons. The decoupling power was quite critical: too much, and the coupling to the aromatic protons was perturbed; too little, and the coupling from the methyl protons was not completely eliminated. The carbon–proton coupling constants determined by this technique are best taken as lower limits to the true values. The long-range carbon–proton coupling constants in the methyl-substituted heterocycles are given in Table II.

Table II

Long-Range Carbon–Proton Coupling in Hertz for Methyl-Substituted Nitrogen Heterocycles

| Compound | Registry no. | Carbon | H-2 | H-3 | H-4 | H-5 | H-6 |
|---|---|---|---|---|---|---|---|
| 2-Methylpyridine | 109-06-8 | 2 | | 2.4 | 6.7 | 0.0 | 11.2 |
| | | 3 | | | 0.0 | 6.5 | 1.5 |
| | | 4 | | 0.0 | | 0.0 | 6.3 |
| | | 5 | | 6.3 | 0.0 | | 8.7 |
| | | 6 | | 0.0 | 6.5 | 3.8 | |
| 3-Methylpyridine | 108-99-6 | 2 | | | 5.25 | 0.0 | 10.95 |
| | | 3 | 6.7 | | 0.0 | 6.7 | 0.0 |
| | | 5 | 1.45 | | 0.0 | | 10.2 |
| | | 6 | 10.6 | | 6.4 | 2.1 | |
| 4-Methylpyridine | 108-89-4 | 2 | | 4.2 | | −0.7 | 10.6 |
| | | 3 | 8.7 | | | 5.6 | 1.6 |
| | | 4 | 6.35 | 0.0 | | 0.0 | 6.35 |
| 3,5-Dimethylpyridine | 591-22-0 | 2 | | | 5.8 | | 11.2 |
| | | 3 | 7.7 | | 0.0 | | 1.6 |
| | | 4 | 5.3 | | | | 5.3 |
| 2,6-Dimethylpyridine | 108-48-5 | 2 | | 2.5 | 6.4 | −0.7 | |
| | | 3 | | | 0.0 | 5.1 | |
| | | 4 | | <0.3 | | <0.3 | |
| 2,4-Dimethylpyridine | 108-47-4 | 2 | | 11.3 | | 1.6 | 11.3 |
| | | 4 | | 0.0 | | 0.0 | 6.7 |
| | | 5 | | 5.5 | | | 8.6 |
| | | 6 | | 0.0 | | 4.0 | |
| 2,4,6-Trimethylpyridine | 108-75-8 | 3 | | | | 5.1 | |
| 3-Methylpyridazine | 1632-76-4 | 4 | | | | 0.0 | 5.5 |
| | | 5 | | | 0.0 | | 7.45 |
| | | 6 | | | *a* | *a* | |
| 5-Methylpyrimidine | 2036-41-1 | 2 | | | 10.6 | | 10.6 |
| | | 4 | 9.1 | | | | 4.35 |
| 2,5-Dimethylpyrazine | 123-32-0 | 2 | | 9.4 | | | 9.4 |
| | | 3 | | | | | 1.4 |
| 2,6-Dimethylpyrazine | 108-50-9 | 2 | | 9.95 | | 1.25 | |
| | | 3 | | | | 9.7 | |
| Mesitylene[b] | 108-67-8 | 1 | 0.0 | | 0.0 | | 0.0 |
| | | 2 | | | 6.4 | | 6.4 |

[a] The average of these two coupling constants is 4.7 Hz. [b] The geminal carbon–proton coupling to the methyl protons is 6.0 Hz; the vicinal carbon–proton coupling is 4.25 Hz.

Two slightly different sets of proton–proton coupling constants have been reported for pyridine.[11,12] Both give good agreement with a 100-MHz spectrum of pyridine and both can be used equally well to match the $^{13}$C spectrum. To a first-order approximation, the spectrum of C-4 is a doublet (H-4) of triplets (H-2, H-5). However, with the extremely slow passage conditions of Figure 3, an additional splitting is resolved. The splitting, however, is consistent with a value of 0.0 ± 0.1 Hz for the coupling with H-3 and H-5.

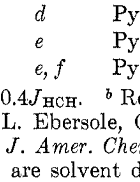
The $^{13}C(\alpha)$–H couplings in pyridazine were obtained using the proton–proton coupling constants derived from the $^{13}$C satellites of the proton spectrum.[13] The best fit to the experimental spectrum of the $\alpha$ carbon was obtained with a $^{13}$C isotope effect on the chemical shift of the directly attached and nearest neighbor proton of 2.0 and 1.7 Hz, respectively, relative to the shifts of the more remote protons.

The proton–proton coupling constants in pyrazine were assumed to be the same as those of the monomethyl derivative.[14]

The 25-MHz $^{13}$C spectrum of C-1 of mesitylene[15] shows a 1:3:3:1 quartet from coupling with the methyl protons. Coupling with the geminal ring protons was zero. The undecoupled $^{13}$C spectrum of C-2 is a broad doublet ($J$ = 160 Hz) with no obvious fine structure. On decoupling the methyl protons, a triplet with $J$ = 6.4 Hz is seen from coupling with the vicinal ring pro-

Table III

A Comparison of Proton–Proton Couplings $^2J_{HH}$ in Substituted Ethylenes with Carbon–Proton Couplings $^2J_{CH}$ in Aromatic Heterocycles



| X | Y | $J_{CCH}$, Hz (pred)[a] | Reference | Compd | $J_{CCH}$, Hz (obsd) |
|---|---|---|---|---|---|
| C | $H_2$ | +1.0 | *b* | Benzene | +1.0 |
| C | $CH_3$ | +0.8 | *c* | Mesitylene | 0.0 |
| N | C | +6.4 | *d* | Pyridine, C-3 | +8.7 |
| N | N | +4.4 | *d* | Pyridazine, C-4 | 6.4 |
| C | N, H | 0.0 | *e* | Pyridine, C-4 | 0.0 |
| C | H | 6.4 | *e, f* | Pyridine, C-4 | 6.4 |

[a] In Hz, from $J_{CCH} = 0.4 J_{HCH}$. [b] Reference 18. [c] Reference 19. [d] B. L. Shapiro, S. L. Ebersole, G. J. Karabatsos, F. M. Vane, and S. L. Manatt, *J. Amer. Chem. Soc.*, **85**, 4041 (1963). These coupling constants are solvent dependent. [e] W. Brügel, Th. Ankel, and F. Krückeberg, *Z. Elektrochem.*, **64**, 1121 (1960), [f] The comparison here is between $^3J_{CCCH}$ and $^3J_{HCCH}$ (trans).

---

(11) C. Sun and R. Kostelnik, *J. Chem. Phys.*, **46**, 328 (1967).

(12) J. B. Merry and J. H. Goldstein, *J. Amer. Chem. Soc.*, **88**, 5560 (1966).

(13) V. M. S. Gil and A. J. L. Pinto, *Mol. Phys.*, **16**, 623 (1969); see also J. A. Elvidge and P. D. Ralph, *J. Chem. Soc. B*, 249 (1966).

(14) R. H. Cox and A. A. Bothner-By, *J. Phys. Chem.*, **72**, 1642 (1968).

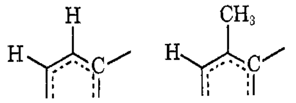
(15) *Chem. Eng. News*, **45**, 46 (1967).

tons. On weak irradiation of the ring protons, each half of the doublet becomes a septet ($J = 4.25$ Hz) from the vicinal coupling to two adjacent methyl groups.

## Discussion

Karabatsos and coworkers[16] have extended the valence-bond treatment of geminal proton–proton couplings[17] to geminal carbon–proton couplings. Such comparisons explain many trends in geminal and vicinal carbon–proton coupling in benzene[8] and the five-membered nitrogen heterocycles[9] if proper models are chosen. Some models and predicted and observed coupling constants are given in Table III. Although the quantitative agreement with Karabatsos' theory is best for benzene, the qualitative trends are correctly predicted throughout the heterocyclic series.

Vicinal carbon–proton couplings across a methyl group are approximately 0.9 times the corresponding couplings in compounds without the methyl. The ratio is the same as for the trans proton–proton couplings in ethylene (19.1 Hz)[18] and propene (16.8 Hz).[19]



---

[16] G. J. Karabatsos, F. D. Graham, and F. M. Vane, *J. Amer. Chem. Soc.*, **84**, 37 (1962).

[17] H. S. Gutowsky, M. Karplus, and D. M. Grant, *J. Chem. Phys.*, **31**, 2278 (1959).

[18] R. M. Lynden-Bell, *Mol. Phys.*, **6**, 537 (1963).

[19] A. A. Bothner-By and C. Naar-Colin, *J. Amer. Chem. Soc.*, **83**, 231 (1961).

---

# The Synthesis of Aryl Isocyanates from Nitro Compounds and Carbon Monoxide

F. J. WEIGERT

*Contribution No. 1963 from the Central Research Department,*
*E. I. du Pont de Nemours and Company, Wilmington, Delaware 19898*

*Received October 17, 1972*

The $PdCl_2$-catalyzed reaction of nitrobenzenes and the thermal reaction of phenyl azides with CO show similar variations of isocyanate yields with pressure and similar by-products. The by-products from 4-fluoronitrobenzene, diphenylurea, triphenylbiuret, and an imidazolinone **3a** may arise from proton abstraction from a nitrene-like intermediate. Labelling of a phenyl with a 4-fluorine gives convenient quantitative analysis of crude reaction mixtures, but is unreliable as a single method for qualitative analysis.

The formation of phenyl isocyanate from nitrobenzene[1] or phenyl azide[2] and carbon monoxide in the presence of $PdCl_2$ is of both academic and practical interest.[3] The only by-products described have been diphenylurea and azobenzene, and the urea has been presumed to arise from reaction of the isocyanate with water.[1] The results presented here suggest that side reactions of nitrene-like intermediates are responsible for the by-products.[4]

$$ArNO_2 + 3CO \xrightarrow{PdCl_2} ArNCO + 2CO_2$$

## Results

Over the range of 50–600 atm, the yield of 4-chlorophenyl isocyanate increases linearly with the square root of pressure (Table I). Yields are independent of temperature or palladium concentration (Table II). High pressure slows the reaction, but on extended heating the yield improvement is maintained.

The diphenylurea from pentadeuterionitrobenzene gave after sublimation infrared bands which were attributed to nitrogen–deuterium stretching vibrations.

An extensive study was made using 4-fluoronitrobenzene as substrate because $^{19}F$ nmr provided convenient analyses of the crude reaction mixtures. First, however, the various by-products were individually isolated by column chromatography over neutral SilicAR. In order of elution, the by-products isolated were 4,4-difluoroazobenzene, an imidazolinone **3a** discussed in detail below, 1,3,5-tris(4-fluorophenyl)biuret, and 1,3-bis(4-fluorophenyl)urea.

TABLE I

EFFECT OF CO PRESSURE ON THE REACTION OF 4-CHLORONITROBENZENE WITH CO[a]

| CO, atm[b] | Time, hr | Conversion of $ArNO_2$, % | Yield of ArNCO, % |
|---|---|---|---|
| 20 | 2 | 53[c] | 7 |
| 75 | 2 | 97 | 13 |
| 150 | 2 | 90 | 35 |
| 300 | 2 | 97 | 46 |
| 600 | 2 | 30 | 72 |
| 600 | 4 | 97 | 68 |

[a] Charge: 4-chloronitrobenzene (5 mmol) in 2 ml of $CH_3CN$ solution, $NO_2$/Pd ratio 5000/1. Run at 250° in 9-ml bomb. [b] At 25°. [c] Insufficient CO is present to react with all the nitrobenzene present.

TABLE II

EFFECT OF REACTION VARIABLES ON ISOCYANATE YIELD[a]

| CO, atm[b] | Temp, °C | Time, hr[c] | $ArNO_2$/Pd | Yield of ArNCO, % |
|---|---|---|---|---|
| 100 | 225 | 10 | 10,000 | 15 |
| 100 | 275 | 1 | 10,000 | 10 |
| 300 | 200 | 2 | 200 | 45 |
| 300 | 250 | 2 | 200 | 46 |
| 400 | 225 | 15 | 10,000 | 44 |
| 400 | 275 | 2 | 10,000 | 50 |

[a] Charge: 5 mmol of 4-chloronitrobenzene + $PdCl_2$ in 2 ml of $CH_3CN$ solution in 9-ml bomb. [b] At 25°. [c] The time is adjusted to give 100% conversion of nitrobenzene.

---

[1] W. B. Hardy and R. P. Bennett, *Tetrahedron Lett.*, 961 (1967).

[2] R. P. Bennett and W. B. Hardy, *J. Amer. Chem. Soc.*, **90**, 3295 (1968).

[3] W. W. Prichard, U. S. Patent 3,576,836 to Du Pont; G. F. Ottmann, E. H. Kober, and D. F. Gavin, U. S. Patent 3,523,962 to Olin Matheson; W. B. Hardy and R. P. Bennett, U. S. Patent 3,461,149 to American Cyanamide.

[4] Similar conclusions have been advanced by F. L'Eplattenier, P. Matthys, and F. Calderazzo, *Inorg. Chem.*, **9**, 343 (1970), for the Ru-catalyzed reaction.