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Reaction of 4-Picoline *N*-Oxide with Acetic Anhydride as Studied by Chemically Induced Dynamic ^{13}C Polarization (CIDNP)[1]

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The ^{13}C spectrum taken during the reaction of 4-picoline *N*-oxide with acetic anhydride at 110 °C in the NMR cavity (23.5 kG) shows a pair of emission lines at 15.8 and 154.4 ppm and enhanced absorption at 29.6 and 125.0 ppm (TMS-based). The signals are found to be due to 4-ethylpyridine formed as a minor product of the reaction and are interpreted in terms of the memory effect of the polarization induced in the precursor 4-picolyl–acetoxy radical pair.

The chemically induced dynamic nuclear polarization (CIDNP) of ^{13}C nuclei is expected to give valuable information on the spin distribution among the carbon atoms in radical species and on the rates of formation and decomposition of radical pair intermediates. Simplified spectra due only to net polarization can be obtained since the multiplet effect derived from the ^{1}H–^{13}C coupling is excluded when the wide-band proton decoupling technique is employed, as is usually the case in ^{13}C NMR spectroscopy. The wide variety of spin-lattice relaxation time of ^{13}C compared to that of ^{1}H may also be of help in interpreting the observed polarization in terms of the kinetics and mechanisms of free radical reactions. However, experimental studies have so far been hampered by the technical difficulty caused by short sampling time of the polarization signals over the wide ^{13}C chemical shift region in question in the course of fast free radical reactions.[2] In contrast with conventional continuous wave NMR, a recently introduced Fourier transform pulsed NMR spectroscopy adequately meets the above requirement for the CIDNP study. We wish to report on the ^{13}C CIDNP spectra obtained during the reaction of 4-picoline *N*-oxide with acetic anhydride.

Results and Discussion

^{13}C CIDNP Spectra. A 3 M solution of 4-picoline *N*-oxide in acetic anhydride was heated at 110 °C in the magnetic cavity of a ^{13}C NMR spectrometer (25.15 MHz). The Fourier transform pulsed NMR spectra were obtained from the time domain signals accumulated nine times during a given 10 s span in the course of the reaction (see Experimental for details). At the beginning of the reaction, the absorption signals at 127.0 and 138.7 ppm (TMS based) due to the ring $C_{(3)}$ and $C_{(2)}$ atoms, respectively, of 4-picoline *N*-oxide were seen in addition to those at 21.0 (for CH_3)[3] and 167.2 ppm (for C=O) of the solvent (see Fig. 1a). As the reaction proceeded, the singals of the starting materials diminished gradually and disappeared in 140 s after the start of the reaction. At 100 s we observed growth of a pair of emission lines at 15.8 and 154.4 ppm and absorption signals at 29.6 and 125.0 ppm. The intensity of these peaks increased until about 140 s (Fig. 1b), when it started to decrease and was null in 300 s. Time development of the polarization during the reaction is summarized in Fig. 2. At the end of the reaction, only two absorption peaks of the products were barely detected under the signal to noise ratios of the experimental conditions. We found on a chart of 100 scan accumulation signals due mainly to 4-picolyl acetate; 19.8 (CH_3), 64.5 (CH_2), 122.5 ($C_{(3)}$), 146.1 ($C_{(4)}$), 148.8 ($C_{(2)}$), and 174.4 ppm (C=O).[4] No signal could be seen at the chemical shifts where the polarized signals appeared (Fig. 3a).

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[1] Part IV of the Mechanism of the Reaction of Picoline *N*-Oxides with Carboxylic Anhydrides Studied by NMR. For Part III see H. Iwamura, M. Iwamura, M. Imanari, and M. Takeuchi, *Tetrahedron Lett.*, **1973**, 2325.

[2] Only a few ^{13}C CIDNP papers have been given: a) E. Lippmaa, T. Pehk, A. L. Buchachenko, and S. V. Rykov, *Chem. Phys. Lett.*, **5**, 521 (1970); b) S. Berger, S. Hauff, P. Niederer, and A. Rieker, *Tetrahedron Lett.*, **1972**, 2581; c) R. Kaptein, J. Brokken-Zijp, and F. J. J. de Kanter, *J. Amer. Chem. Soc.*, **94**, 6280 (1972); d) E. M. Schulman, R. D. Bertrand, D. M. Grant, A. R. Lepley, and C. Walling, *ibid.*, **94**, 5972 (1972).

[3] Also for the CH_3 signal of 4-picoline *N*-oxide.

[4] The carbonyl chemical shift of acetic acid coincided.

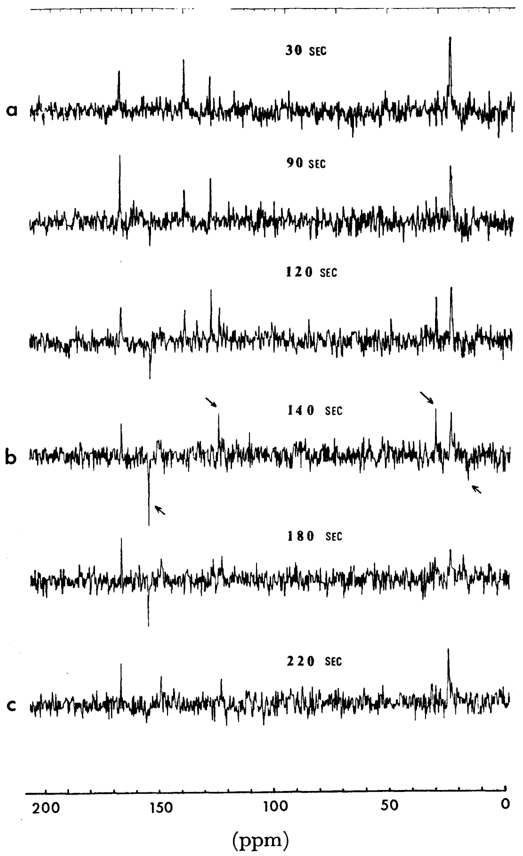


Fig. 1. 25.15 MHz ^{13}C spectra obtained during the course of the reaction of 4-picoline *N*-oxide with acetic anhydride at 110 °C.

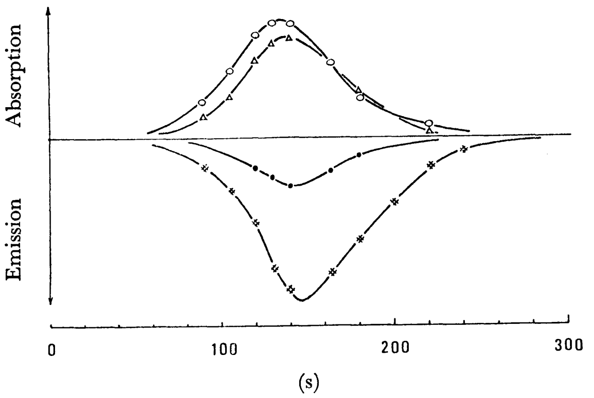


Fig. 2. Time development of the polarization signals due to 4-ethylpyridine during the reaction of 4-picoline *N*-oxide in acetic anhydride at 110 °C. The signal intensities are in arbitrary unit.

By comparison with the ^{13}C spectrum of the authentic sample (Fig. 3b), the emission signals observed during the reaction were assigned to the methyl carbon and ring $C_{(4)}$ while the enhanced absorption peaks corresponded to the methylene carbon and ring $C_{(3)}$ of 4-ethylpyridine formed as a minor product according to Scheme 1. It is reasoned that the chemical yield of 4-ethylpyridine was so low that its NMR absorption could not be observed in the final reaction mixture (Fig. 3a). At the maximum intensity of polarization, we could not detect the signals due to 4-picolyl acetate which should have been formed approximately fifty times as much as 4-ethylpyridine. Since the signal to noise ratio of the strongest emission line was five (Fig. 1b), the apparent enhancement factor of polarization is roughly estimated to be 250.

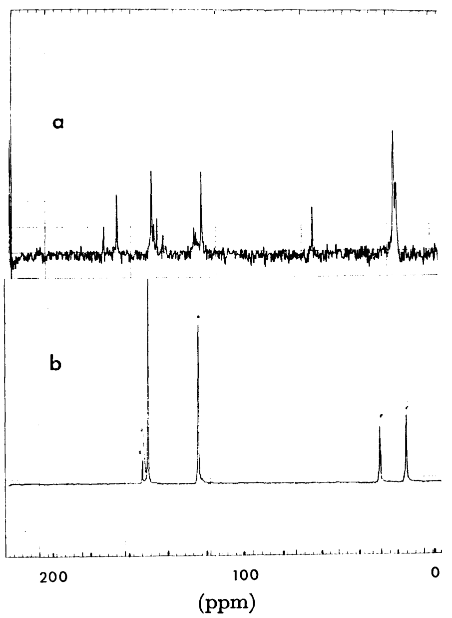
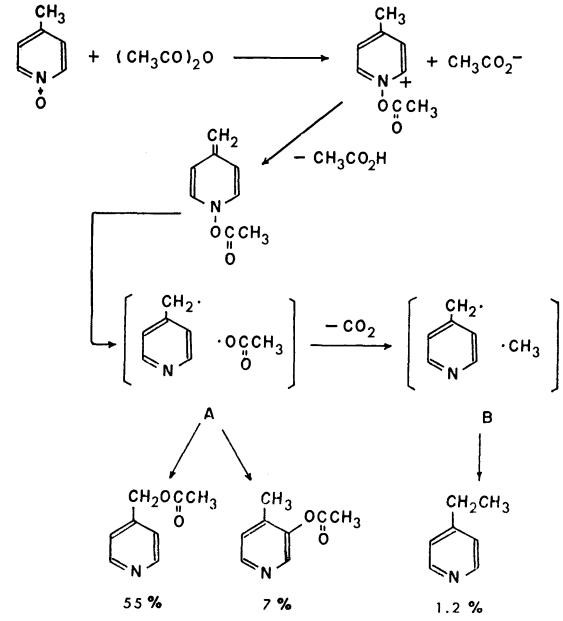


Fig. 3. ^{13}C spectra obtained after the end of the reaction of 4-picoline *N*-oxide in acetic anhydride at 110 °C (a), and of authentic 4-ethylpyridine (b). See text for the assignment of the signals.



Scheme 1. (Yields of the products were determined by vpc.)[5]

Origin of the 4-Ethylpyridine Polarization. Examination of the polarization pattern in terms of the current radical pair theory of CIDNP[6] enables us to confirm

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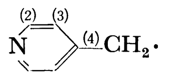
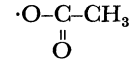
[5] See also H. J. Shine, "Aromatic Rearrangements," Elsevier, Amsterdam (1967), p. 284.

[6] G. L. Closs and A. D. Trifunac, *J. Amer. Chem. Soc.*, **92**, 2183, 2186 (1970); R. Kaptein and L. J. Oosterhoff, *Chem. Phys. Lett.*, **4** 195 (1969); H. Fischer, *Z. Naturforsch.*, **25a**, 1957 (1970); R. Kaptein, *J. Amer. Chem. Soc.*, **94**, 6251 (1971); F. J. Adrian, *J. Chem. Phys.*, **53**, 3374 (1970); **54**, 3912 (1971).

the assignment of the polarization signals and to deduce the origin of the 4-ethylpyridine polarization. Since 4-picolyl and methyl radicals are both carbon radicals and differ only slightly in g factors, their pairing as in B cannot induce the observed net polarization. Polarization with high enhancement factors should have arisen in the precursor 4-picolyl–acetoxy radial pair (A), in which the acetoxy radical decarboxylated before recombination. The 4-picolyl–methyl radical pair (B) thus formed can in principle superimpose the multiplet effect on the net polarization already present in the radical pair. The former effect cannot be observed in the present example for lack of spin coupling as the result of application of the wide-band proton decoupling and of low statistical probability of ^{13}C–^{13}C coupling in the samples of natural ^{13}C abundance.

The ESR parameters for the unstable radical components in A are not experimentally available, but the following assumption based mostly on analogy with the data of benzyl and some oxygen radicals for 4-picolyl and acetoxy radicals, respectively (Table 1), may not be far from reality. In A, the acetoxy radical undoubtedly has a larger g value by *ca.* 0.003 due to the presence of the oxygen atom.[2c,7] In reference to the simple rules on the sign of net effects of CIDNP,[8] ring $C_{(4)}$ in 4-picolyl radicals which is expected to carry a negative value of the isotropic hyperfine coupling constant[9] is predicted to give net emission in the cage recombination product. Positive signs in hyperfine coupling of the CH_2 carbon and ring $C_{(3)}$ in 4-picolyl radicals should correspond to enhanced absorption.[10] The polarity of the polarized signals with respect to the sign of hyperfine coupling constants is reversed in acetoxy radicals which have larger g values than their counterpart. Our prediction was exactly what was observed in 4-ethylpyridine formed in an NMR cavity (Fig. 1b).

Table 1. ESR parameters assumed for the radical components of 4-picolyl–acetoxy pair (A)

	g	$a_{^{13}C}$ (G)[a]
	2.0026[b]	32.6, 38.3[b] (CH_2) −12.3, −13.6[c] ($C_{(4)}$) 11.7 ($C_{(3)}$) −8.5 ($C_{(2)}$)
 $\cdot O\!-\!\overset{\overset{\displaystyle O}{\|}}{C}\!-\!CH_3$	2.0058[2c]	3∼5 (CH_3)[2c]

a) The calculated values for benzyl radicals unless otherwise stated.[9]

b) Data for methyl radicals.[10]

c) Data for ethyl sadicals.[11]

The memory effect of polarization induced in the earlier radical pair A is in accord with the time scale of the whole process. Nuclear relaxation times of radicals are usually short in the range 10^{-5}—10^{-4} s [2c,12] as a result of efficient fluctuation of the local magnetic field produced by the spins of unpaired electrons. The life-time of acetoxy radicals and consequently of A could well be shorter (10^{-9} s)[13] than their relaxation time, giving polarization patterns due to A in 4-ethylpyridine.

From a comparison with the ^{1}H CIDNP spectra in which net emission is observed at δ 4.98 for CH_2 of 4-picolyl acetate and a pair of emission/absorption multiplets is eminent for the ethyl signals of 4-ethylpyridine,[14] we note that net polarization for the latter product is detected but not that due to 4-picolyl acetate under the S/N of the present ^{13}C study. As a possible mechanism which might account for the difference, a faster reaction rate at a slightly higher temperature (110°) than that in the previous ^{1}H study (95°) is suggested. As the decay rate of radical pair A increases at the vicinity of $k=10^9$ s^{-1}, the enhancement factor of polarization in 4-picolyl acetate starts to decrease because of loss of efficiency of the S–T_0 mixing in A. In other words the nuclear spin independent part of the product formation increases. With respect to the efficiency of development of polarization, the same is true for 4-ethylpyridine formed later *via* B. However, shortening of the time span before product formation is advantageous for the long time spin correlation which is indispensable for the memory effect. As a result, the polarization for 4-ethylpyridine drops off much more slowly as the rate of reaction increases. Thus, in the case of rapid reactions, it might even happen that polarization in 4-ethylpyridine is more than ten times as strong as in 4-picolyl acetate. Secondly, higher polarity of the reaction medium in the present ^{13}C study (acetic anhydride *vs.* benzene) might be another reason for the detection of net polarization only for 4-ethylpyridine. It is possible that a dual mechanism in which the anhydro-base intermediate cleaves to both radical and ion pairs is operative.[14] The ester product can result from both, but only the radical manifold should give polarization. The fraction of the ion pair mechanism increases naturally with polarity of the medium, making the detection of CIDNP spectrum of 4-picolyl acetate difficult.

The Effect of ^{13}C Spin-Lattice Relaxation Rates. While the ^{13}C signal due to ring $C_{(4)}$ of 4-ethylpyridine has the weakest resonance intensity under the spin

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7) H. Fischer, "Magnetic Properties of Free Radicals," Landolt-Börnstein, New Series, Group II, Vol. 1, ed. by K.-H. Hellwege, Springer-Verlag, Berlin (1965).

8) R. Kaptein, *Chem. Commun.*, **1971**, 732; R. Kaptein and J. A. den Hollander, *J. Amer. Chem. Soc.*, **94**, 6269 (1972). The signs (Γ_{ne}, + for absorption and − for emission) of net polarization are given by $\Gamma_{ne}=\mu\varepsilon\Delta g A_i$ where μ, ε, and A_i labels indicate the multiplicity of the radical pair (− for S precursor), the type of product (+ for cage recombination), and the sign of hyperfine coupling of the nucleus i under consideration, respectively.

9) J. A. Pople, D. L. Beveridge, and P. A. Dobosh, *J. Amer. Chem. Soc.*, **90**, 4201 (1968).

10) R. W. Fessenden, *J. Phys. Chem.*, **71**, 74 (1967).

11) M. Karplus and G. K. Fraenkel, *J. Chem. Phys.*, **35**, 1312 (1961).

12) G. L. Closs and D. R. Paulson, *J. Amer. Chem. Soc.*, **92**, 7229 (1970); N. Bloembergen, *J. Chem. Phys.*, **27**, 572 (1957).

13) M. Szwarc, "Peroxide Reaction Mechanisms," ed. by J. O. Edwards, Interscience, New York, N. Y. (1962); A. Rembaum and M. Szwarc, *J. Amer. Chem. Soc.*, **77**, 3486 (1955); W. Braun, L. Rajbenbach, and F. R. Eirich, *J. Phys. Chem.*, **66**, 1591 (1962).

14) H. Iwamura, M. Iwamura, T. Nishida, and S. Sato, *J. Amer. Chem. Soc.*, **92**, 7474 (1970).

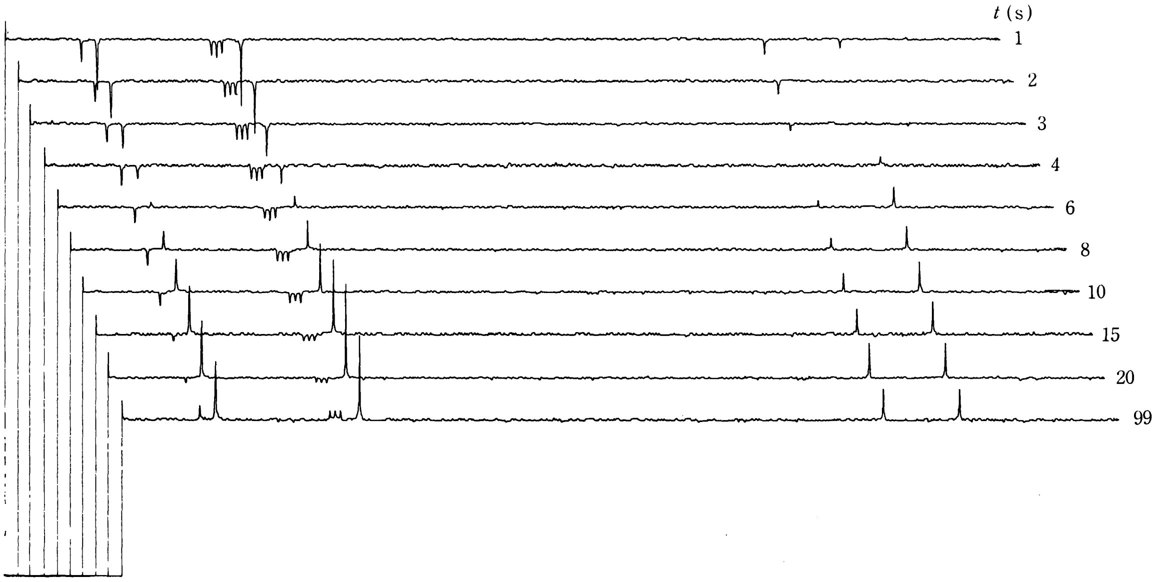

Fig. 4. Carbon-13 partially relaxed Fourier transform spectra of 4-ethylpyridine (containing 30% benzene-d_6 as an internal lock). A waiting period t in a 180 °–t–90 ° pulse sequence is indicated. See text and Fig. 3b for the signal assignment.

equilibrated conditions as the result of lack of signal enhancement due to operation of a ^{13}C–H Overhauser effect (Fig. 3b), it shows the strongest amplitude in polarization spectrum (Fig. 1b, 2). The hyperfine coupling constant is not necessarily the largest for the carbon atom. The effect is considered to originate from the slower spin-lattice relaxation rate of the quaternary carbon atom which usually has relaxation times an order of magnitude greater than those of carbon atoms carrying a proton. The intensities of CIDNP spectra are approximately proportional to the nuclear spin relaxation times.[15] In order to verify the above reasoning for the effect, T_1 measurements were performed by means of 180°–t–90° pulse sequence method. The results are summarized in Table 2.

Table 2. ^{13}C spin-lattice relaxation times (T_1) for 4-ethylpyridine

^{13}C	T_1 (s)
CH_3	3.8
CH_2	6.7
$C_{(2)}$	7.8
$C_{(3)}$	7.8
$C_{(4)}$	96.8

As expected, ring $C_{(4)}$ of 4-ethylpyridine which lacks the dipole-dipole relaxation mechanism with the attached proton has a T_1 value almost ten times as great as that of the other carbons. As another manifestation of the relaxation effect on CIDNP spectra, we note in Fig. 2 that the relative intensity of the $C_{(4)}$ signal is prominent at a later stage (150—300 s) of the reaction wkere intensities are more susceptible to relaxation mechanism in the product.

Experimental

The Fourier transform pulsed NMR spectra were taken on a JNM-PFT-100 FT NMR System. An internal D lock at 15.359 MHz was made on DMSO-d_6 sealed in a capillary and placed concentrically in a sample tube of 8 mm o.d. The sample temperature was controlled by preheated nitrogen and was measured by a calibrated thermocouple in an effluent gas stream. A short radiofrequency 40° pulse of 8 μsec width was applied with a repetition time of 1.1 s over the ^{13}C spectrum width of 6.25 kHz. Nine scans on 2048 data points were accumulated in a magnetic dram of 16 kW which allowed us to obtain four separate spectra in the course of a single run of the reaction. After completion of the sampling, each accumulated time domain signal was Fourier transformed. The signals of individual ^{13}C were obtained as a single line with the use of wide-band proton decoupling with 100.00 MHz radiofrequency of 35—40 W. All the spectra were of v-mode which was phase corrected by computer calculation. Five runs of the reaction on a 3 M batch solution were carried out in order to construct Fig. 2.

For T_1 measurements, 180°–t–90° pulse sequences were used, and the values of T_1 were obtained from least-squares fits of the logarithm of the heights of the 90° pulse responses as a function of t. The original data are shown in Fig. 4. A sample of 4-ethylpyridine was neat liquid with approximately 30% benzene-d_6 as an internal lock and was not degassed to simulate the reaction conditions.

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15) R. G. Lawler, *ibid.*, **89**, 5519 (1967); G. L. Closs and L. E. Closs, *ibid.*, **91**, 4549 (1969).