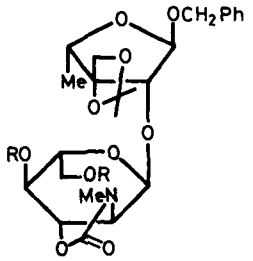
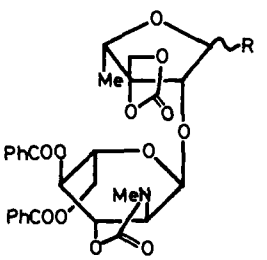
(cyclic carbamate). Partial hydrolysis of **7** (25% AcOH in MeOH, reflux) gave the diol **8** (95%): mp 190–190.5°; $[\alpha]^{23}D$ −177° (*c* 1, MeOH). This was converted (PhCOCl–pyridine, 91%) into the dibenzoyl derivative **9**: $[\alpha]^{18}D$ −145° (*c* 1, $CHCl_3$). Partial hydrolysis (75% AcOH, 70° 83%) removed the isopropylidene group, giving a diol, $[\alpha]^{18}D$ −177° (*c* 1, $CHCl_3$), which was transformed (*p*-$NO_2C_6H_4$-OCOCl, pyridine) into the carbonate **10** (91%): $[\alpha]^{18}D$ −145° (*c* 1, $CHCl_3$); ir ($\nu_{C=O}$) 1815 (carbonate), 1775 (cyclic carbamate), 1725 cm^{-1} (ester). Hydrogenolysis of the glycosidic linkage (Palladium Black, dioxane, 99%) gave the free sugar **11**: $[\alpha]^{18}D$ −95° (*c* 1, $CHCl_3$). Reaction with thionyl chloride at room temperature afforded the α-glycosyl chloride **12** in



8, R = H
9, R = COPh

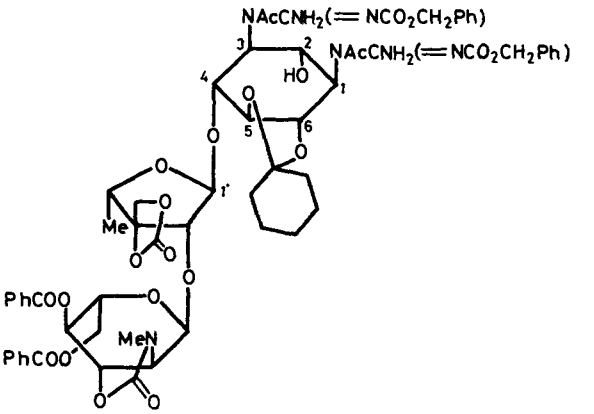


10, R = OCH_2Ph (α-anomeric)
11, R = OH
12, R = Cl (α-anomeric)

77% yield.[13]

Direct treatment of **6** with *p*-nitrophenoxycarbonyl chloride or phosgene followed by benzoylation gave a poor yield of **10**. Transformation of **9** into a chloride corresponding to **12** by similar hydrogenolysis followed by chlorination was avoided, because the authors observed that transketalization occurred in the chlorination of 2-*O*-acetyl-3,3′-*O*-isopropylidenedihydrostreptose with thionyl chloride.

Finally, condensation of **12** with di-*N*-acetyl-di-*N*-benzyloxycarbonyl-*O*-cyclohexylidenestreptidine[14] (**13**) (Ag_2CO_3–$AgClO_4$, molecular sieve type 3A, benzene, 50°) gave four condensation products and one of them having $[\alpha]^{25}D$ −70° (*c* 2, $CHCl_3$) proved to be the 4-*O*-glycoside[16] **14** (10%). Hydrolysis (0.05 *N* $Ba(OH)_2$, dioxane, 60°) selectively removed the carbamate, carbonate, benzoyl, and acetyl groups to give a di-*N*-benzyloxycarbonyl-*O*-cyclohexylidene derivative (73%), $[\alpha]^{28}D$ −63° (*c* 1, MeOH). Removal of the remaining



14

protecting groups with 50% acetic acid and hydrogenolysis with Palladium Black afforded dihydrostreptomycin[17,18] (60% as sesquisulfate; $[\alpha]^{25}D$ −88° (*c* 0.1, H_2O), identical[19] with a natural specimen in optical rotation; ir and pmr spectra (in D_2O, H-1′ had J = 1.3 Hz)). The C-4 glycosidic linkage was confirmed by the $\Delta[M]^{10}_{436(CuAm)}$ value[20] (−1200°) identical with that of natural dihydrostreptomycin.

Acknowledgment. The authors are grateful to Professor Hamao Umezawa of Tokyo University and of the Institute of Microbial Chemistry for his important ideas and encouragement.

(13) Compound **12**: mp 114–116°; $[\alpha]^{18}D$ −170° (*c* 1, $CHCl_3$); ir 1820, 1770, 1725 cm^{-1}; pmr ($CDCl_3$) δ 1.26 (d, 3, $CHCH_3$), 2.94 (s, 3, NCH_3), 5.32 (d, J = 3 Hz, H-1′), 6.33 (d, J = 1.5 Hz, H-1).

(14) Compound **13**; reaction of streptidine[15] with excess benzyloxycarbonyl chloride and 2 *N* NaOH in aqueous dioxane followed by partial hydrolysis with 2 *N* NaOH in dioxane gave di-*N*-benzyloxycarbonylstreptidine (50%), which, by treatment with 3,4-dihydro-2*H*-pyran and *p*-toluenesulfonic acid in DMF, gave a tetra-*O*-tetrahydropyranyl derivative (70%). Acetylation with acetic anhydride–pyridine containing triethylamine then gave a di-*N*-acetyl derivative (98%), which, by removal of the tetrahydropyranyl group by acid hydrolysis followed by reaction with 1,1-dimethoxycyclohexane, led to **13** (racemate, 40%), mp 117–118°, which is satisfactorily soluble in benzene. The positions of acetyl and benzyloxycarbonyl groups attached to nitrogen are arbitrary and the assignment is under study. This is the first preparation of a useful intermediate for the synthesis of streptidine glycosides.

(15) M. L. Wolfrom and W. J. Polglase, *J. Amer. Chem. Soc.*, **70**, 1672 (1948); M. L. Wolfrom, S. M. Olin, and W. J. Polglase, *J. Amer. Chem. Soc.*, **72**, 1724 (1950).

(16) Compound **14** was isolated by silica gel chromatography with C_6H_6–$CHCl_3$–EtOH–concentrated NH_4OH (50:50:4:0.5) and C_6H_6–90% EtOH (25:1); ir ($\nu_{C=O}$) 1810, 1775, 1725, 1640, 1570 cm^{-1}; pmr ($CDCl_3$) δ 1.30 (d, 3, $CHCH_3$), 2.18 (s, 6, Ac), 2.94 (s, 3, NCH_3), 7.40 (s, 10, CH_2Ph), 7.4 and 8.1 (br, 6 and 4, respectively, COPh).

(17) See ref 5 for the structure of dihydrostreptomycin.

(18) After submission of the manuscript, dihydrostreptomycin has been converted into streptomycin by oxidation with Me_2SO–DCC followed by chromatographic separation.

(19) Identity was further established by thin layer and paper chromatographic behavior, paper electrophoresis mobility, and antibacterial spectra.

(20) S. Umezawa, T. Tsuchiya, and K. Tatsuta, *Bull. Chem. Soc. Jap.*, **39**, 1235 (1966).

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Received September 7, 1973

Photochemistry of Methyl Diazoacetate in Chloromethanes Studied by CIDNP

Sir:

In sharp contrast with the photolysis of diazomethane, a radical chain mechanism was considered a remote possibility in the reactions of methyl diazoacetate with halomethanes. The overall product yields as well as the quantum yield in these reactions are usually low.[1,2] Migita and coworkers provided chemical evidence in support of the nonradical chain mechanism by obtaining different products from the benzoyl peroxide initiated decomposition of ethyl diazoacetate in chloromethanes.[3] On the other hand, Cocivera and Roth argued for a radical chain mechanism originally proposed by Urry and coworkers[4] by showing that the CIDNP emission signal for the α-proton of methyl 2,3,3,3-tetrachloropropionate (**1**) formed on photolysis of methyl diazo-

(1) C. Walling, "Free Radicals in Solution," Wiley, New York, N. Y., 1957, p 272.

(2) J. W. Wilt, Ph.D. Dissertation, University of Chicago, 1964.

(3) T. Migita, W. Ando, S. Kondo, H. Matsuyama, and M. Kosugi, *J. Chem. Soc. Jap., Pure Chem. Sect.*, **91**, 374 (1970).

(4) W. H. Urry and J. W. Wilt, *J. Amer. Chem. Soc.*, **76**, 2504 (1954).

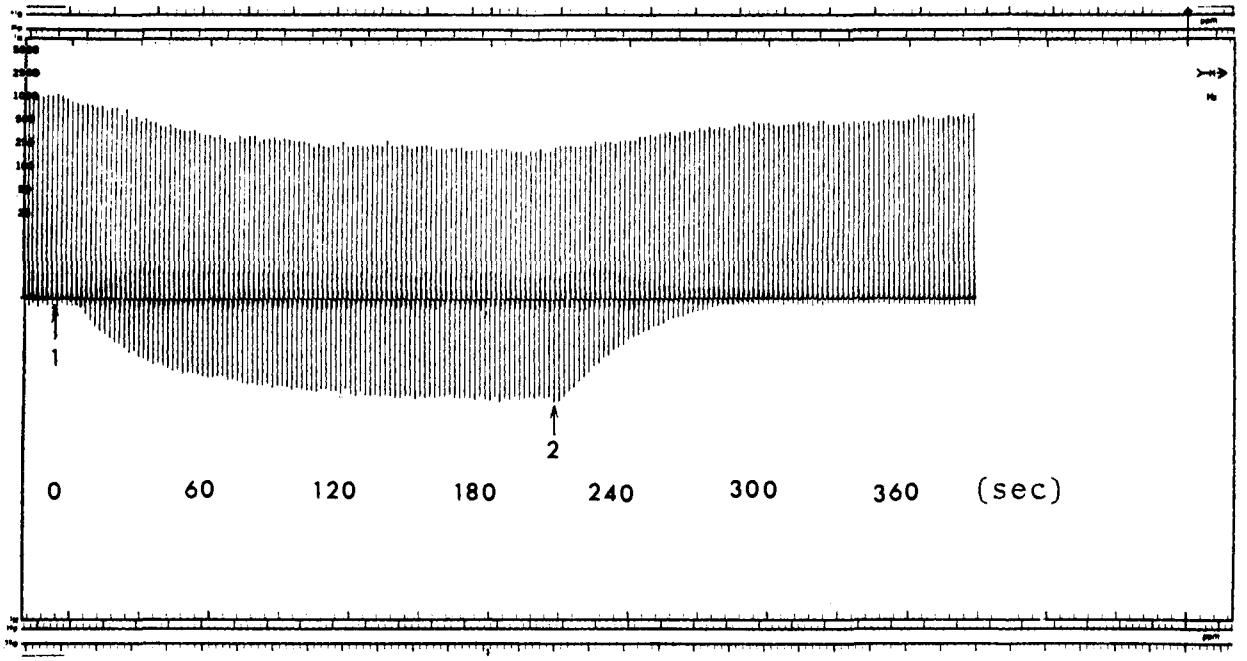


Figure 1. Time development of CIDNP emission signal due to the α-proton of **1** during irradiation of methyl diazoacetate in CCl_4, obtained by repeated sweeping through the δ 4.5–4.8 region. Arrows 1 and 2 indicate the start and interruption of irradiation, respectively.[9]

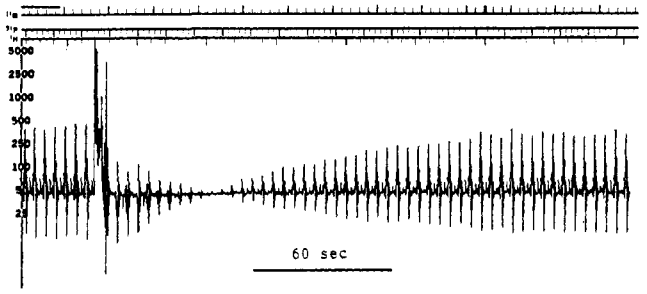


Figure 2. Reversal and recovery of the nuclear magnetization of the α-proton signal of **1** measured by the adiabatic rapid passage through resonance.

acetate in carbon tetrachloride has a decay lifetime (*ca.* 70 sec) considerably longer than the nuclear spin–lattice relaxation time T_1 (*ca.* 1 sec).[5]

We have reexamined the photochemical decomposition of methyl diazoacetate in solutions of carbon tetrachloride and chloroform and found that the T_1 of the α proton of **1** is not so short as reported under the experimental conditions. The relaxation time coincides within the experimental errors with the decay lifetime of the emission signal after interruption of uv irradiation. The ^{13}C CIDNP patterns are also in accord with the cage recombination of radical pairs **2** but are inconsistent with a radical chain mechanism in reference to the current theory of CIDNP.[6]

$$\overline{Cl_2XC\cdot} \quad \overline{\cdot CHClCO_2CH_3}$$
2 X = Cl, H, or D

The proton nmr spectra[7] for a degassed 10 mol % solution of methyl diazoacetate in carbon tetrachloride before, during, and after irradiation are practically the same as those given by Cocivera and Roth.[5,8] Figure 1 gives the time development of the emission singlet at δ 4.72 due to the α-proton of **1** when the light is turned on and off. The plateau of the envelope of the downward spikes indicates the steady-state concentration of the polarized product established.[9] The reported relaxation time of about 70 sec is reproduced for the exponential decay of the emission signals right after irradiation is stopped. Since only small amounts of **1** have been formed during the few minute period of irradiation, no absorption lines due to **1** can be detected after the polarization is completely relaxed. Figure 2 shows the saturation recovery of the same α-proton signal measured on a degassed 2.5 mol % solution of the authentic sample of **1** at 52° by the adiabatic rapid passage through resonance technique.[10] The spin–lattice relaxation time is calculated to be 74 ± 4 sec. The spin–lattice relaxation time usually decreases as the temperature is lowered and the concentration of the substrate is increased.[11,12] In the present example, a decidedly lower T_1 value can-

(5) M. Cocivera and H. D. Roth, *J. Amer. Chem. Soc.*, **92**, 2573 (1970).

(6) (a) G. L. Closs and L. E. Closs, *J. Amer. Chem. Soc.*, **91**, 4549, 4550 (1969); (b) G. L. Closs, *ibid.*, **91**, 4552 (1969); (c) G. L. Closs and A. D. Trifunac, *ibid.*, **91**, 4554 (1969); **92**, 2183 (1970); (d) R. Kaptein and L. J. Oosterhoff, *Chem. Phys. Lett.*, **4**, 195, 214 (1969); (e) R. Kaptein, *J. Amer. Chem. Soc.*, **94**, 6251, 6262 (1972).

(7) Measured at 60 MHz with a Varian NV-14 spectrometer. A focused beam of uv light from a Ushio USH-500D high-pressure mercury arc (500 W) was introduced from the bottom of the probe to a Pyrex nmr sample tube of 8 mm o.d.

(8) A 1.3 mol % solution of methyl diazoacetate in chloroform gives a pair of emission signals centered at δ 4.57 and another pair of enhanced absorption lines at δ 5.98 due to the α- and β-protons, respectively, of methyl 2,3,3-trichloropropionate. In deuteriochloroform the emission is now singlet and the enhanced absorption lines are missing.[5]

(9) The upper spikes correspond to the α-proton signal (δ 4.57) of methyl diazoacetate. Slight lowering of their height during irradiation is noted. The phenomenon can be ascribed mostly to the apparent lowering of sample concentration as a result of the rise of temperature (to *ca.* 50°) by irradiation and the volume expansion of the solvent.

(10) J. A. Pople, W. G. Schneider, and H. J. Bernstein, "High-resolution Nuclear Magnetic Resonance," McGraw-Hill, New York, N. Y., 1959, p 83.

(11) Chapter 9 of ref 10.

(12) T. L. Pendred, A. M. Pritchard, and R. E. Richards, *J. Chem. Soc. A*, 1009 (1966).

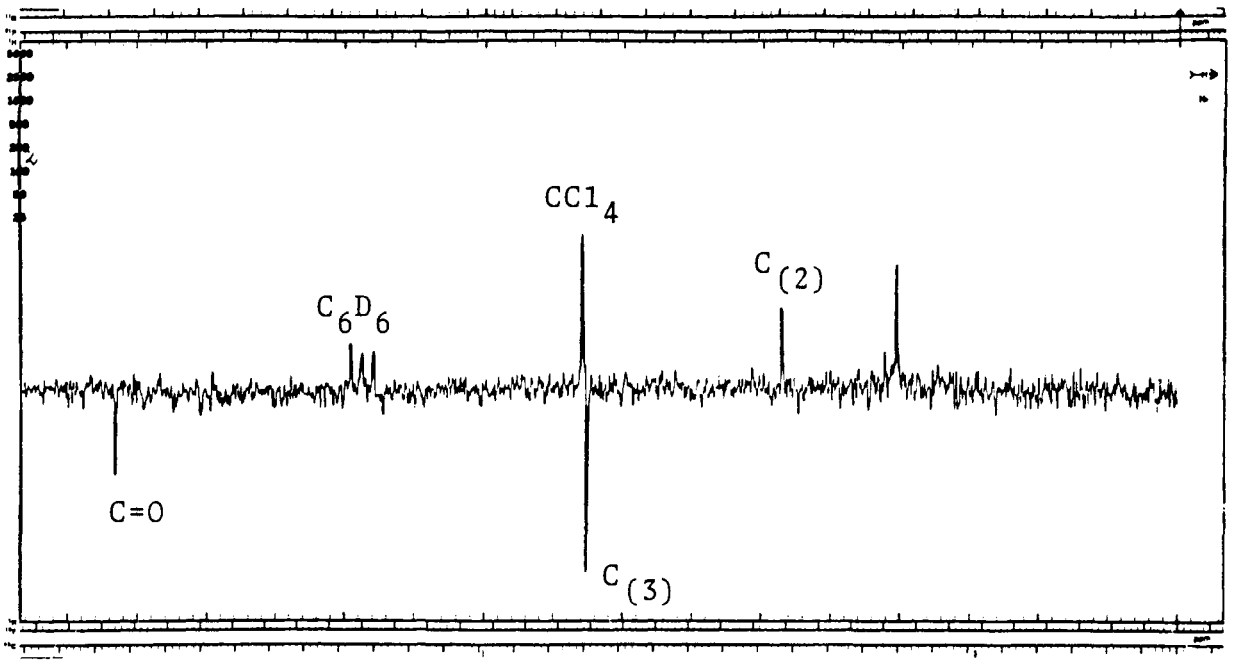
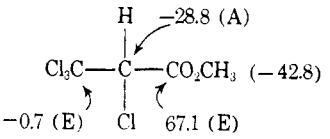


Figure 3. The 15.087-MHz ^{13}C spectrum taken during photolysis of a 8.5 mol % solution of methyl diazoacetate in CCl_4.

not be obtained as long as the measurement is made on a dilute carbon tetrachloride solution at the ambient or higher temperatures.

In Figure 3 is shown the ^{13}C nmr spectrum taken during the photolysis of a 8.5 mol % solution of methyl diazoacetate in carbon tetrachloride.[13] We note two emission lines and an absorption signal in addition to those of the starting material, the solvent and hexadeuteriobenzene used as an internal lock. By comparison with the ^{13}C chemical shifts of the authentic **1**, the following assignment is made.[14] The results are



fully in accord with the mechanism of the ^{13}C polarization induced in radical pairs **2**. Hereby it is assumed that the $\cdot CHClCO_2CH_3$ radical has a reasonably smaller g value than $\cdot CCl_3$ (g = 2.0091).[15] For ^{13}C hyperfine coupling positive signs in $C_{(2)}$ and $C_{(3)}$ and a negative one in the carbonyl carbon are also assumed.[16]

According to the radical pair theory of CIDNP,[6] no polarization results from a radical transfer reaction itself. Polarization ascribed to such a process[17] is considered to originate from a memory of the previous radical pair or from a radical disproportionation reaction instead of the apparent transfer reaction.[6] The memory effect is limited to appear only when the subsequent steps are very rapid, or else the nuclear spin polarization will disappear in one of the intermediate radicals as a result of efficient fluctuation of the local magnetic field produced by the spins of unpaired electrons.[18] Therefore a radical chain mechanism in which $\cdot CXCl_2$ is a chain carrier is unlikely because polarization induced at the earliest stage in pairs **(2)** has to be retained unrelaxed during radical chain transfer steps. CIDNP at nuclei other than $C_{(3)}$ in the products cannot also be explained by a radical chain mechanism.

Thus none of the CIDNP results can be regarded as a support for a radical chain mechanism. The recombination of geminate pairs **(2)** formed presumably by homolysis of chloronium ylides **3** is the more likely mechanism.[19]

$$Cl_2XC\overset{+}{Cl}\overset{-}{C}HCO_2CH_3$$
3

Acknowledgment. The authors gratefully acknowledge support of this work by Ito Science Foundation.

(13) The Fourier transform pulsed nmr spectra were obtained with the aid of a NV-124 computer system from the free induction decay signals accumulated during a given 800-sec span under irradiation on five batch solutions. A short radio frequency pulse of 10-μsec width was applied with the acquisition time of 0.8 sec on the 4096 data points over the 2500-Hz spectral width.

(14) Shifts in ppm downfield from the solvent carbon tetrachloride signal are stated as positive. In chloroform the CIDNP signals are at 88.8 (E, C=O), −6.4 (E, $C_{(3)}$), and −14.9 (A, $C_{(2)}$) in ppm from the chloroform signal.

(15) A. Hudson and H. A. Hussain, *Mol. Phys.*, **16**, 199 (1969).

(16) R. W. Fessenden, *J. Phys. Chem.*, 71, 74 (1967); M. Karplus and G. K. Fraenkel, *J. Chem. Phys.*, **35**, 1312 (1961).

(17) F. Gerhart and G. Ostermann, *Tetrahedron Lett.*, 4705 (1969).

(18) Nuclear relaxation times of organic radicals are usually in the range 10^{-5}–10^{-4} sec. See G. L. Closs and D. R. Paulson, *J. Amer. Chem. Soc.*, **92**, 7229 (1970); R. Kaptein, J. Brokken-Zijp, and F. J. J. de Kanter, *ibid.*, **94**, 6280 (1972); C. Walling and A. R. Lepley, *ibid.*, **94**, 2007 (1972); N. Bloembergen, *J. Chem. Phys.*, **27**, 572 (1957).

(19) There are many examples of the thermal 1,2 rearrangements of nitrogen and sulfur ylides which exhibit CIDNP. See, for example, A R. Lepley, *J. Amer. Chem. Soc.*, **91**, 1237 (1969); *Chem. Commun.*, 1460 (1969); V. Schollkopf, G. Ostermann, and J. Schossig, *Tetrahedron Lett.*, 2619 (1969); J. E. Baldwin, W. F. Erickson, R. E. Hackler, and R. M. Scott, *Chem. Commun.*, 576 (1970); H. Iwamura, M. Iwamura, T. Nishida, M. Yoshida, and J. Nakayama, *Tetrahedron Lett.*, 63 (1971).

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Received September 11, 1973