tion of 5 ml. of ethanol gave a crystalline precipitate which contained *erythro*-β-hydroxyleucine as the sole ninhydrin-positive component. Paper electrophoresis showed the filtrate to contain a number of ninhydrin-positive substances. The *erythro*-amino acid was purified by treating the aqueous solution (10 ml.) with 0.3 g. of activated charcoal, lyophilizing the filtrate, and recrystallizing the residue from water–ethanol; 28 mg. (47%) of *erythro*-β-hydroxy-L-leucine was thus obtained as colorless needles, m.p. 219–222° dec., $[\alpha]^{30}\mathrm{D}$ + 22° (*c* 1.0 in water). The infrared spectrum (KBr) was identical with that of the hydroxyleucine obtained from the acid hydrolysate of Telomycin.

Anal. Calcd. for $C_6H_{13}NO_3$: C, 48.96; H, 8.90; N, 9.52. Found: C, 49.46; H, 8.62; N, 9.55.

2,4-Dinitrophenyl-*erythro*-β-hydroxy-L-leucine.—Dinitrophenylation[17] of both the isolated and synthetic amino acids gave DNP derivatives which were crystallized from aqueous ethanol and had identical m.p.'s (173–174°) and infrared spectra (KBr).

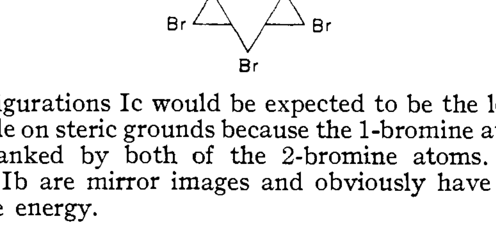
Anal. Calcd. for $C_{12}H_{15}N_3O_7$: C, 46.01; H, 4.82; N, 13.41. Found (for Telomycin product): C, 46.55; H, 5.28; N, 13.70; (for synthetic product): C, 45.83; H, 4.60.

COMMUNICATIONS TO THE EDITOR

OPPOSITE RELATIVE SIGNS OF GEMINAL AND VICINAL FLUORINE-FLUORINE N.M.R. COUPLING CONSTANTS IN A SATURATED FLUOROCARBON BY DOUBLE RESONANCE

Sir:

We wish to report the determination of the relative signs of the geminal and vicinal F^{19}–F^{19} n.m.r coupling constants in a saturated fluorocarbon by use of the audio side band phase detection decoupling technique.[1,2] The utility of this decoupling technique for F^{19}–F^{19} decoupling has been demonstrated recently.[3] In this communication, we describe the results of double irradiation experiments on 1,1,2-trifluoro-1,2,2-tribromoethane (I). The fluorine n.m.r. spectrum of I was studied previously by Nair and Roberts,[4] who have also discussed the temperature dependence of the spectrum of I. They demonstrated that molecules of this type are undergoing rapid rotation about the C–C bond at room temperature but that at low temperature it is possible to "freeze" molecules into a mixture of their various possible rotational configurations. The three possible rotational configurations of I are Ia, Ib and Ic. Of these three configurations Ic would be expected to be the least stable on steric grounds because the 1-bromine atom is flanked by both of the 2-bromine atoms. Ia and Ib are mirror images and obviously have the same energy.



We have studied the low temperature spectrum of I (50% in CS_2) at 56.4 Mc. and found that at −110° the spectrum is that of an ABX type with $J_{\mathrm{AB}} = |165|$ cps., J_{AX} (or $J_{\mathrm{A'X}}$) = 16.2 cps. and J_{BX} (or $J_{\mathrm{B'X}}$) = 18.6 cps. (Fig. 1a). The chemical shift between the center of gravity of the AB region and the X region is about 705 cps.

It would appear that at this temperature I has been "frozen" primarily into a mixture of the magnetically equivalent rotational configurations Ia and Ib. However, there are additional lines in the spectrum indicating the presence of Ic. There is a sharp doublet about 388 cps. upfield from the center of gravity of the AB region and a triplet about 250 cps. upfield from the center of the X region of Ia and Ib. The intensity perturbations and spacings of these sets of lines are consistent with those of an A_2X system with a coupling of 18.8 cps. and a chemical shift of 570 cps. Relative area measurements suggest that Ic is only present to the extent of 5–7%.

At −110° we carried out double irradiation experiments at the audio frequencies of 670 and 756 cps. with a $\gamma H_1/2\pi$ of 25 cps. The results are shown in Fig. 1 where each transition has been numbered. By assigning the neighboring nuclear spin states to each transition in Fig. 1a, it is possible to predict what changes in the spectrum will take place on double irradiation between certain sets of the lines for the various possible relative sign assignments for the three coupling constants. This procedure is described in detail elsewhere.[5,6,7]

When the AB region is observed with a decoupling frequency of 670 cps. lines 10 and 12 are receiving the strong irradiation while lines 5 and 6 are being observed. It is predicted that if J_{AX} and J_{AB} have the same relative signs then no change in lines 5 and 6 should be observed, but if J_{AX} and J_{AB} have different signs then lines 5 and 6 should collapse (as observed in Fig. 1b). When the X region is observed at the same decoupling frequency lines 5 and 6 are being strongly irradiated. If J_{AX} and J_{AB} have the same relative signs then lines 9 and 11 should collapse, but if J_{AX} and J_{AB}

(1) R. Kaiser, *Rev. Sci. Instr.*, **31**, 963 (1960).

(2) R. Freeman, *Mol. Phys.*, **3**, 435 (1960).

(3) D. D. Elleman and S. L. Manatt, *J. Chem. Phys.*, in press.

(4) P. M. Nair and J. D. Roberts, *J. Am. Chem. Soc.*, **79**, 4565 (1957).

(5) R. Freeman and D. H. Whiffen, *Mole. Phys.*, **4**, 321 (1961).

(6) S. L. Manatt and D. D. Elleman, *J. Am. Chem. Soc.*, **84**, May (1962).

(7) D. D. Elleman and S. L. Manatt, *J. Chem. Phys.*, in press.

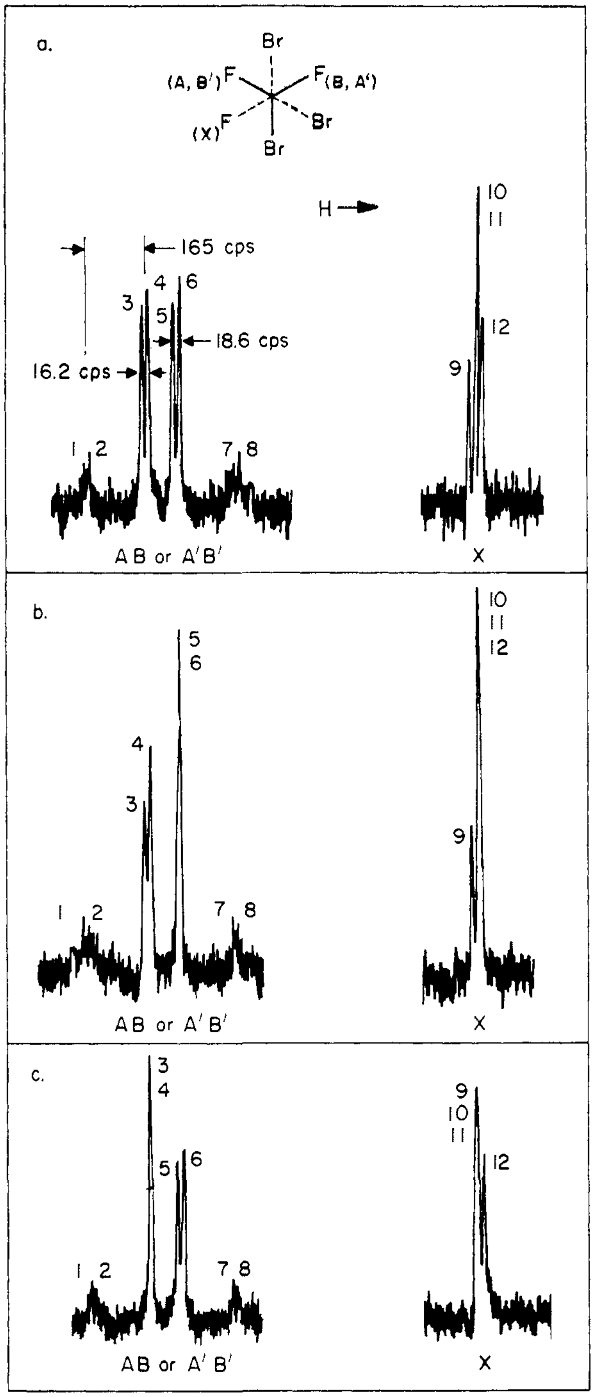


Fig. 1.—The low temperature (−110°) F^{19} n.m.r. spectrum of 1,1,2-trifluoro-1,2,2-tribromoethane (50% in CS_2): a, undecoupled; b, decoupled, $\gamma H_1/2\pi = 25$ cps. and $\Omega = 670$ cps.; c, decoupled, $\gamma H_1/2\pi = 25$ cps. and $\Omega = 756$ cps.

have different signs lines 10 and 12 should collapse (as observed in Figure 1b).

When decoupling at 756 cps. and observing the AB region, lines 9 and 10 are strongly irradiated when lines 3 and 4 are being observed. If J_{BX} and J_{AB} have the same relative signs then lines 3 and 4 should not collapse, but if the signs of J_{BX} and J_{AB} are different, lines 3 and 4 should collapse (as observed in Fig. 1c). On observing the X region at the same decoupling frequency, lines 11 and 12 should collapse if J_{AB} and J_{BX} have the same relative signs, but if J_{AB} and J_{BX} have different signs then lines 9 and 10 should collapse (as observed in Fig. 1c).

The fact that the presence of Ic was detected and that the *gauche* coupling constant in this A_2X system is about 18.8 cps. enables us to unambigously assign $J_{A'X} = 16.2$ cps. (the *trans* coupling) and assign $J_{B'X} = 18.6$ cps. (the *gauche* coupling) in rotational configurations Ia and Ib. The significance of the difference in the magnitudes of the *trans* and *gauche* couplings is being further investigated.

The results of the double resonance experiments on I reported here show unequivocally that J_{AB}, the geminal coupling constant, has a different relative sign from that of $J_{A'X}$ and $J_{B'X}$, the vicinal coupling constants. Thus, the same degree of caution should be exercised in the analyses of F^{19} n.m.r. spectra as is required in the analyses of H^1 n.m.r. spectra where it has recently been demonstrated that likewise the geminal H^1–H^1 coupling constant has a different relative sign than the vicinal H^1–H^1 coupling constants.[8,9]

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(8) R. R. Fraser, R. U. Lemieux and J. D. Stevens, *J. Am. Chem. Soc.*, **83**, 3901 (1961).

(9) F. Kaplan and J. D. Roberts, *ibid.*, **83**, 4667 (1961).

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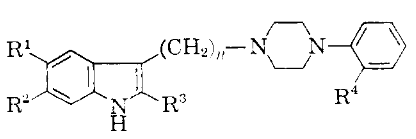
PASADENA, CALIFORNIA DANIEL D. ELLEMAN

RECEIVED FEBRUARY 12, 1962

1-(INDOLYLALKYL)-4-ARYLPIPERAZINES: A NEW CLASS OF TRANQUILIZERS

Sir:

Hiebel[1] probably was the first to suggest that the tranquilizing effect of chlorpromazine derives from its central adrenolytic action. It occurred to us to see whether by appropriate modification, other adrenolytic agents could be transformed to central nervous system depressant drugs. Since we had available from other studies 1-phenylpiperazine, which has been reported to be a relatively weak adrenolytic,[2] we prepared and studied a series of compounds represented by formula I.[3] The indolylalkyl group was selected because of its relationship to serotonin,[4] a normal constituent of the



I

II, $R^1, R^2 = OCH_3, R^3 = CH_3, R^4 = H, n = 2$
III, $R^1, R^2, R^4 = H, R^3 = CH_3, n = 2$
IV, $R^1, R^2 = O\text{-}CH_2\text{-}O, R^3 = H, R^4 = OCH_3, n = 2$
V, $R^1, R^2, R^3, R^4 = H, n = 1$

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(1) G. Hiebel, M. Bonvallet and P. Dell, *Semaine hôp. Paris*, **30**, 2346 (1954); *cf.* D. Bovet, ref. 4.

(2) D. Bovet and F. Bovet-Nitti, "Médicaments du Système Nerveux Végétatif," S. Karger, S. A., Bale, 1948, p. 246.

(3) Analyses of all new compounds were satisfactory. These were performed by Mr. K. D. Fleischer and staff of this Institute.

(4) Since norepinephrine normally is present in the brain too, and certain phenethylamines (*e.g.*, mescaline) show central nervous sys-