Supporting Information

Regio- and stereo-selective glycosylation: Synthesis of 5-haloimidazole α-ribonucleosides

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General methods (S1)

Experimental Section

All reactions were carried out in oven or flame-dried glassware under a nitrogen atmosphere. Solvents were distilled prior to use. Dichloromethane, benzene and ether were distilled from calcium hydride. Purification of reaction products was carried out by flash chromatography using silica gel (230-400 mesh). All reagents were commercially available and used without further purification. All reactions were monitored by thin-layer chromatography (TLC) using silica gel 60, F-254. Column chromatography was conducted using flash silica gel. ^{1}H NMR and ^{13}C NMR spectra were recorded on 500 or 400 NMR spectrometers using the residual proton resonance of the solvent as an internal reference at 25 ^{o}C. Two-dimensional NMR (COSY, NOESY) spectra were obtained at 25 ^{o}C on a NMR spectrometer using TMS as an internal reference. The multiplicities of the ^{13}C NMR signals were determined by HMQC and DEPT techniques.

4-Fluoroimidazole[17, 18] (2) S2: A solution of 4-nitroimidazole (4.5 g., 39 mmol) in 50% tetrafluoroboric acid (200 mL) was cooled to -10 ^{o}C. The solution stirred rapidly and was aerated with argon. Zinc dust (8.2 g., 125 mmol) was added to it slowly maintaining the temperature -5 ^{o}C. Complete reduction was monitored by UV. Finally, a solution of sodium nitrite (3.0 g., 43 mmol) in water (10 mL) was added dropwise to it in 30 minutes. The resulting solution was diluted with 50% cold tetrafluoroboric acid (200 mL) and then photolysed. The photolysis reactions were carried out in in a glass vessel using a high pressure Xe-Hg photolysis lamp (254 nm principal wavelength) for 2-3 hr at ambient temperature. After complete conversion of the reactant, the reaction mixture was cooled to 0 ^{o}C and neutralized with cold concentrated sodium hydroxide solution. The

viscous mixture was extracted with ethyl acetate (3x100 mL). The ethyl acetate was dried over Na_2SO_4, concentrated and finally passed through a silica gel plug column to remove the inorganic salts. Yield: 20-30%; white crystalline solid; R_f. 0.6; ^{1}H NMR ($CDCl_3$): δ 6.39 (dd, J = Hz, 1H), 7.07 (s, 1H), ^{13}C NMR ($CDCl_3$): δ 93.9 (d, J = 37.87 Hz), 128.5 (d, J = 15.87 Hz), 155.6 (d, J = 233.5 Hz); ^{19}F NMR ($CDCl_3$): -136.61 (d, J = 8 Hz).

1-(Trimethylsilanyl)-4- Bromoimidazole (4) S3:

A mixture of 4- bromoimidazole (1.0 g., 7 mmol) and hexamethyldisilazane (1.0 g., 29 mmol) was refluxed for 6 hr. Excess HMDS was removed under reduced pressure and the residue was dried under high vacuum for 3 h. Yield: 95%; white solid; ^{1}H NMR ($CDCl_3$): δ 0.47 (s, 9H), 6.90 (s, 1H), 7.43 (s, 1H); HRMS: *m/z*: 218.9961 (calcd. for $C_6H_{12}BrSiN_2$; 218.9952) (M +H).

1-(Trimethylsilanyl)-4- Iodooimidazole (5) S4:

This compound was prepared similarly to **4,** starting from 4-iodoimidazole. Yield: 97%; white solid; ^{1}H NMR ($CDCl_3$): δ 0.57 (s, 9H), 6.97 (s, 1H), 7.40 (s, 1H), ^{13}C NMR ($CDCl_3$): δ -0.70 ($SiMe_3$), 83.65 (Cquat), 125.69 (CH), 141.35 (CH); HRMS: *m/z*: 266.9661 (calcd. for $C_6H_{12}ISiN_2$; 266.9773) (M +H).

TABLE 1. Crystal data and structure refinement for compound 8 (S-5)

empirical formula	$C_{30}H_{29}F_1N_2O_4$
formula weight	500.55
color of crystal	colorless
crystal system	orthorhombic
space group	$P2_12_12_1$
a, Å	8.2594(4)
b, Å	14.7704(8)
c, Å	20.8394(9)
α, deg.	90.058(4)
β, deg.	89.990(4)
γ, deg.	89.935(2)
V, Å^3	2542.3(2)
Z	4
ρ_{calcd}, g/cm^3	1.308
T, K	100
λ, Å	0.71073
Goodness-of-fit[a] on F^2	0.994
Final R indices[b]	R1 = 0.0378,
[I>2sigma(I)]	wR2 = 0.0924
R indices[c] (all data)	R1 = 0.0463,
	wR2 = 0.0953
Largest diff. peak and hole	0.471 and -0.195 e.Å^{-3}

[a]Goodness-of-fit = $[\Sigma[w(F_o^2 - F_c^2)^2]/N_{observns} - N_{params})]^{1/2}$, all data.
[b]R1 = $\Sigma(|F_o| - |F_c|) / \Sigma |F_o|$. [c]wR2 = $[\Sigma[w(F_o^2 - F_c^2)^2] / \Sigma [w(F_o^2)^2]]^{1/2}$.

TABLE 2. Selected Bond Length and Angles* for Compound 8, (S-6)

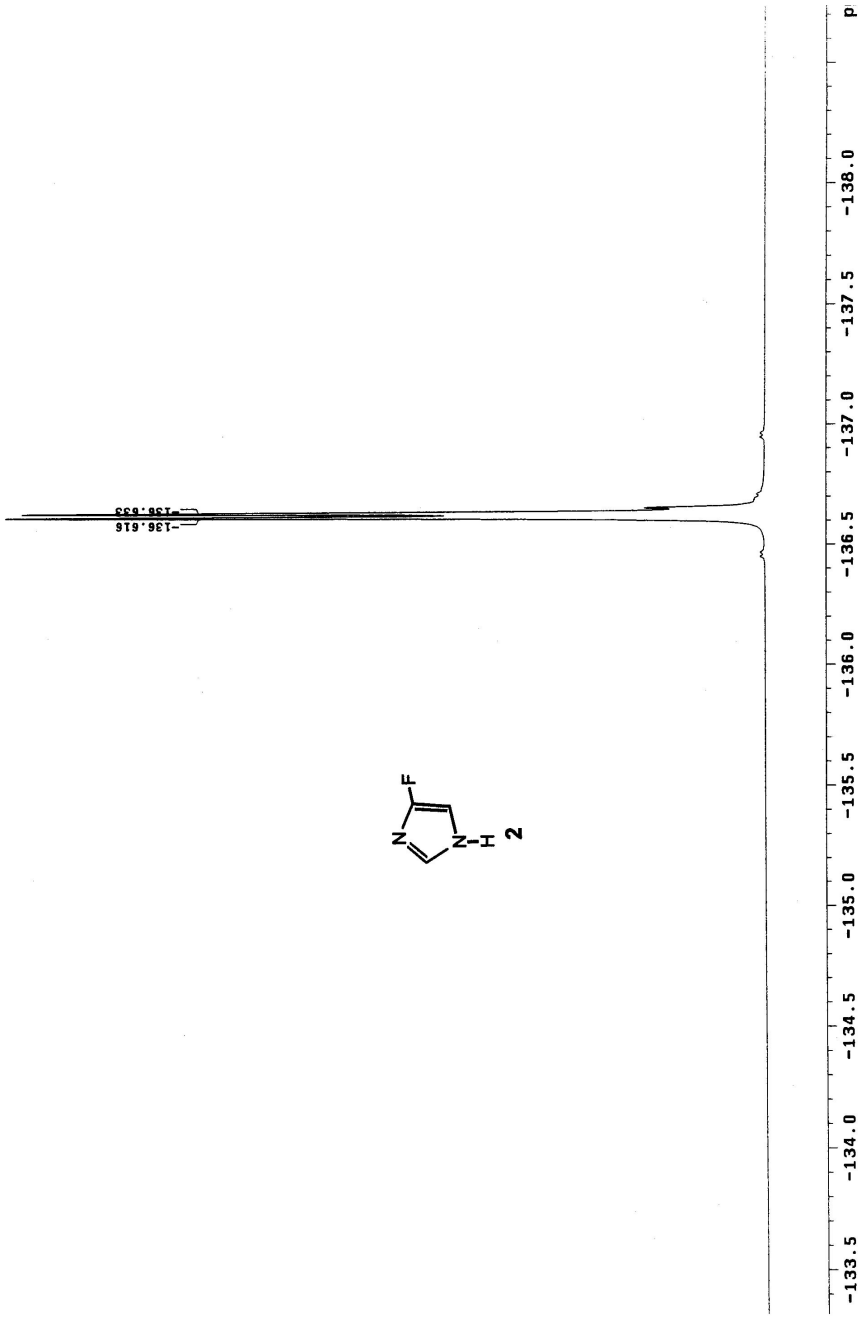
Bond	Length (Å)	Bond angle	Angle (deg)
N1-C1	1.446	C1-O1-C10	107.60
N1-C2	1.373	C3-N2-C4	106.05
C1-H1	0.961	O1-C1-C5	105.75
C1-C5	1.528	F1-C2-N1	119.21
O1-C1	1.421	O1-C10-C11	111.87
O1-C10	1.445	C1-N1-C4	128.91

Errors in bond distances are estimated at about 0.001 Å, and in inter bond angles about 0.05 - 0.08 degrees

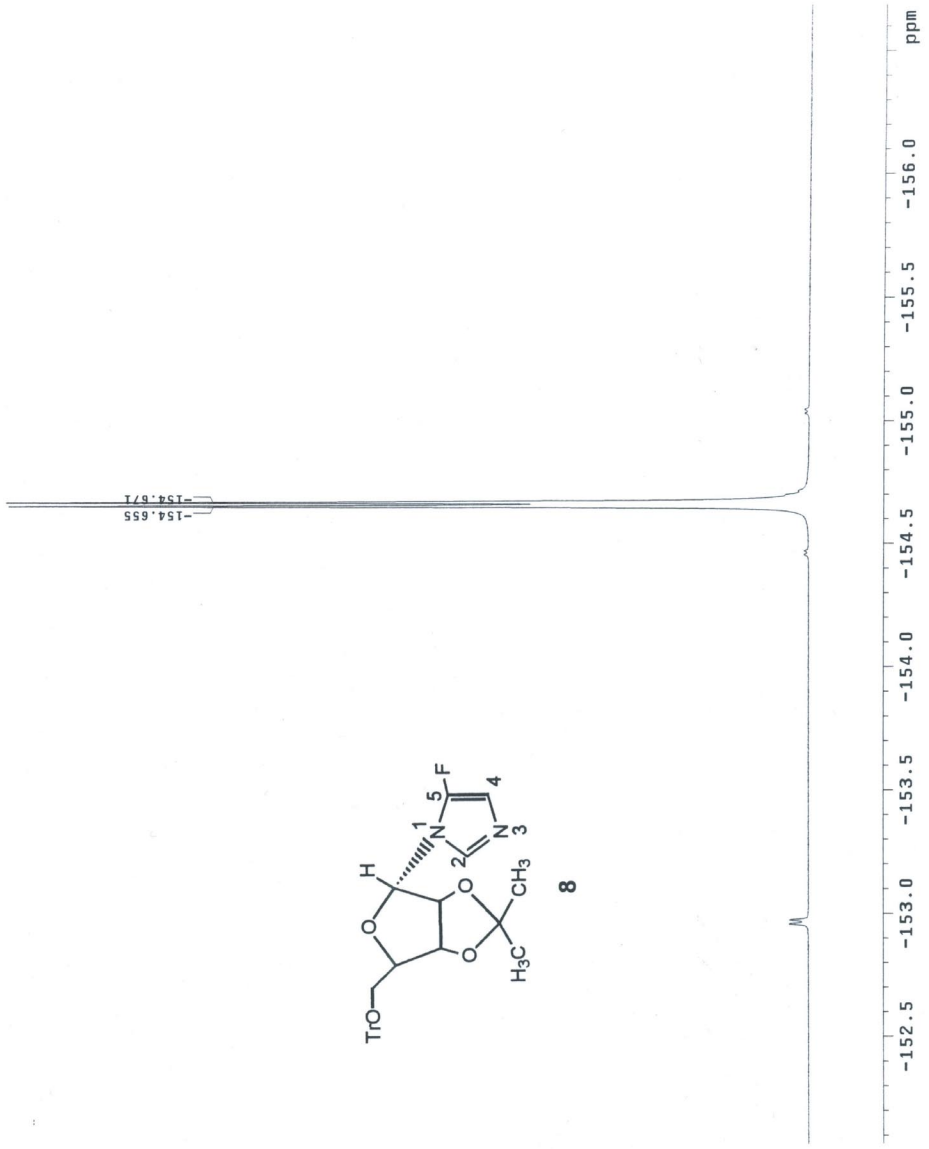
TABLE 3. Selected Torsion Angles for Compound 8 (S-7)

Torsion	angle (°)	Torsion	angle (°)	Torsion	angle (°)
C2-N1-C1-O1	115.62	C4-N1-C1-C5	65.98	C10-O1-C1-N1	161.37
C2-N1-C1-H1	-3.23	C1-N1-C2-F1	10.27	C10-O1-C1-H1	83.73
C2-N1-C1-C5	-125.84	C1-N1-C2-C3	-170.95	C10-O1-C1-C5	36.41
C4-N1-C1-O1	-52.55	C4-N1-C2-F1	-179.22	C1-O1-C10C9	-28.93
C4-N1-C1-H1	-171.40	C4-N1-C2-C3	-0.45	C1-C5-C9-C10	10.79

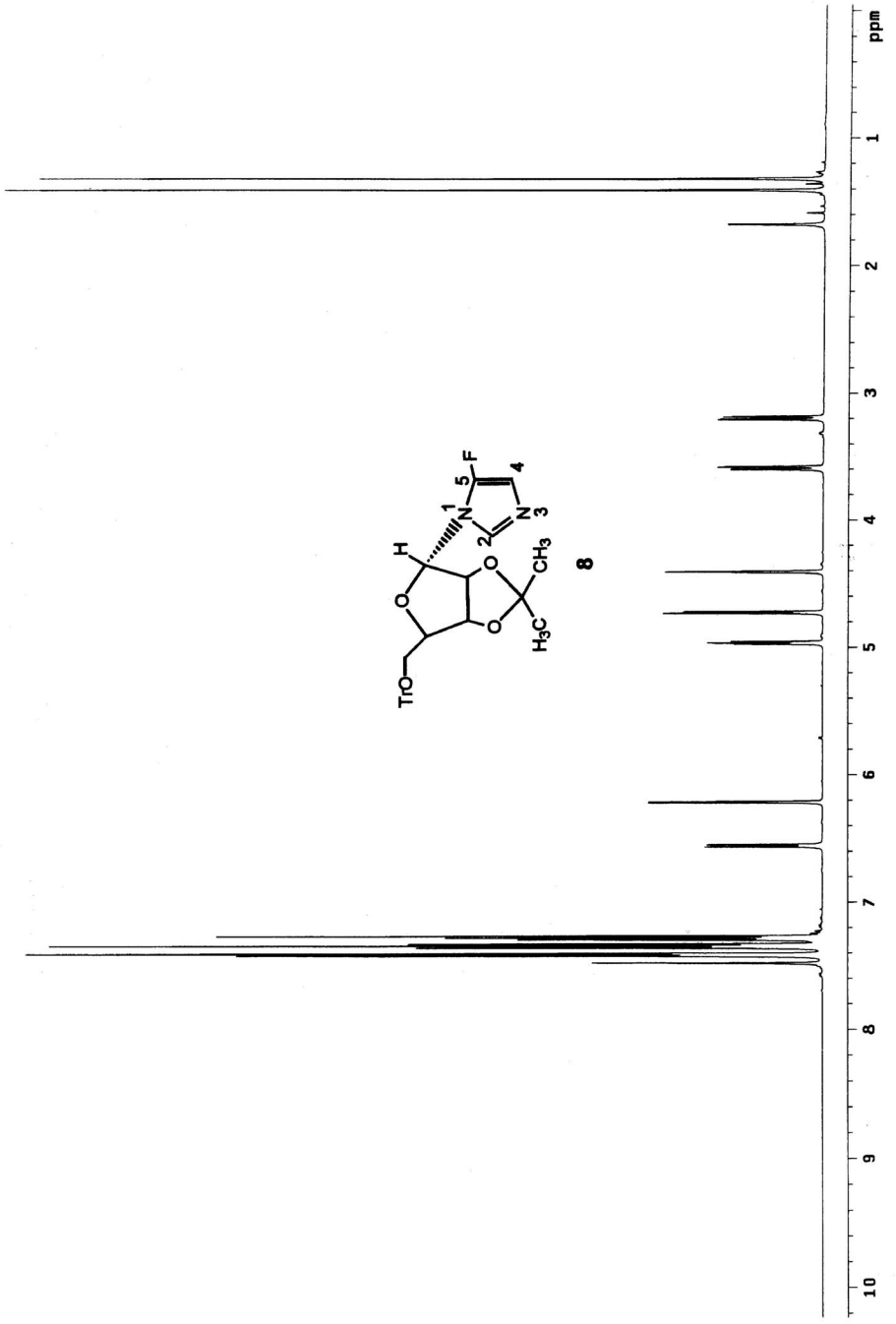
Errors in torsion angles are estimated at about 0.6 - 0.9 degrees



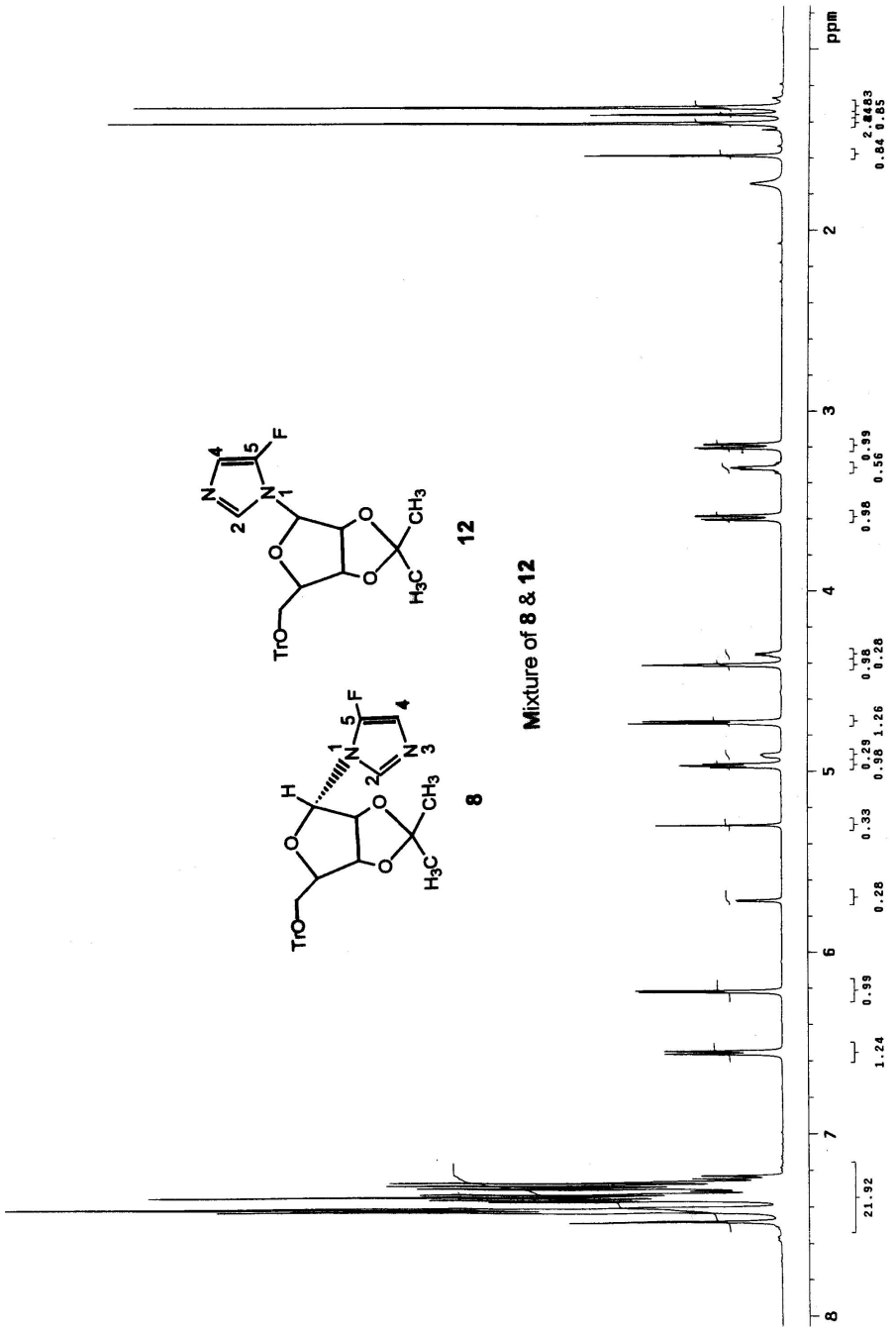
S-8, ^{19}F spectrum of compound **2**



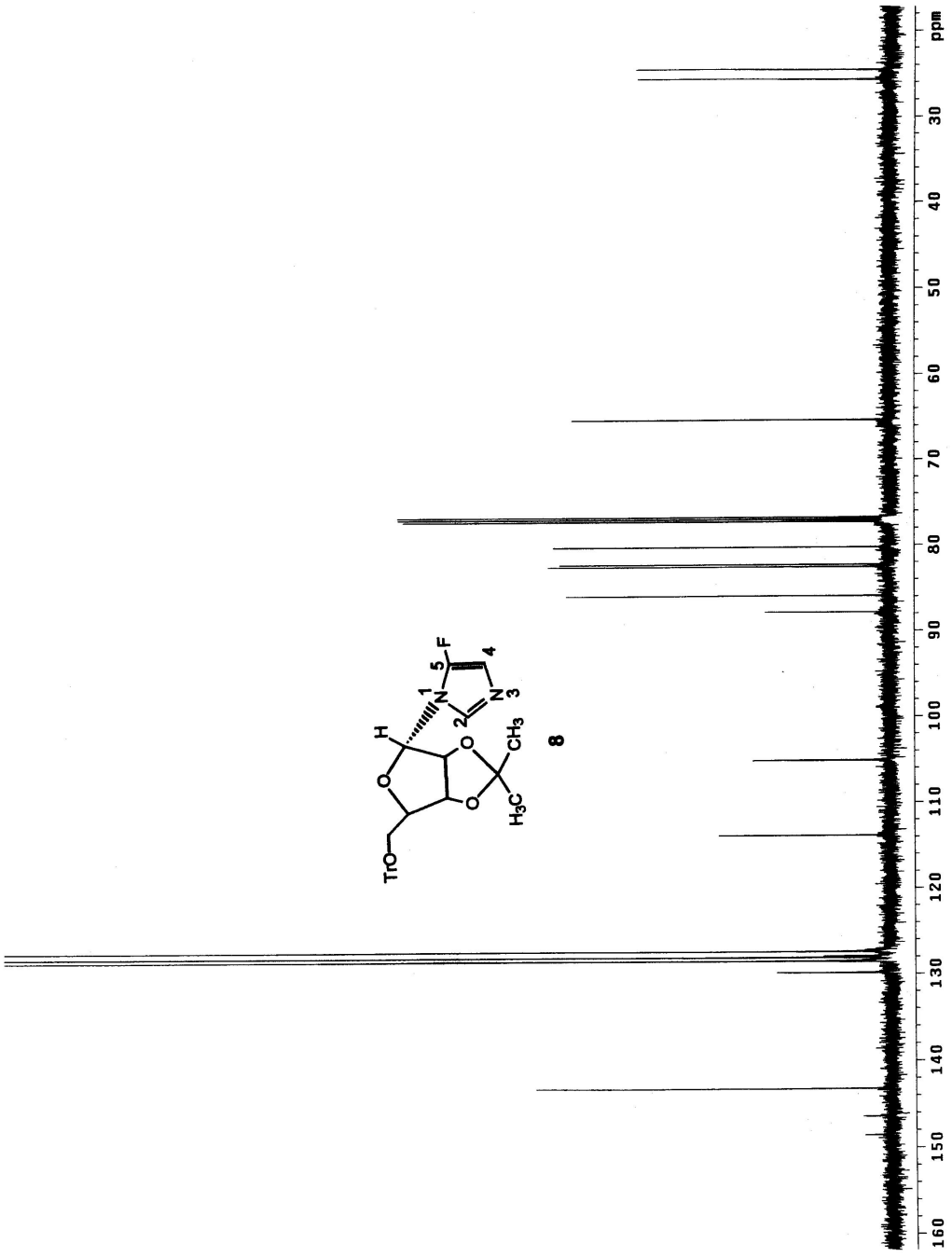
S-9 ^{19}F spectrum of compound **8**



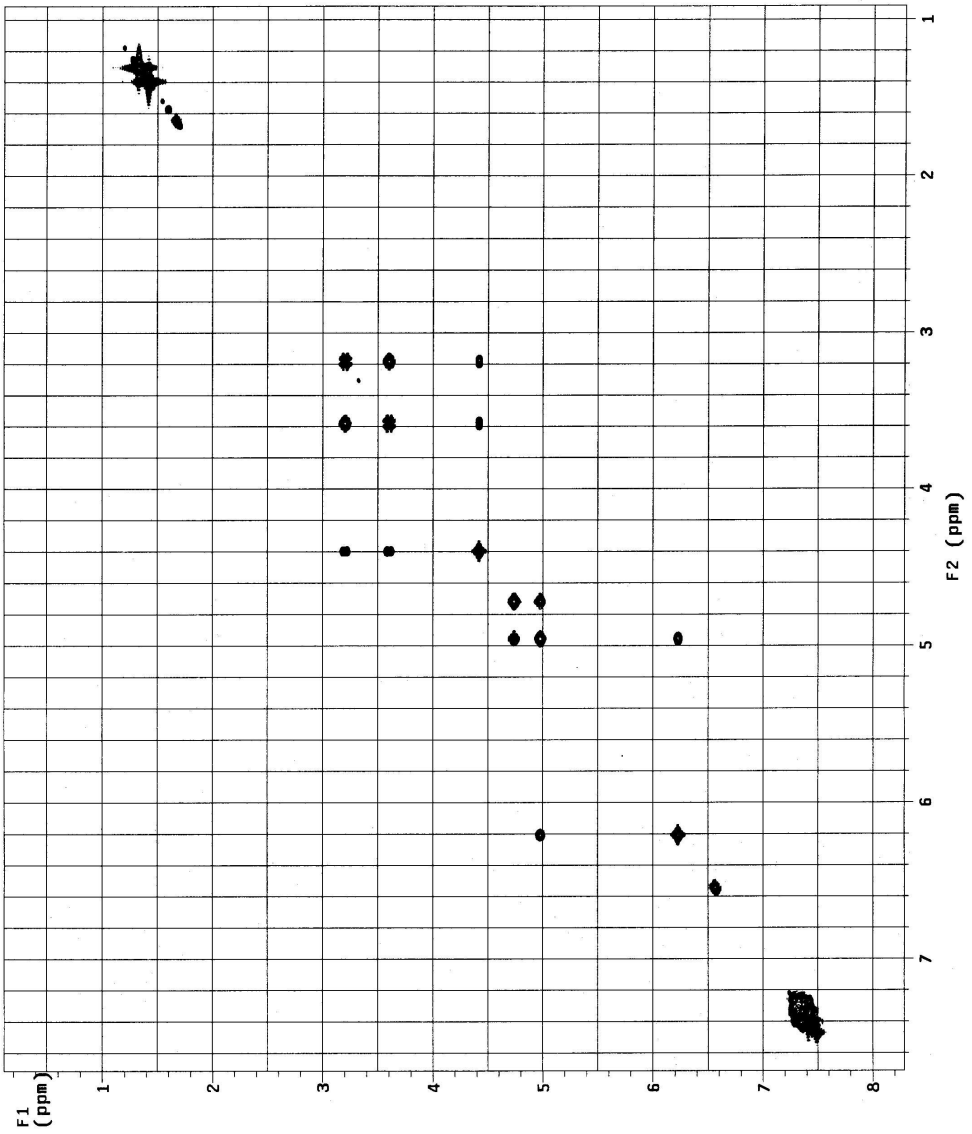
S-10 ^{1}H spectrum of compound **8**



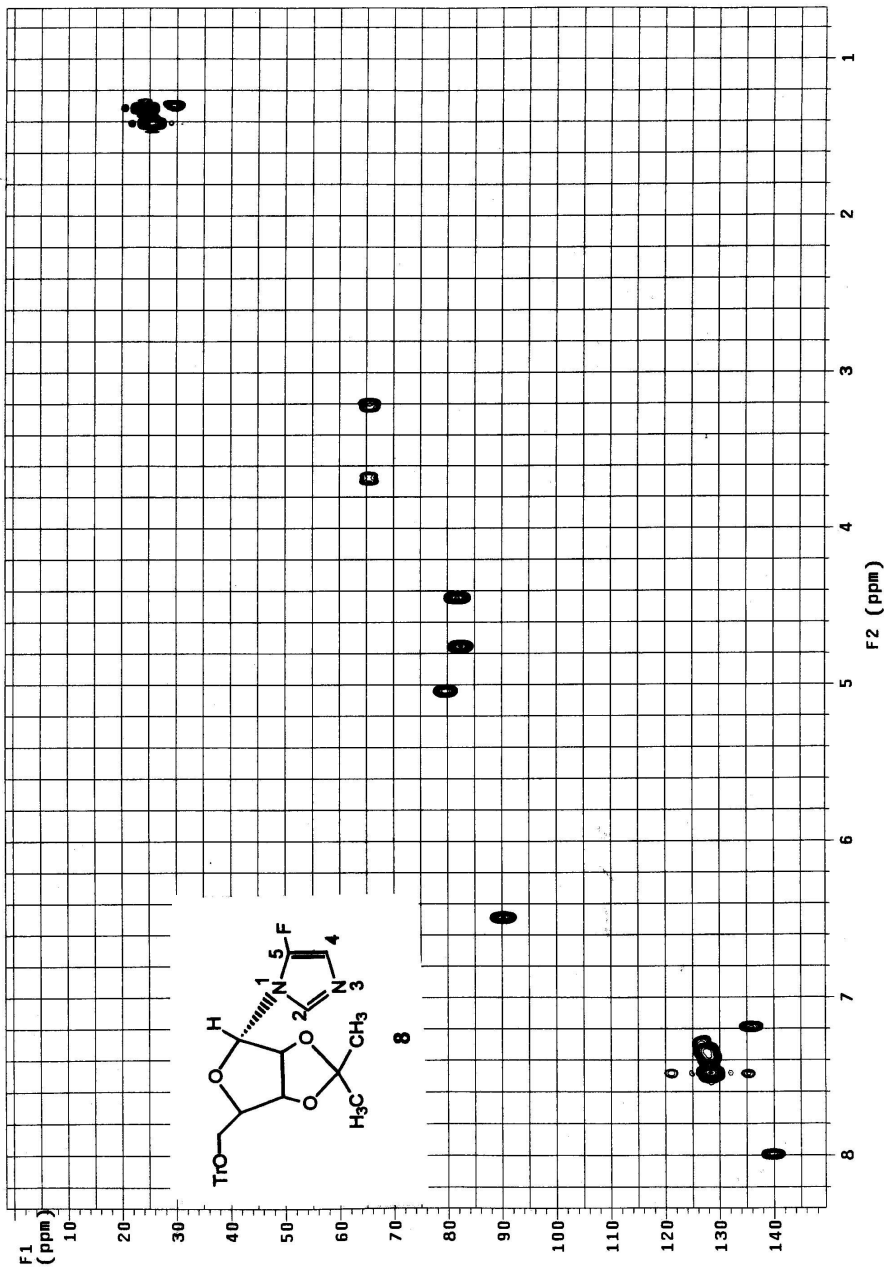
S-11 ^{1}H spectrum of compound **8**&**12** (reaction mixture)



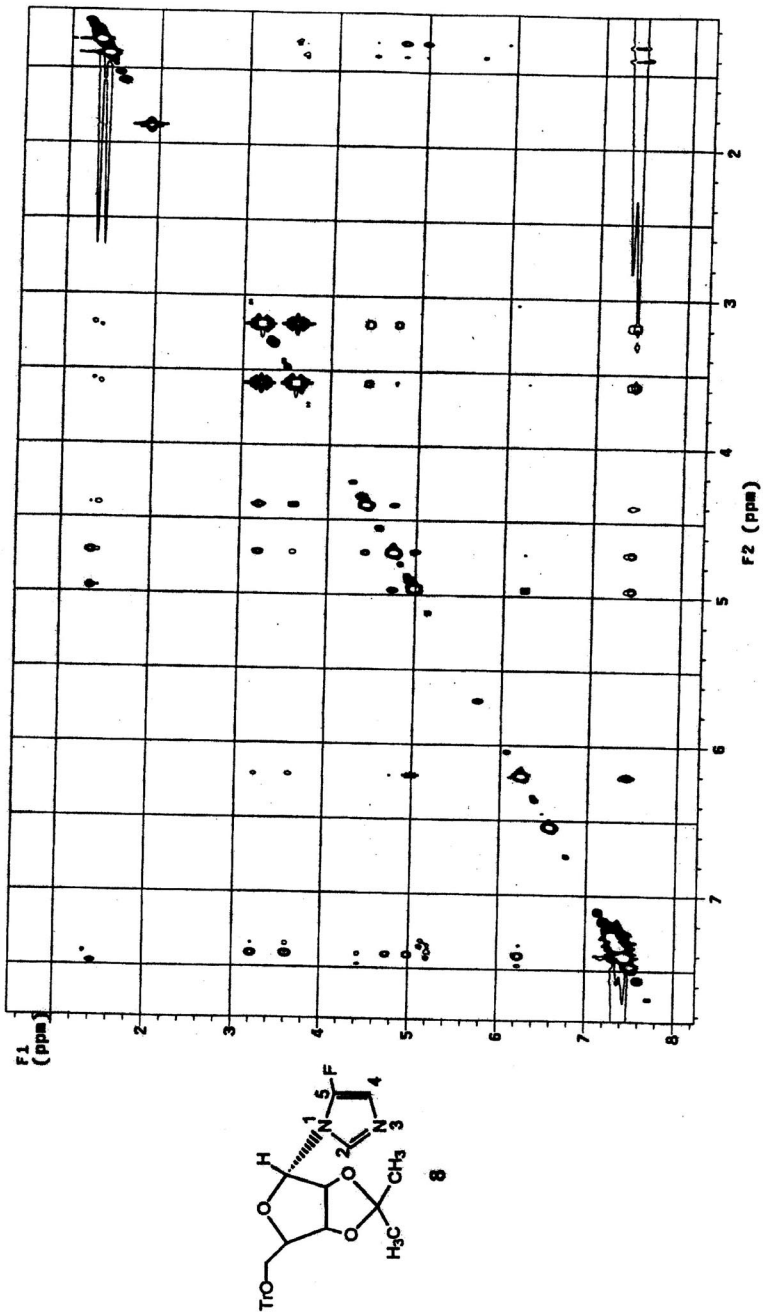
S-12 ^{13}C spectrum of compound **8**



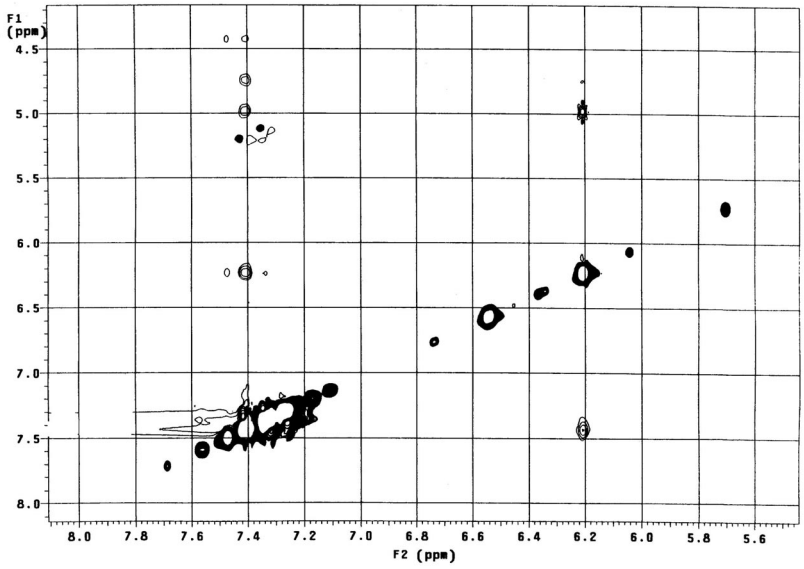
S-13 COSY of compound **8**



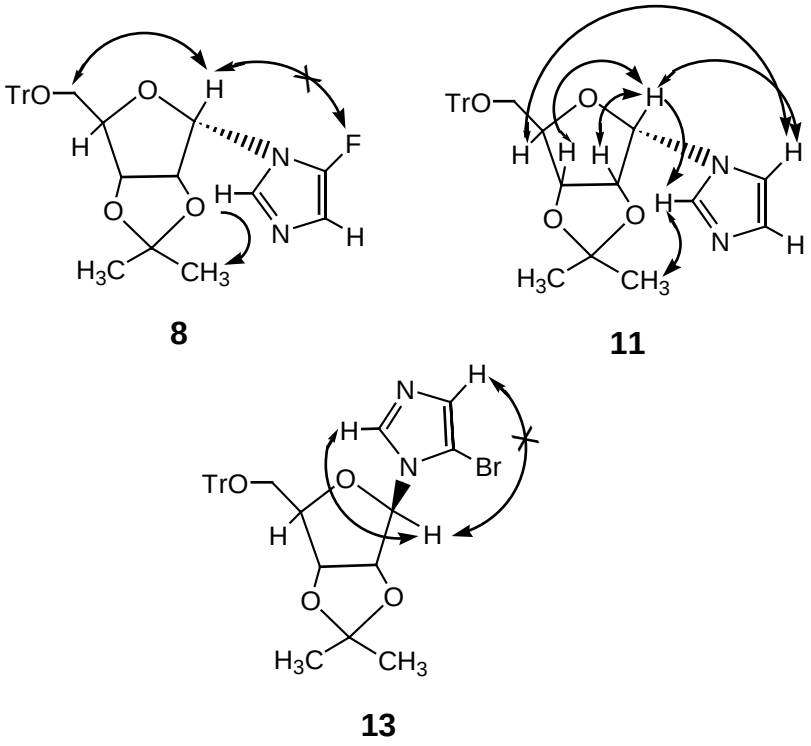
S-14 HMQC of compound **8**



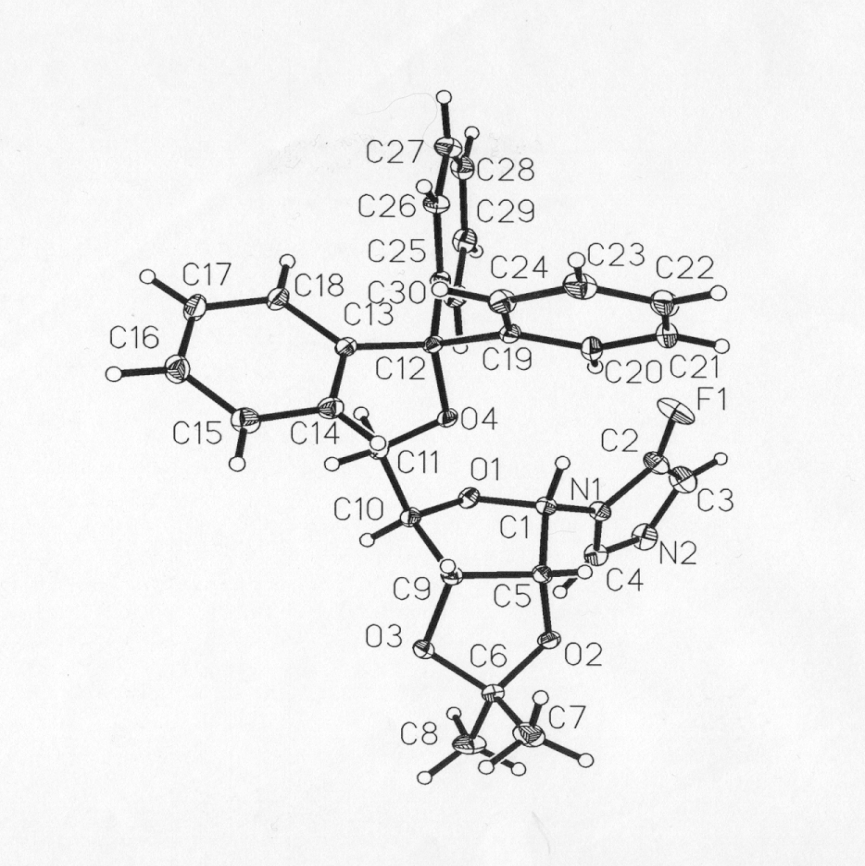
S-15 [1]NOESY spectrum of compound **8**



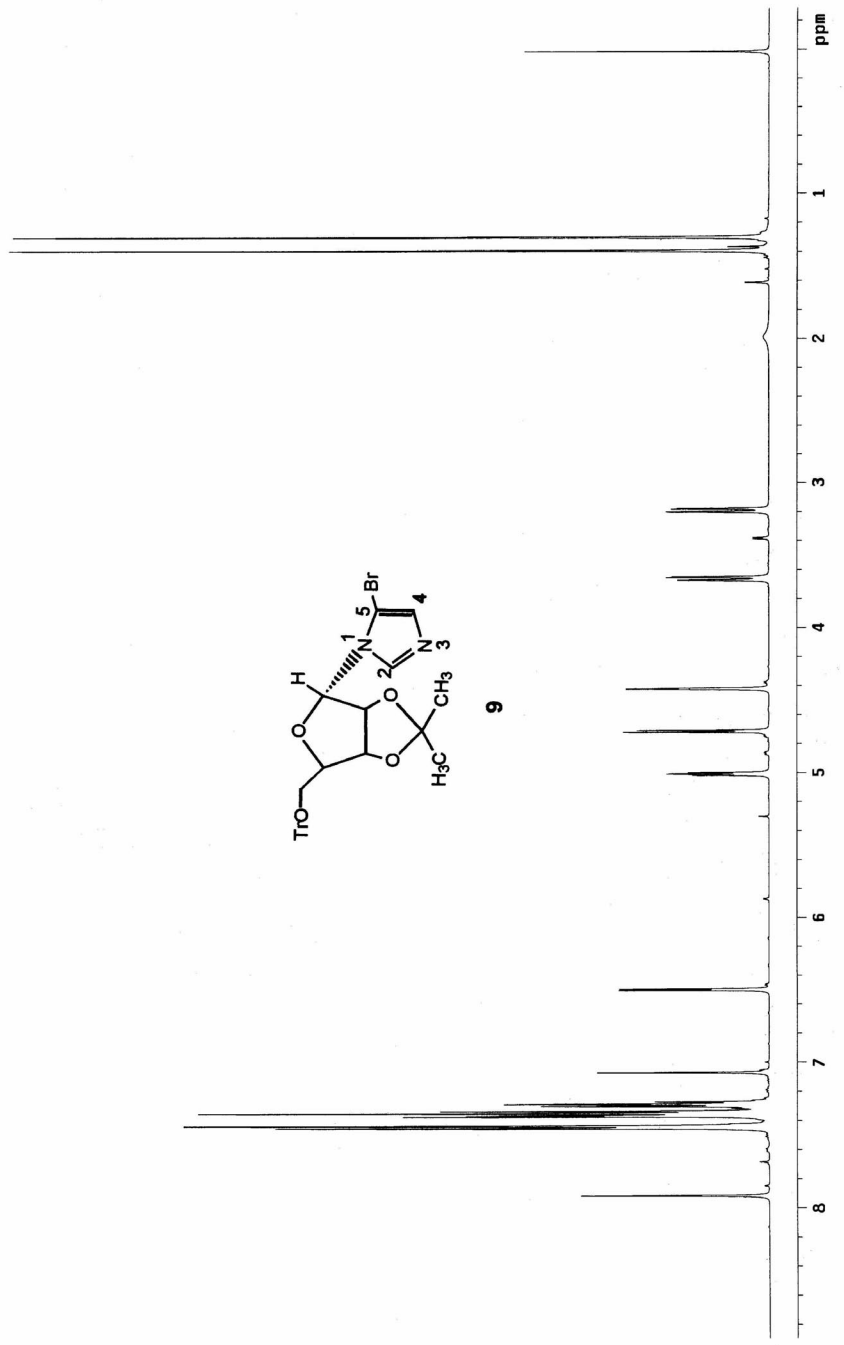
S-16 Down field region NOESY of compound **8**



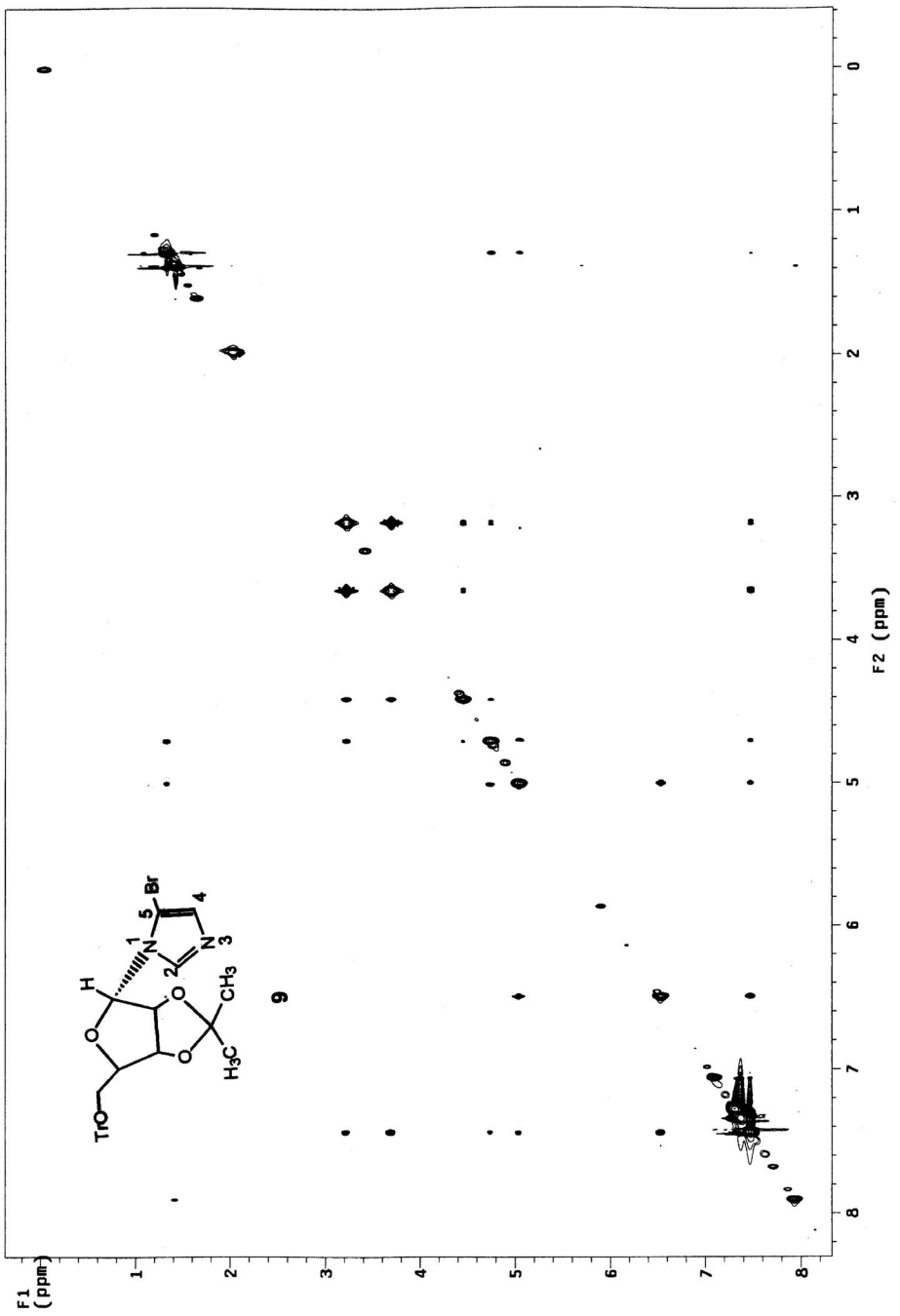
S-17 nOe's of α/β 5-haloimidazole ribonucleosides



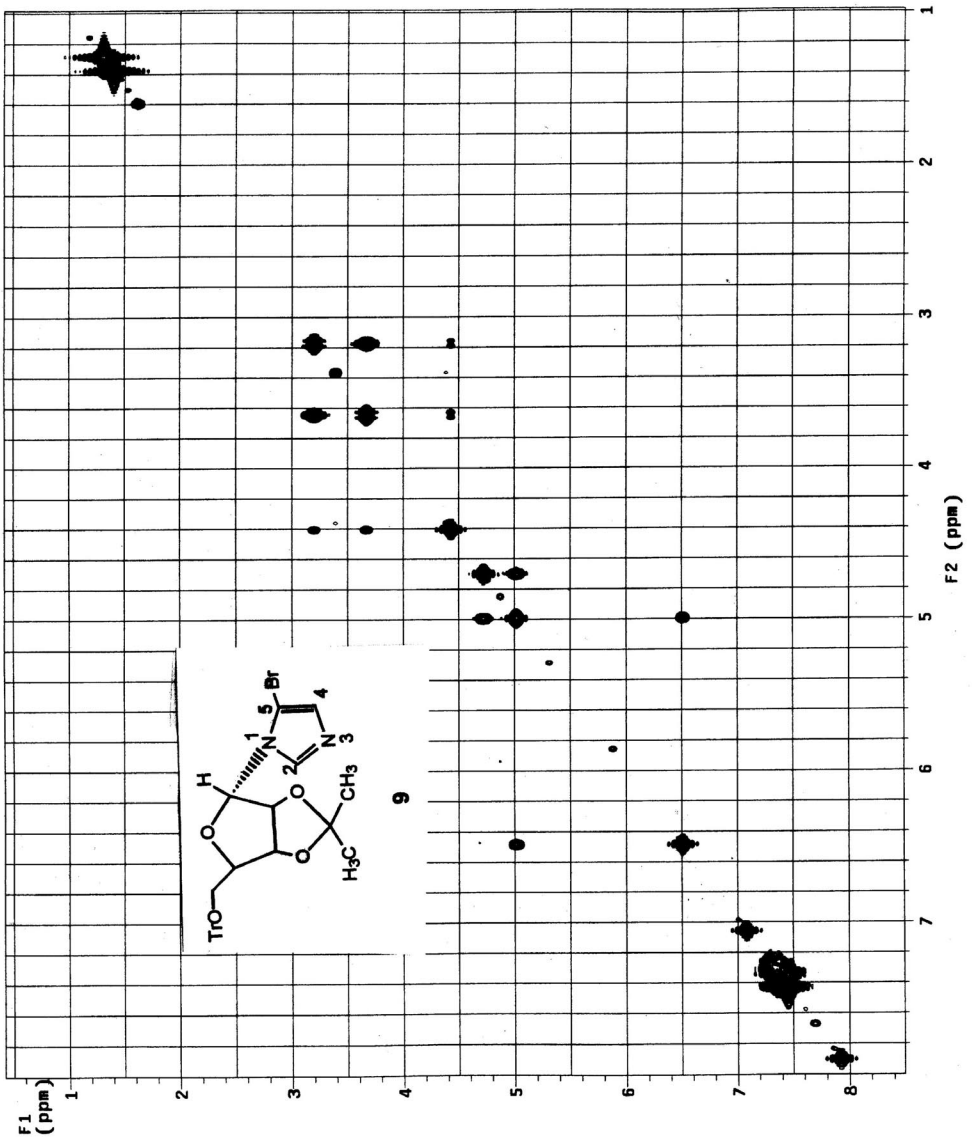
S-18 ORTEP diagram of compound **8**



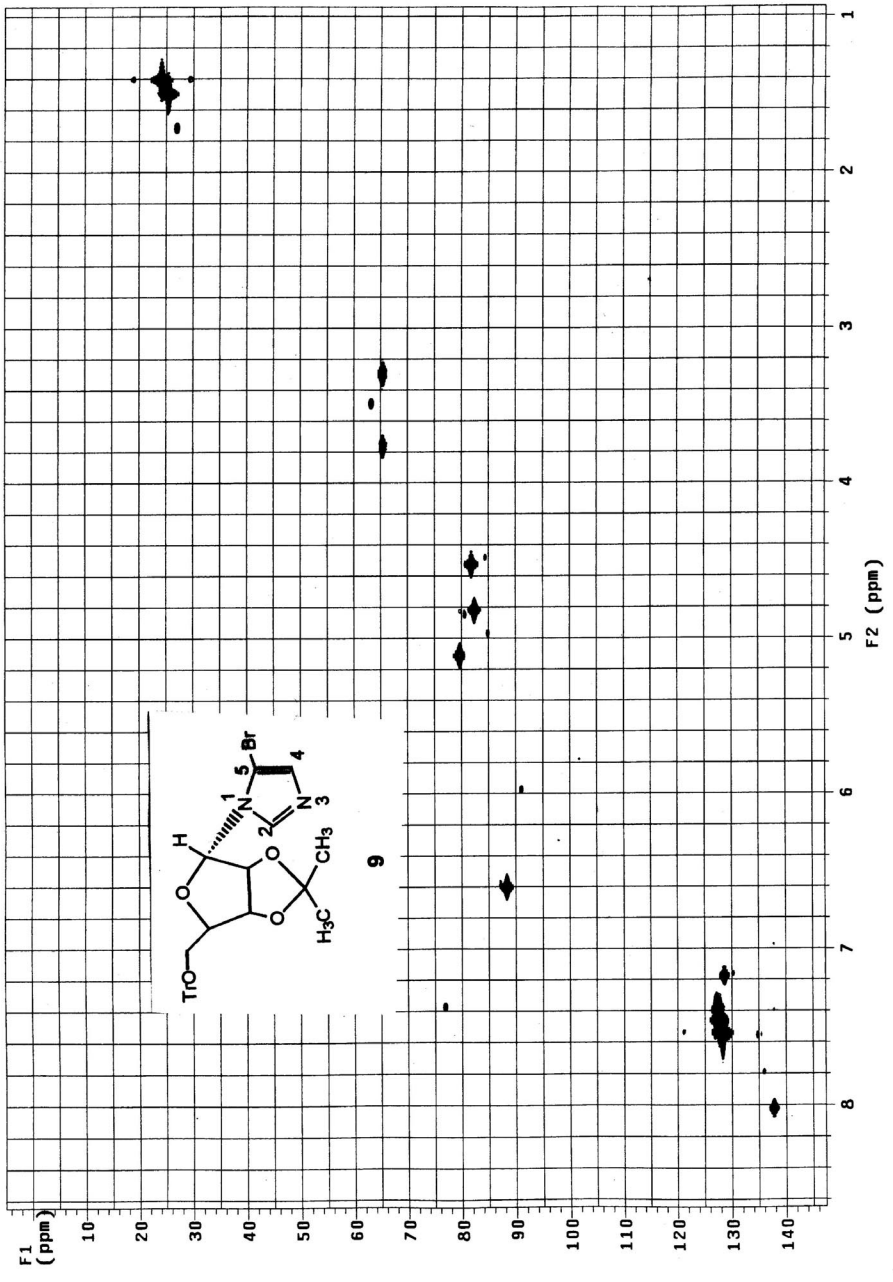
S-19 ^{1}H spectrum of compound **9**



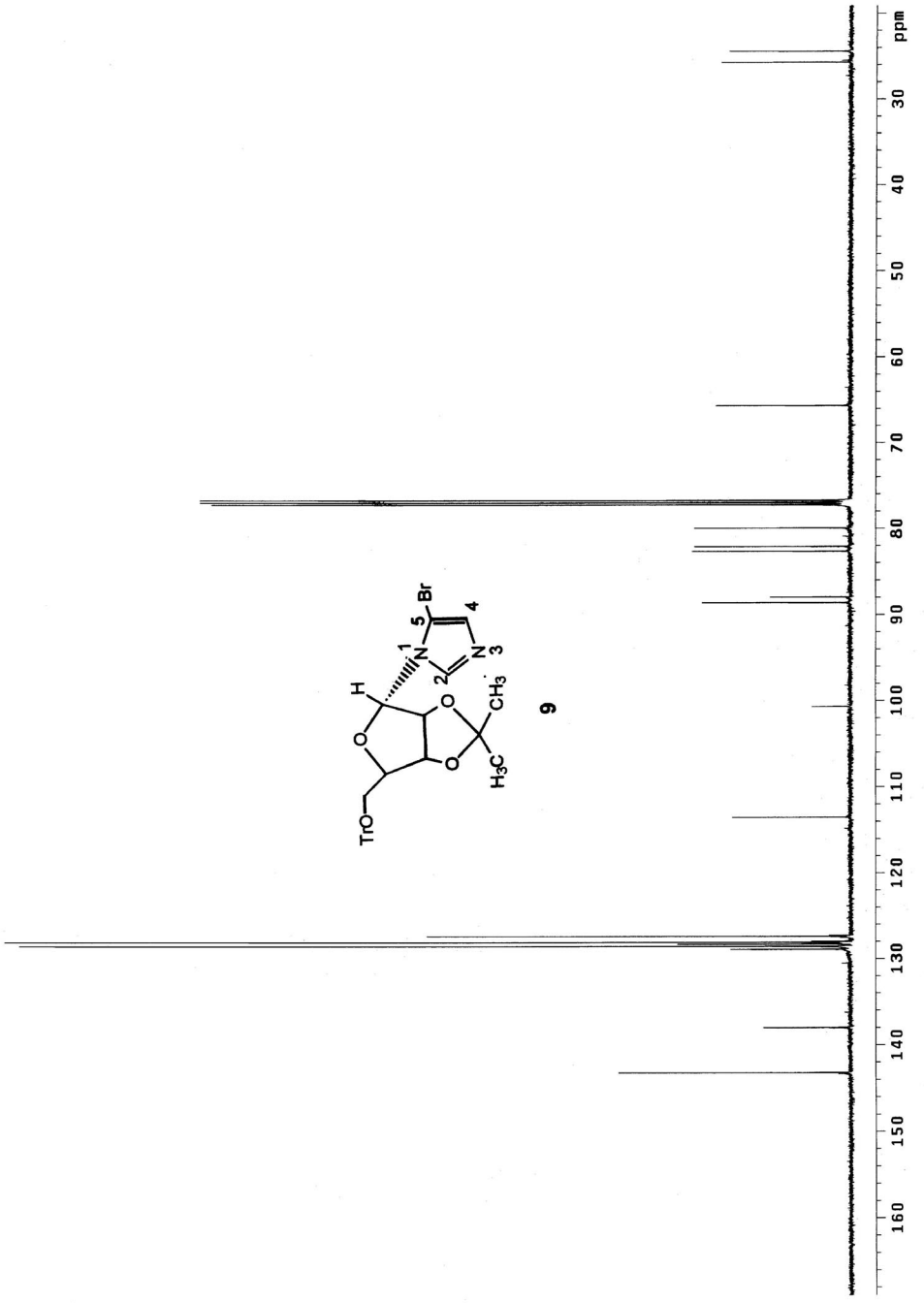
S-20 NOESY of compound **9**



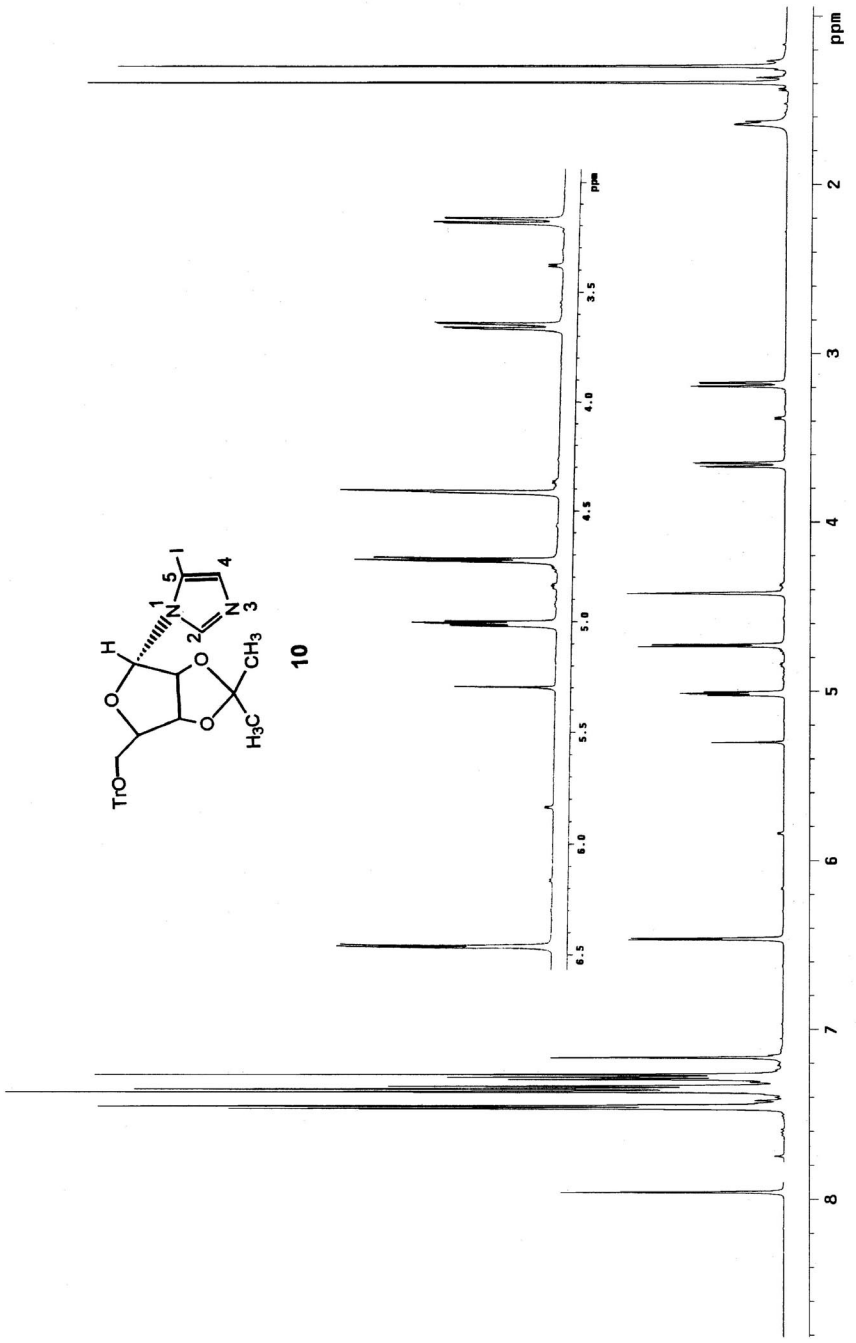
S-21 COSY for compound **9**



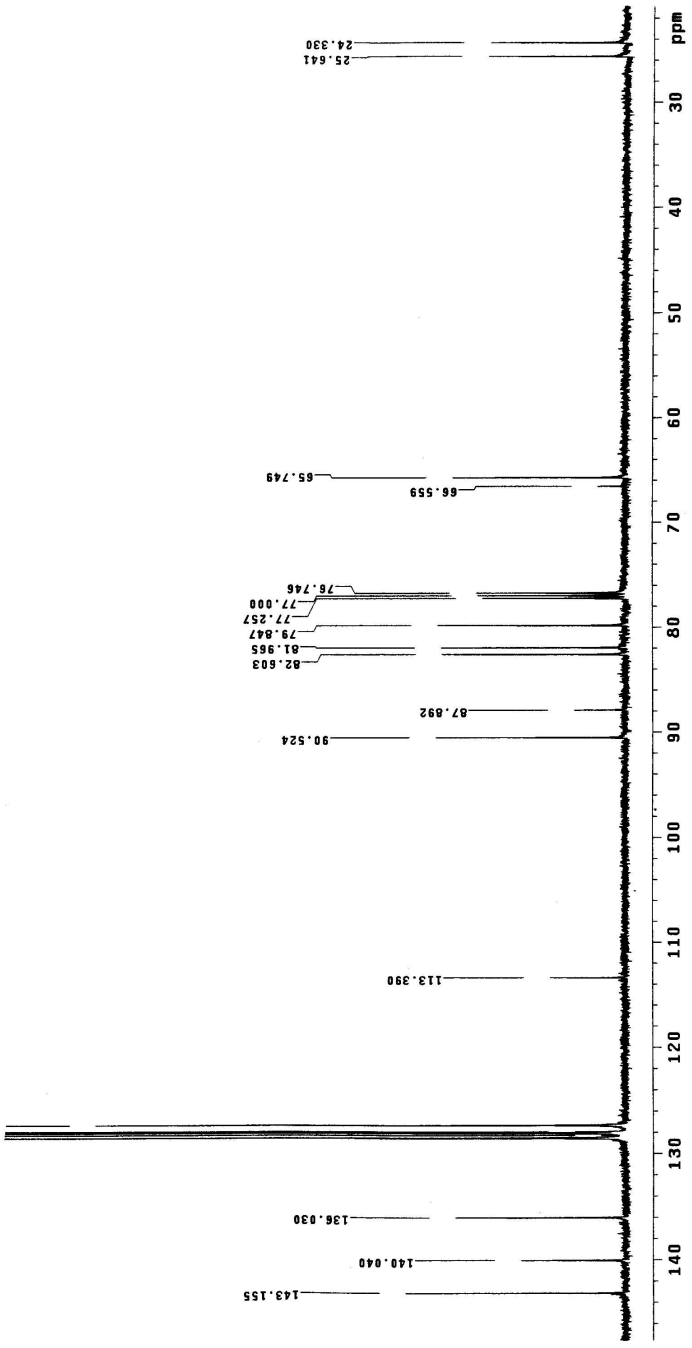
S-22 HMQC



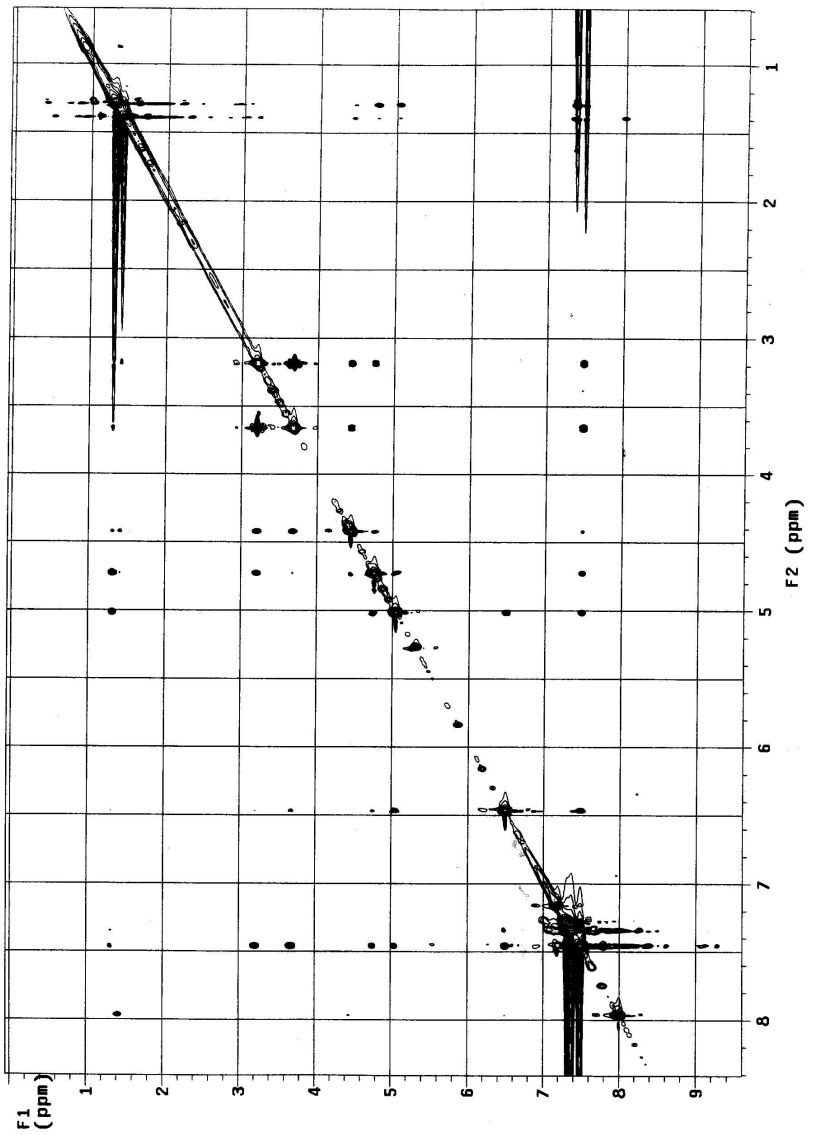
S-23 ^{13}C spectrum of compound **9**



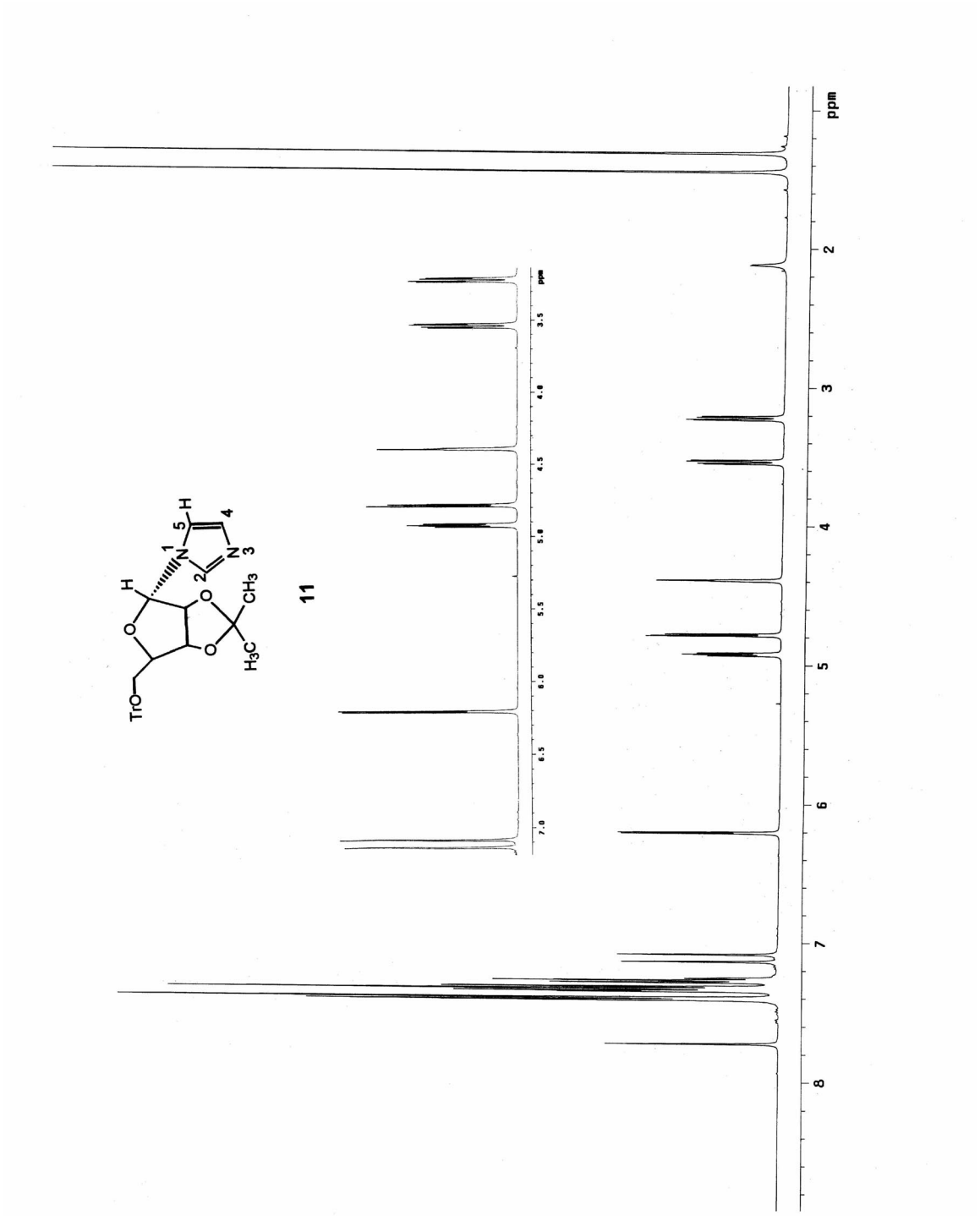
S-24 ^{1}H spectrum of compound **10**



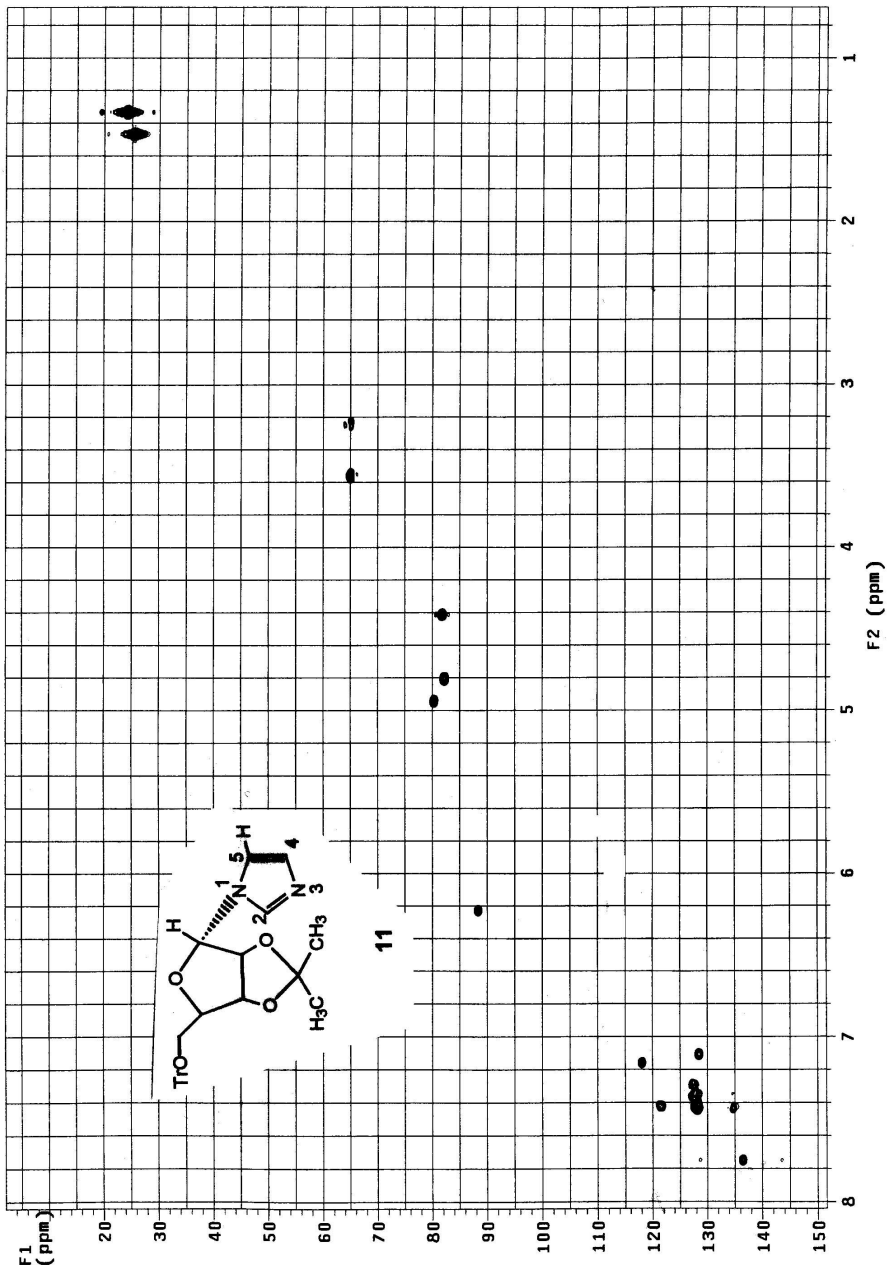
S-25 ^{13}C spectrum of compound **10**



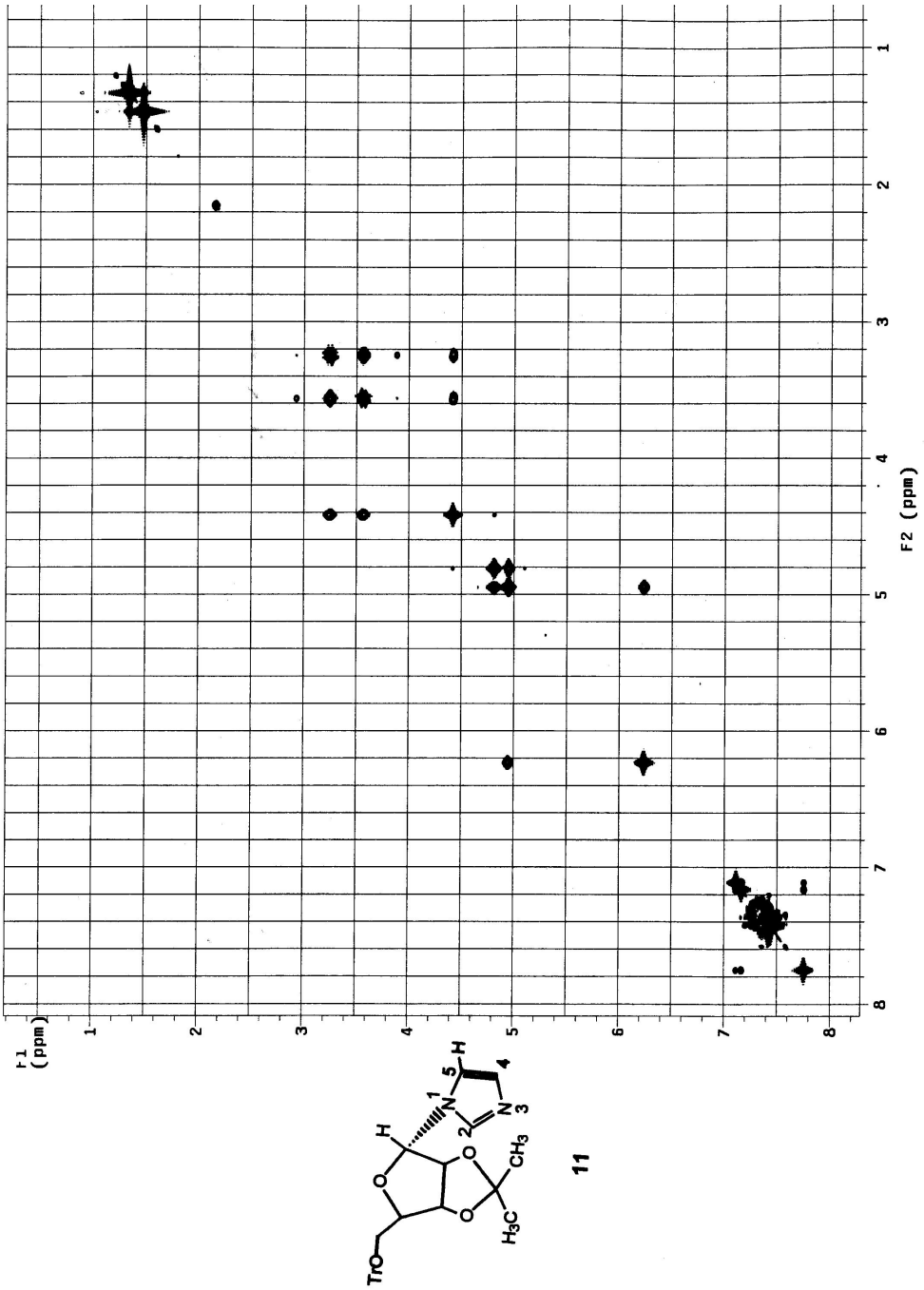
S-26 NOESY of compound **10**



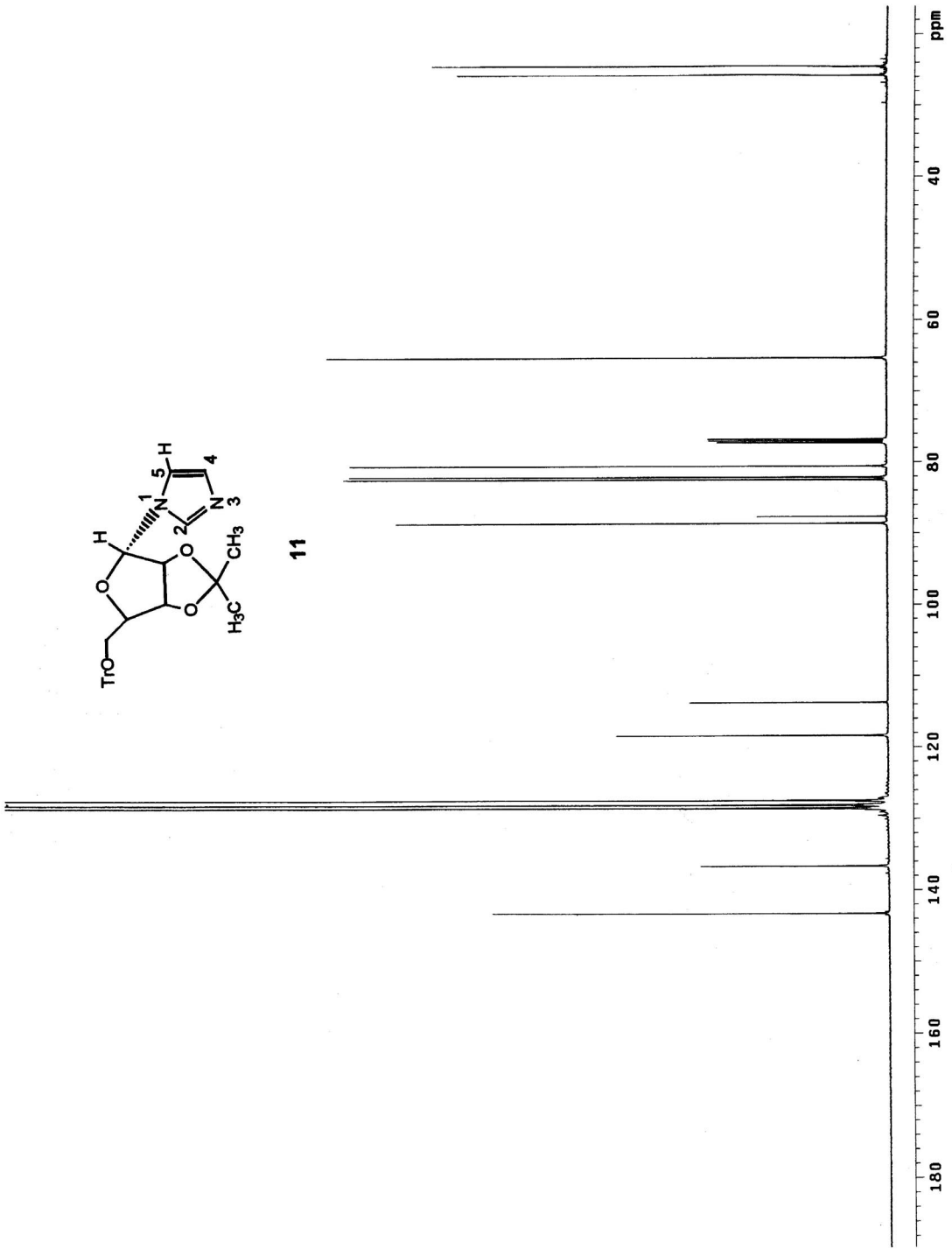
S-27 ^{1}H spectrum of compound **11**



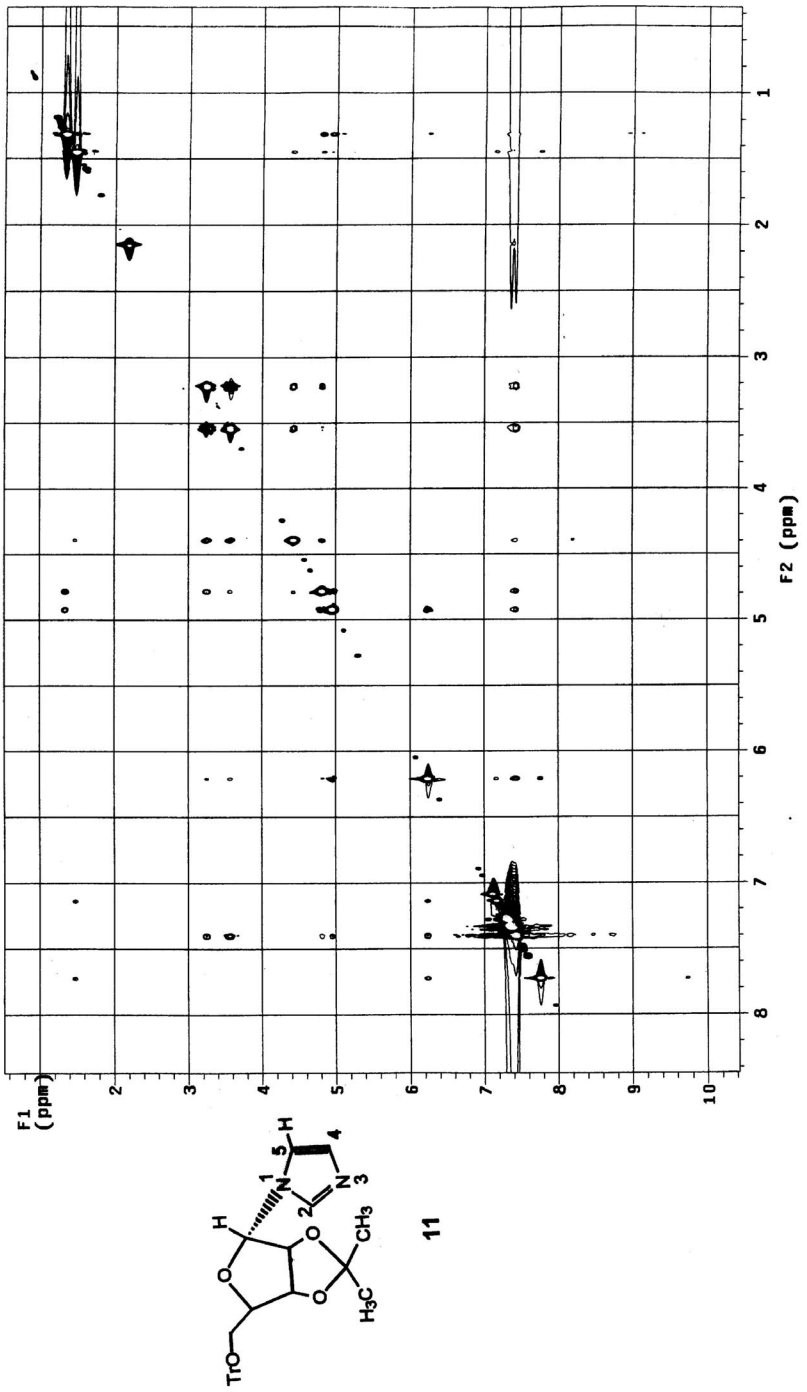
S-28 HMQC of compound **11**



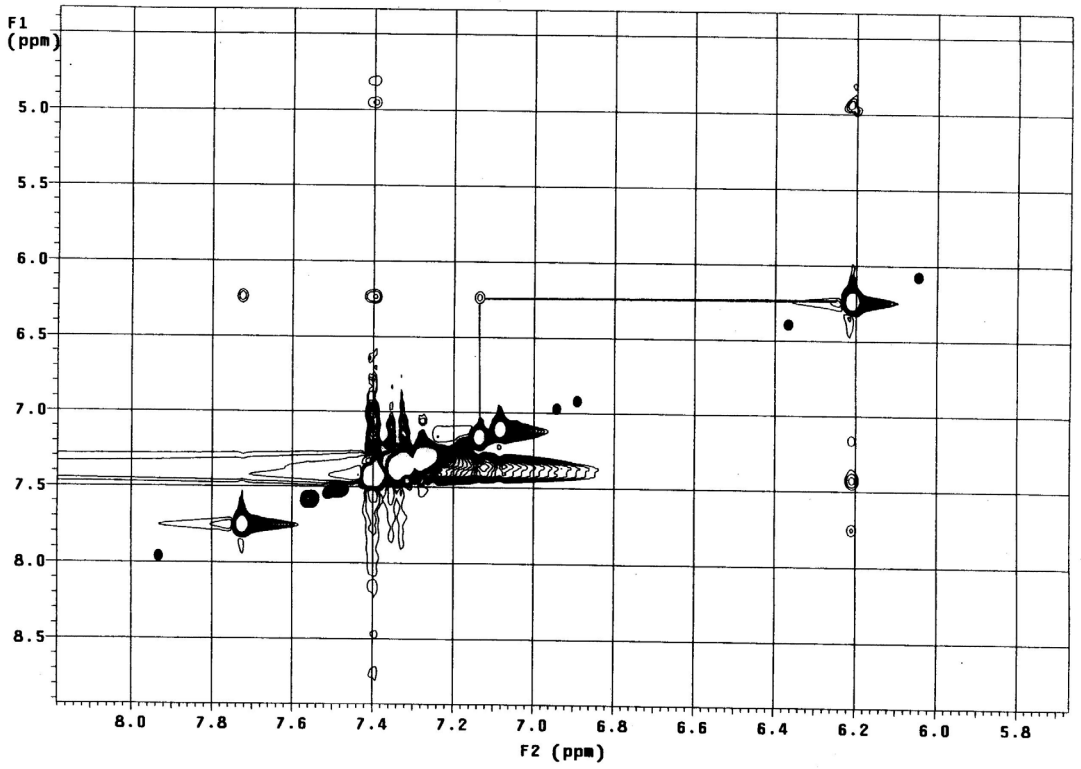
S-29



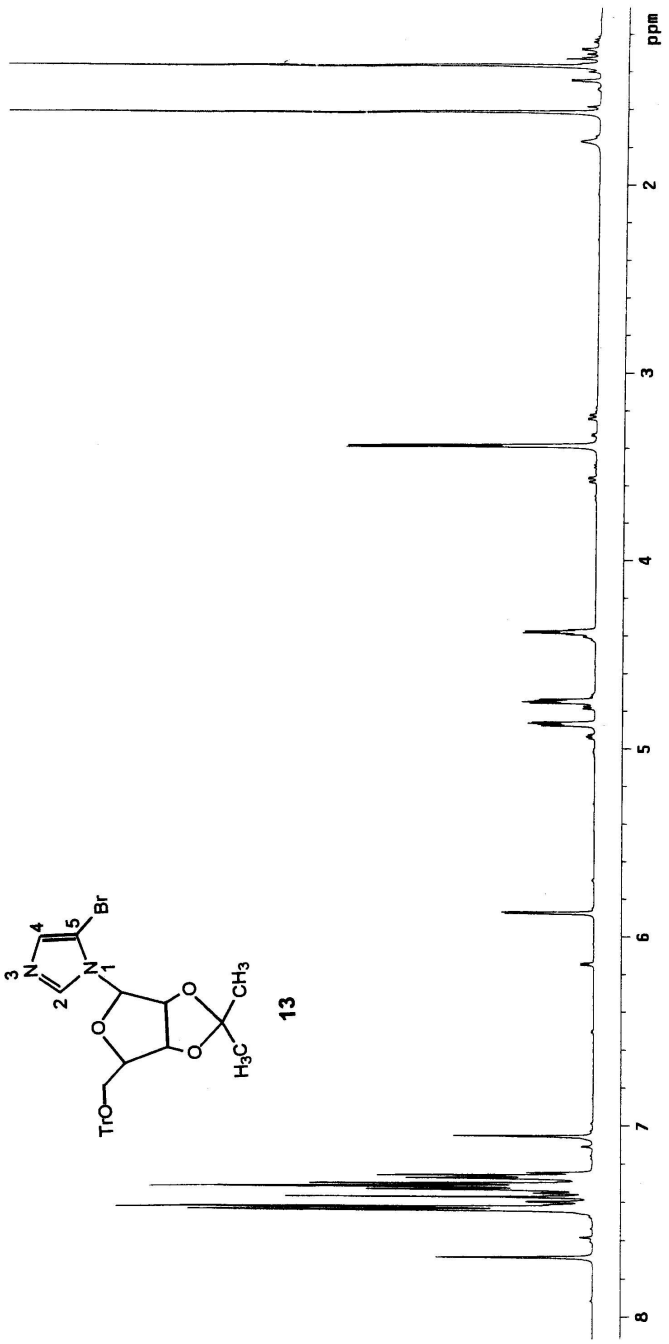
S-30 ^{13}C spectrum of compound **11**



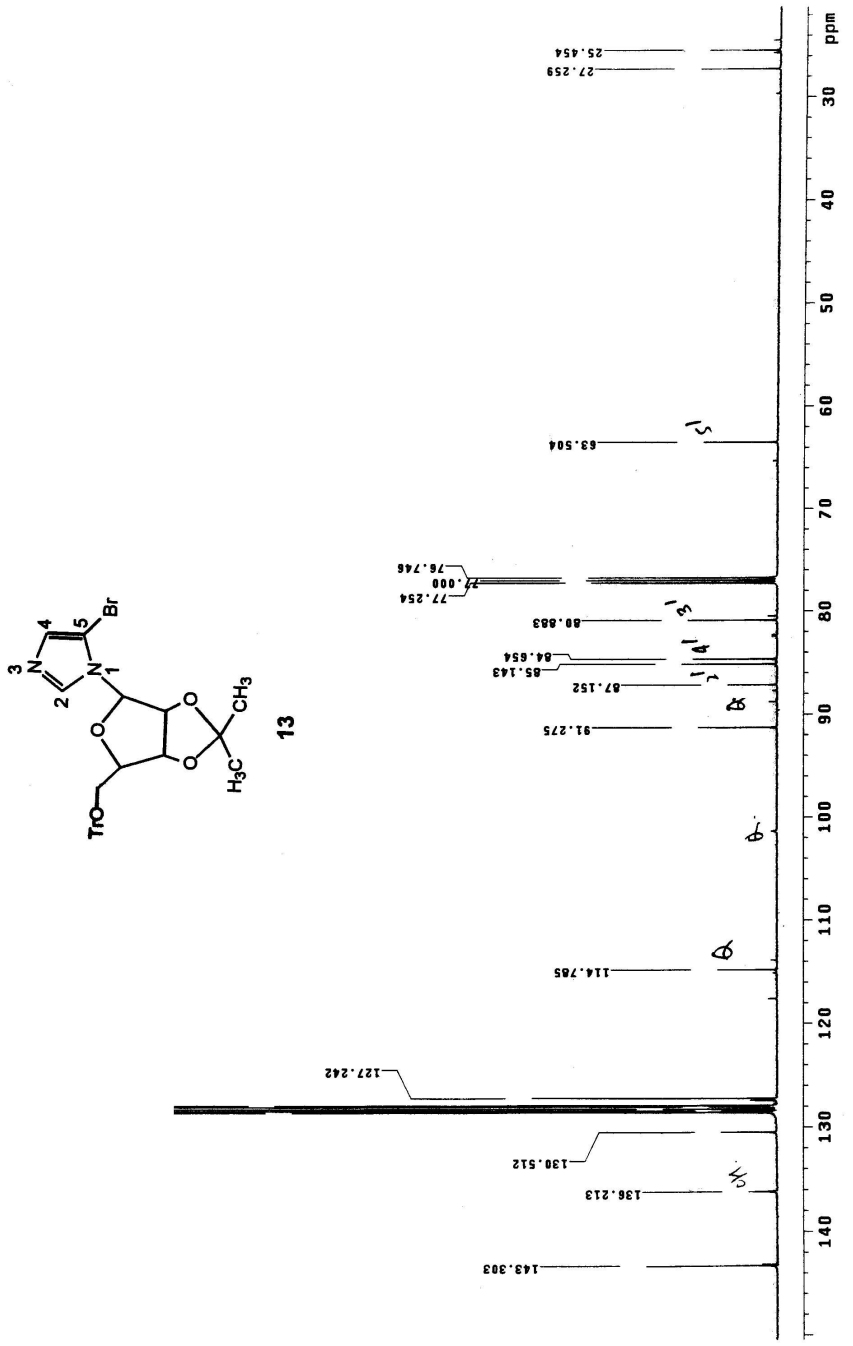
S-31 NOESY of compound **11**



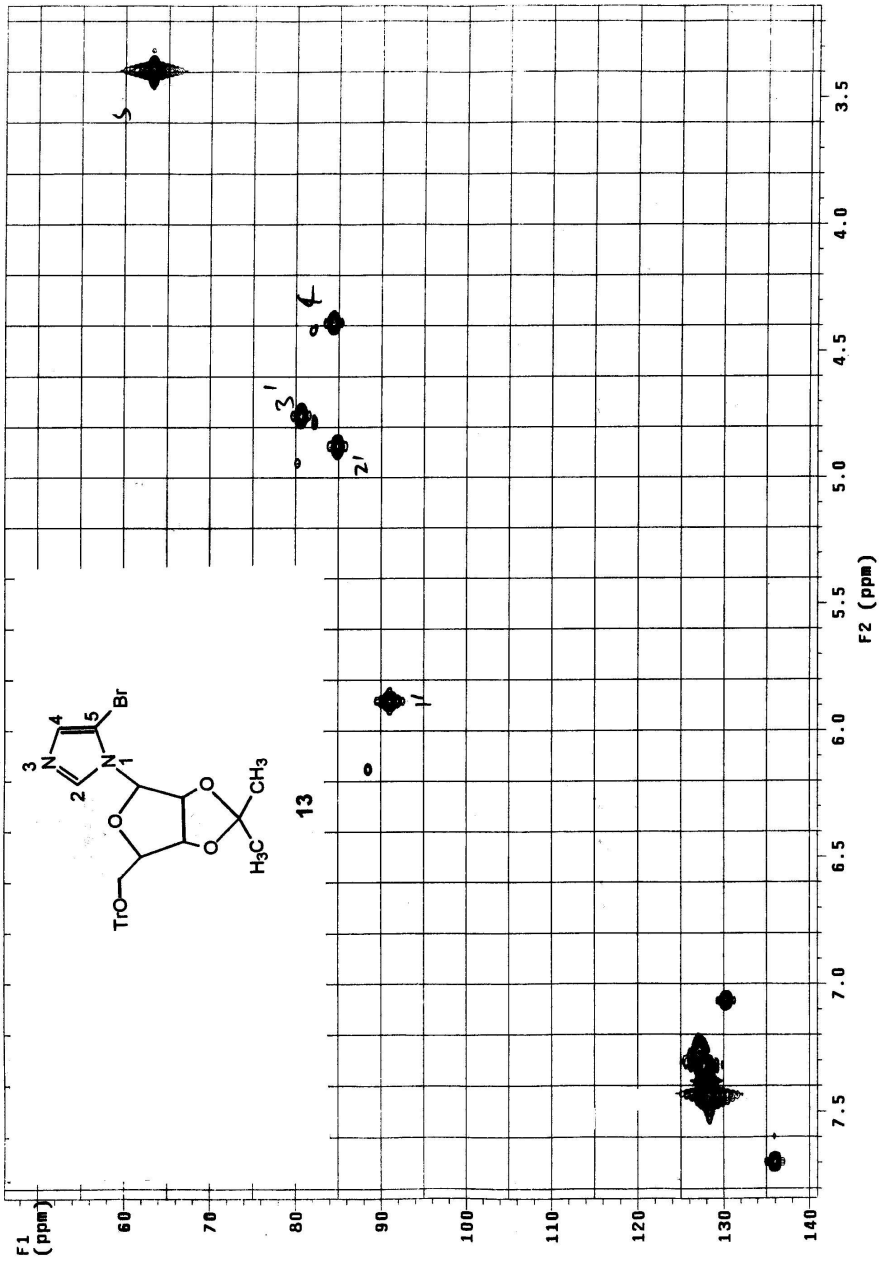
S-32 Down field region NOESY of compound **11** showing nOe between anomeric proton and C-5 imidazole proton



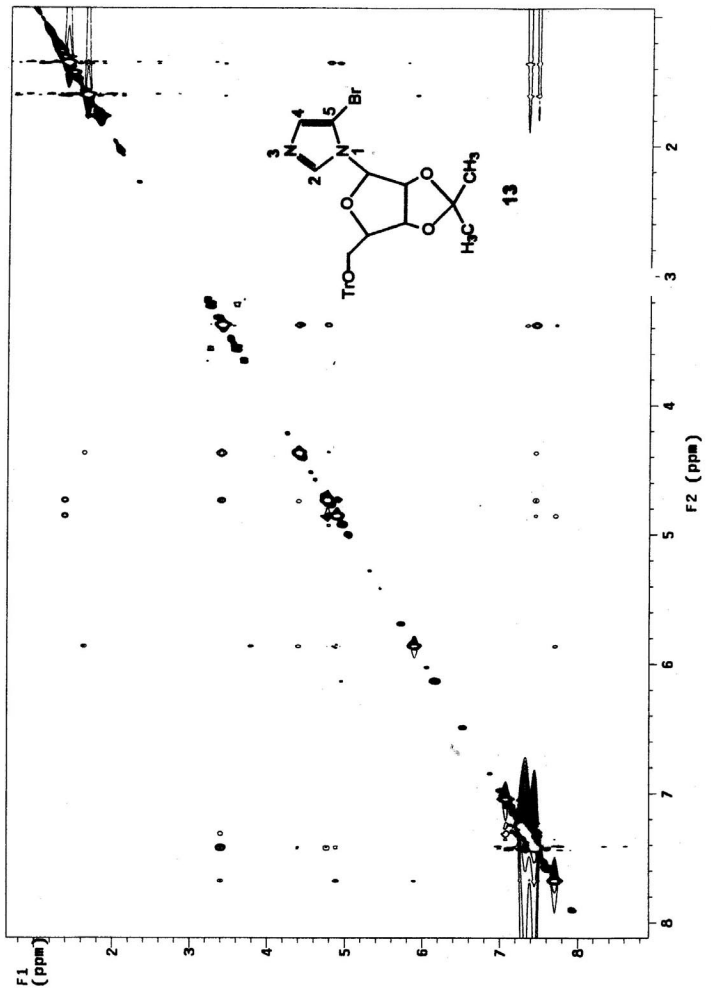
S-33 ^{1}H spectrum of compound **13**



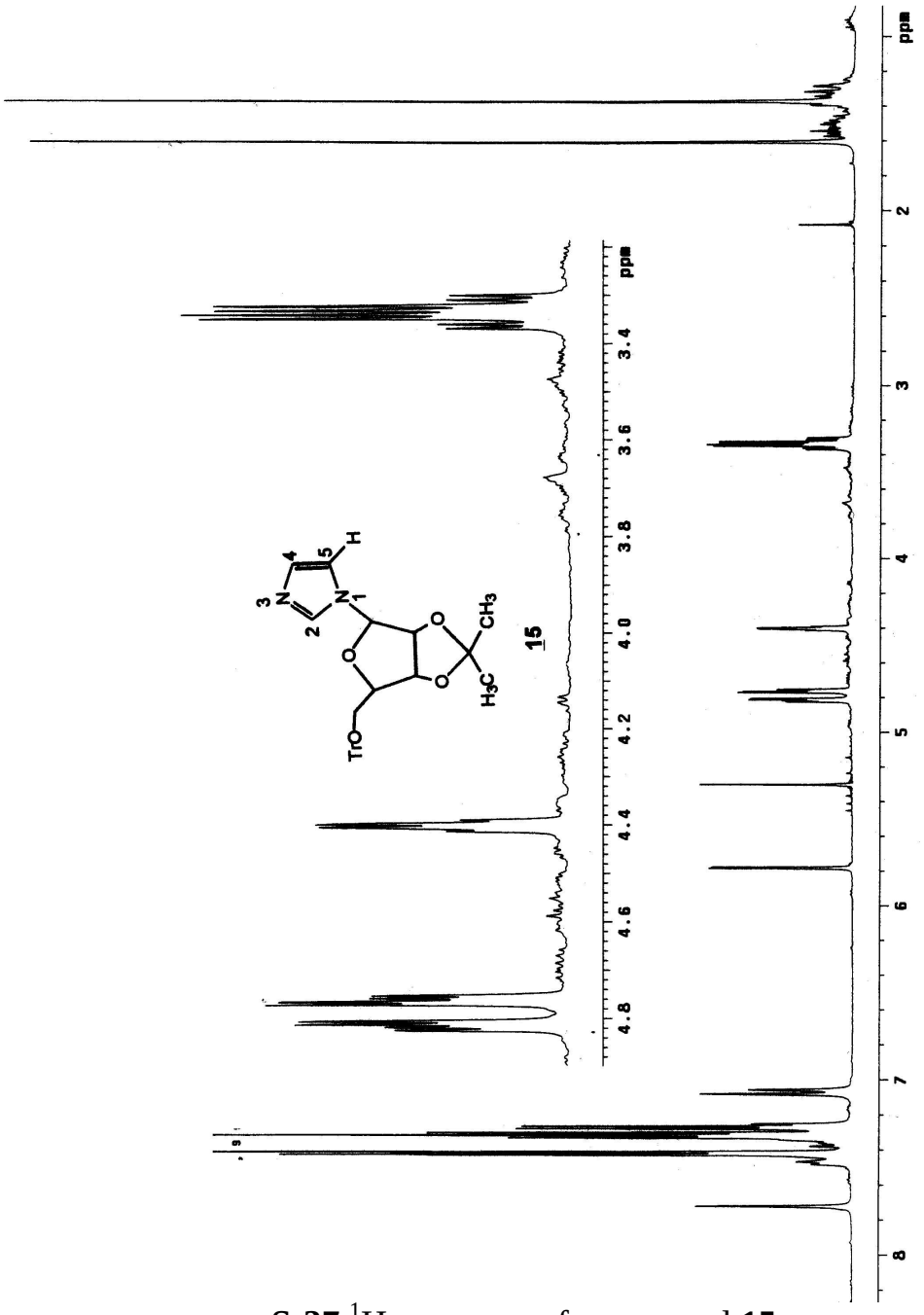
S-34 ^{13}C spectrum of compound **13**



S-35 HMQC of compound **13**



S-36 NOESY of compound 13



S-37 ^{1}H spectrum of compound **15**