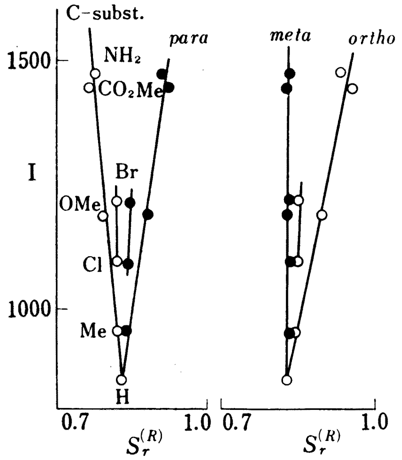

Fig. 1. Correlations between Retention Indices I and Free Radical Superdelocalizabilities $S_r^{(R)}$ on the Ring Carbon of Monosubstituted Benzenes

stationary phase: Emulphor-O; temp.: 150°

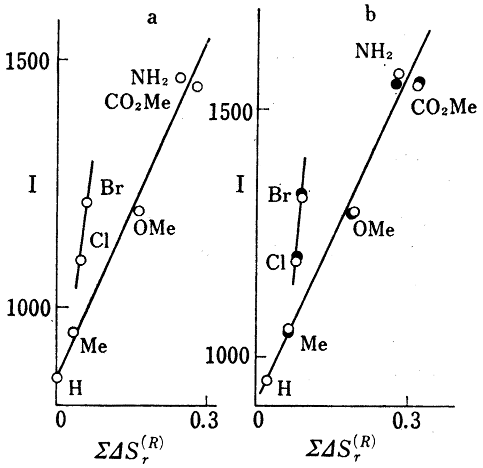

Fig. 2. Correlations between Retention Indices I and Sum of Excess Free Radical Superdelocalizabilities $\sum\Delta S_r^{(R)}$

stationay phase: Emulphor-O; temp.: 150°
a: monosubstituted benzenes
b: *meta*- and *para*-substituted toluene series
meta: ○ *para*: ●

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Synthesis and Properties of 8,2′-Cyclothioguanosine and Related Compounds

Recently, the synthesis and properties of a variety of adenosine-8-cyclonucleosides have been reported.[1-4] These cyclonucleosides are important intermediates for the transformation of ribonucleosides to deoxynucleosides or arabinonucleosides. However, because of the difficulty of application of mono-tosylation or mono-triisopropylbenzenesulfonylation to guanine nucleosides,[5] 8,2′-cyclothioguanosine derivatives have not hitherto been reported.

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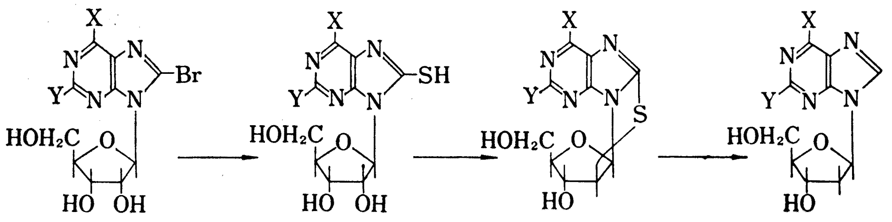
In the present paper we wish to report the synthesis of 8,2′-cyclothioguanosine and its related compounds using diphenylcarbonate as a cyclizing agent. Treatment of 8-mercaptoguanosine (IIa)[6] with 1.2 equivalent of diphenylcarbonate and a small amount of sodium bicarbonate in dimethylformamide at 150° under anhydrous conditions for 30 min, yielded 83% of powdery 8,2′-cyclothioguanosine following the treatment with ether and recrystallization from hot water.

The structures of this 8,2′-cyclothioguanosine and other 8,2′-cyclothiopurinenucleosides described below were decided on the basis of: i) good agreement of the elemental analytical data with calculated value; ii) the coupling constants between H1′ and H2′ in the nuclear magnetic resonance (NMR) spectra are nearly same as those of 8,2′-cyclothioadenosine; iii) the presence of strong molecular ion peaks in the mass spectra and iv) desulfurization with Raney nickel to give corresponding 2′-deoxyribonucleosides.

In addition, 8,2′-cyclothioxanthosine and 8,2′-cyclothio-6-thioguanosine were synthesized by the same procedure used for 8,2′-cyclothioguanosine from 8-mercaptoxanthosine[7] and 6,8-dimercaptoguanosine,[8] respectively.



I

II

IIa : X=OH, Y=NH$_2$
IIb : X=OH, Y=OH
IIc : X=SH, Y=NH$_2$
IId : X=OH, Y=H
IIe : X=SH, Y=H

III

IIIa : X=OH, Y=NH$_2$
IIIb : X=OH, Y=OH
IIIc : X=SH, Y=NH$_2$
IIId : X=OH, Y=H
IIIe : X=SH, Y=H
IIIf : X=H, Y=H

IV

IVa : X=OH, Y=NH$_2$
IVb : X=OH, Y=OH
IVc : X=H, Y=NH$_2$
IVd : X=OH, Y=H
IVe : X=H, Y=H

Chart 1

Desulfurization of these 8,2′-cyclothionucleosides gave the corresponding 2′-deoxyguanosine,[9] 2′-deoxyxanthosine[9] and 2′-deoxy-2-aminopurineribonucleoside.[10] These 2′-deoxyribonucleosides revealed a pink color with cystein sulfuric acid spray on paper chromatograms. In the case of desulfurization of 8,2′-cyclothio-6-thioguanosine, 8,2′-cyclothio-2-aminopurineribonucleoside was obtained using a restricted amount of Raney nickel.

The elemental analytical data and the physical properties are shown in Table I.

During the course of this investigation, Ogilvie, *et al.*[11] reported only briefly that 8-bromoadenosine-2′,3′-cyclic carbonate gave 8,2′-cyclothioadenosine by refluxing in butanol with thiourea. The method described above is also applicable to adenosine derivatives in high yields. Applications of these reactions to other purine cyclonucleosides are in progress in this laboratory.

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Table I. Physical Properties of 8,2′-Cyclothiopurinenucleosides

Compound	mp (°C)	UV $\lambda_{\max}$ (mμ)	NMR (ppm) H1′ (cps)	Elemental analysis (%)			
					C	H	N
IIIa	>220	$\mathrm{H^+}$ 267 $\mathrm{H_2O}$ 265, 280(sh) $\mathrm{OH^-}$ 279	6.30[a] (6.0)	Calcd. Found	39.21 39.44	3.95 3.94	22.87 23.05
IIIb	278 (decomp.)	$\mathrm{H^+}$ 249, 278 $\mathrm{H_2O}$ 255, 282 $\mathrm{OH^-}$ 257.5, 287	6.40 (6.0)	Calcd. Found	40.26 40.17	3.39 3.25	18.78 18.54
IIIc	220—228	$\mathrm{H^+}$ 235, 261, 355 $\mathrm{H_2O}$ 235, 261, 355 $\mathrm{OH^-}$ 258, 331	6.38 (7.0)	Calcd. Found	36.75 36.84	4.01 4.01	21.43 21.69
IIId	280 (decomp.)	$\mathrm{H^+}$ 206.5, 264 $\mathrm{H_2O}$ 205, 263.5 $\mathrm{OH^-}$ 268	6.55 (7.0)	Calcd. Found	41.23 41.63	3.81 3.88	19.24 19.69
IIIe	251 (decomp.)	$\mathrm{H^+}$ 251, 336 $\mathrm{H_2O}$ 250, 336 $\mathrm{OH^-}$ 248.5, 321	6.59 (6.5)	Calcd. Found	37.75 37.71	3.83 3.43	17.71 17.75
IIIf	256—275 (decomp.)	$\mathrm{H^+}$ 225.5, 243, 323 $\mathrm{H_2O}$ 223.5, 252, 315 $\mathrm{OH^-}$ 252, 316	6.45 (6.0)	Calcd. Found	41.83 41.67	4.21 4.12	24.38 24.22

a) taken at 130°

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