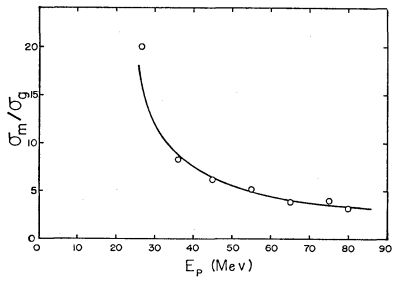

FIG. 1. Ratio of formation cross sections of the metastable and ground states of Cs^{134} as a function of proton bombarding energy.

energy range, and is formed almost exclusively at the lower energies. However, the low-spin ground state (4+) becomes increasingly favored with increasing excitation energy. This is not in agreement with the conclusions of Bailey (2), who reasoned that, since high-energy fission is a high angular momentum process, the low-spin isomer ought to be less favored at higher energies.

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6-O-METHANESULPHONYL-D-GALACTOSE

D. L. MITCHELL

Acid hydrolysis of the *O*-isopropylidene groups of 1,2:3,4-di-*O*-isopropylidene-6-*O*-toluene-*p*-sulphonyl-D-galactose with retention of the 6-*O*-toluene-*p*-sulphonyl ester offers little difficulty and the product, 6-*O*-toluene-*p*-sulphonyl-D-galactose, has been described as a crystalline solid (1). Because the methanesulphonyl ester of a primary alcohol is more easily hydrolyzed by acid than the corresponding toluene-*p*-sulphonyl ester, and because the liberated methanesulphonic acid renders the reaction autocatalytic, selective removal of the *O*-isopropylidene groups of 1,2:3,4-di-*O*-isopropylidene-6-*O*-methanesulphonyl-D-galactose has offered greater difficulty and the product, 6-*O*-methanesulphonyl-D-galactose, has hitherto been obtained only as a syrup although two crystalline thioacetal derivatives have been reported (2).

Hydrolysis conditions are now described for the preparation of 6-*O*-methanesulphonyl-D-galactose as a crystalline compound. The product was the α-anomer since an aqueous solution mutarotated to a less positive equilibrium value. Chromatographic examination of the equilibrium solution revealed the absence of possible dehydration products, thus confirming that the rotational change originated from a mutarotation and not from the formation of 3,6-*O*-anhydro-D-galactose or other products. Acetonation of the crystalline

mono-*O*-methanesulphonyl-D-galactose regenerated the starting material, 1,2:3,4-di-*O*-isopropylidene-6-*O*-methanesulphonyl-D-galactose, and the location of the methanesulphonyl ester at the primary alcohol (carbon 6) was therefore confirmed. Quantitative periodate oxidation of the crystalline ester also gave data consistent with that expected for an aldohexopyranose substituted at the primary alcohol. Similar results were also obtained for the periodate oxidation of crystalline 6-*O*-toluene-*p*-sulphonyl-D-galactose.

Attempts to form the 2,5-dichlorophenylhydrazone and the *N*-benzylphenylhydrazone derivatives by the usual method of gentle warming of an alcoholic solution of the substituted hydrazine and 6-*O*-methanesulphonyl-D-galactose gave crystalline products that contained no sulphur. Analyses corresponded to those of anhydrohexose phenylhydrazones and the products have been tentatively identified as 3,6-*O*-anhydro-D-galactose 2,5-dichlorophenylhydrazone and 3,6-*O*-anhydro-D-galactose *N*-benzylphenylhydrazone respectively. Under refluxing conditions during the attempted formation of the phenylosazone, loss of the 6-*O*-methanesulphonyl group occurred and an anhydrohexose phenylosazone was isolated, which was most likely 3,6-*O*-anhydro-D-*lyxo*-hexose phenylosazone.

When a lower reaction temperature was employed (i.e. reaction at room temperature for several days), the expected hydrazone derivatives were obtained without the anhydro compound being simultaneously formed. Several new substituted hydrazone derivatives of 6-*O*-(methanesulphonyl- and toluene-*p*-sulphonyl-)D-galactose have been described in Table III.

EXPERIMENTAL

For paper chromatographic examination, the following solvent system was used (v:v): ethyl acetate – acetic acid – water (9:2:2). 1,2:3,4-Di-*O*-isopropylidene-D-galactose was prepared in 66% yield by a procedure adapted from the preparation of 1,2:5,6-di-*O*-isopropylidene-D-glucose (3). $[\alpha]_D^{20}$ −54.1° (*c*, 1.0, chloroform) (lit. $[\alpha]_D^{24}$ −54.7° (4)).

The above compound was methanesulphonated in 85% yield, by the usual method employing methanesulphonyl chloride and pyridine. The product, obtained as a solid when the reaction mixture was poured into ice-cold water, had m.p. 122–123° C and $[\alpha]_D^{24}$ −63.4° (*c*, 1.7, chloroform) after several recrystallizations from methanol (lit. m.p. 122° C and $[\alpha]_D^{20}$ −62° (chloroform) (5)).

6-O-Methanesulphonyl-D-galactose

1,2:3,4-Di-*O*-isopropylidene-6-*O*-methanesulphonyl-D-galactose (46.2 g) was dissolved in ethanol (200 ml), water (200 ml), and 2 *N* sulphuric acid (20 ml) and the solution was heated to 80° C for 3 hours. The cooled solution (0° C) was neutralized on columns of Amberlite IR-45 (acetate) and IR-120 (H) ion exchange resins and the eluate was concentrated under reduced pressure to a small volume (50 ml). Some of the starting material (ca. 1 g) separated and was recovered. The mother liquors were concentrated to a syrup which was repeatedly dissolved in a small volume of ethanol and reconcentrated to remove traces of water. The syrup was dissolved in acetone (50 ml), warmed slightly, and light petroleum (b.p. 60–80° C) was added to incipient turbidity. Storage at 4° C for 4 days induced crystallization (rosettes, 14.6 g, 42%). Recrystallization from ethanol–water (25:1) gave fine needles of m.p. 124–125° C, $[\alpha]_D^{23}$ 83.9° (13 minutes) → 55.2° (3.5 hours) → 52.8° (constant value) (*c*, 0.9, water), and a R_f 0.45 and R_{Rh} 1.06. Anal. Calc. for $C_7H_{14}O_8S$: C, 32.7; H, 5.5; S, 12.4. Found: C, 32.6; H, 5.5; S, 12.4. Syrupy 6-*O*-methanesulphonyl-D-galactose, obtained by using the hydrolysis conditions (dilute acetic acid) described by Stacey (2), crystallized after nucleation with the above crystalline specimen.

The above hydrolysis conditions were found to be too mild for the preparation of the corresponding 6-*O*-toluene-*p*-sulphonyl-D-galactose and a modified procedure was adopted. A solution of 1,2:3,4-di-*O*-isopropylidene-6-*O*-toluene-*p*-sulphonyl-D-galactose (20 g) in ethanol (140 ml), water (60 ml), and dilute sulphuric acid (2 *N*, 25 ml) was heated to 80° C for 4 hours. Using the above isolation procedure, 31% yield of 6-*O*-toluene-*p*-sulphonyl-D-galactose was obtained, m.p. 133–134° C and $[\alpha]_D^{23}$ 32.8° → 46.7° (24 hours) (*c*, 1.22, water).

Periodate Oxidation Experiments

Periodate oxidation at room temperature of samples (38.7 mg, 1.5×10^{-4} mole) with sodium metaperiodate solution (12×10^{-4} mole in 25 ml) under unbuffered and buffered conditions is described in Tables I and II.

Re-formation of 1,2:3,4-Di-O-isopropylidene-6-O-methanesulphonyl-D-galactose

A solution of 6-*O*-methanesulphonyl-D-galactose (110 mg) in acetone (20 ml) containing concentrated

TABLE I

Periodate oxidation of 6-*O*-methanesulphonyl-D-galactose

Determination	pH	Time (min) 5	10	20	30	60	120	180		
Uptake*	U	3.72	3.74	—	3.76	3.78	—	—	3.93 (210 min)	3.99 (21 hr)
Uptake	3.7	3.08	3.10	3.46	—	3.87	3.89	3.94	3.52 (40 min)	
Titratable acid†	U	2.6	2.7	2.9	3.1	3.8	—	—	3.8 (7.5 hr)	3.9 (17 hr)
Formaldehyde‡	U	—	—	—	—	—	—	—	Nil (21 hr)	

*Reference 9.
†An end point using the screened methyl red indicator was taken.
‡Reference 10.

TABLE II

Periodate oxidation of 6-*O*-toluene-*p*-sulphonyl-D-galactose

Determination	pH	Time (min) 10	30	60	90	21 hr	24 hr	
Uptake	U	—	2.21	—	2.63	3.83	4.13 (constant)	
Titratable acid	U	1.17	2.17	2.50	—	—	3.75	3.96 (40 hr)
Formaldehyde	U	—	—	—	—	—	Trace	

sulphuric acid (1 drop) was stored for 24 hours at room temperature. After neutralization (barium carbonate) and filtration from the inorganic salts, the solution was concentrated to a crystalline mass. This material was recrystallized from methanol and had a melting point of 121–122° C which was not depressed upon admixture with an authentic specimen of 1,2:3,4-di-*O*-isopropylidene-6-*O*-methanesulphonyl-D-galactose. The derived product possessed an infrared absorption spectrum identical with that of the authentic specimen. Both comparisons using solid material (potassium bromide disk) and chloroform solutions were employed.

6-O-Methanesulphonyl-D-galactose 2,5-Dichlorophenylhydrazone

A suspension of 6-*O*-methanesulphonyl-D-galactose (0.20 g) and 2,5-dichlorophenylhydrazine (0.17 g) in dry methanol was stored in a stoppered flask at room temperature. After 24 hours, the reactants formed a solution, which was stored for a further 24 hours. Concentration under reduced pressure afforded a solid which was recrystallized from a small volume of ethanol, m.p. 143–145° C, $[\alpha]_D^{23}$ +30° (*c*, 0.53, pyridine) (Table III).

The preparations of 6-*O*-methanesulphonyl-D-galactose *N*-benzylphenylhydrazone, and 6-*O*-toluene-*p*-sulphonyl-D-galactose 2,5-dichlorophenylhydrazone were also carried out by the above method (Table III) (6).

6-O-Methanesulphonyl-D-galactose 2,4-Dinitrophenylhydrazone

The 2,4-dinitrophenylhydrazones were prepared by mixing a warm alcoholic solution of the D-galactose sulphonyl ester with an excess of Brady's reagent. After 30 minutes' reaction, the precipitate was collected by centrifugation and repeatedly washed with ether. The physical constants are reported in Table III.

(?) 3,6-O-Anhydro-D-galactose N-Benzylphenylhydrazone

A solution of 6-*O*-methanesulphonyl-D-galactose (0.24 g) and *N*-benzylphenylhydrazine (0.50 g) in methanol (5 ml) was cautiously warmed to ca. 45–50° C intermittently for 1 hour and stored for a further 48 hours. Concentration to dryness afforded a crystalline solid that was repeatedly triturated with cold (−10° C) ether followed by hexane–ether solutions. A portion was recrystallized from ethanol to give white needles of m.p. 155–156° and $[\alpha]_D^{23}$ −22° (12 hours) (*c*, 1.2, pyridine). Anal. Calc. for $C_{19}H_{22}N_2O$: C, 66.7; H, 6.5; N, 8.2; S, nil. Found: C, 67.3; H, 6.5; N, 8.1; S, nil.

(?) 3,6-O-Anhydro-D-galactose 2,5-Dichlorophenylhydrazone

A solution of 6-*O*-methanesulphonyl-D-galactose (0.050 g) and 2,5-dichlorophenylhydrazine (0.040 g) in

TABLE III

Hydrazone derivatives of 6-*O*-(methanesulphonyl- and toluene-*p*-sulphonyl-)D-galactose

Hydrazone	Ester	M.p.* (°C)	$[\alpha]_D^{23}$ †	Formula	C		H		N		S	
					Calc.	Found	Calc.	Found	Calc.	Found	Calc.	Found
2,5-Dichlorophenyl	6-*O*-Methanesulphonyl	143–145	30°	$C_{13}H_{18}Cl_2N_2O_7S$	37.4	37.7	4.4	4.5	6.7	6.3		
2,4-Dinitrophenyl	6-*O*-Methanesulphonyl	148–150	—	$C_{13}H_{18}N_4O_{11}S$	35.8	35.6	4.4	4.1			7.3	7.9
N-Benzylphenyl	6-*O*-Methanesulphonyl	124–126	7.7°	$C_{20}H_{26}N_2O_7S$	54.8	54.8	6.0	6.2	6.4	6.5		
2,5-Dichlorophenyl	6-*O*-Toluene-*p*-sulphonyl	131–133	17.6° 8.8° (12 hr)	$C_{19}H_{22}Cl_2N_2O_7S$	46.2	46.5	4.5	4.6	5.7	5.5	6.5	6.5
2,4-Dinitrophenyl	6-*O*-Toluene-*p*-sulphonyl	148–150	—	$C_{19}H_{22}N_4O_{11}S$	44.4	44.4	4.3	4.4	10.9	10.5		

*All samples melted with decomposition.
†All observations were carried out in pyridine solutions.

methanol (5 ml) was heated to 80° C for 2 hours. The solution was concentrated to a crystalline mass which was repeatedly triturated with cold ether to yield pale yellow flakes (0.025 g) of m.p. 191–193° C (preliminary shrinking). Anal. Calc. for $C_{12}H_{14}Cl_2N_2O_4$: N, 8.7; S, nil. Found: N, 9.0; S, nil.

3,6-O-Anhydro-D-lyxo-*hexose Phenylosazone*

Attempts to prepare the phenylosazone of 6-*O*-methanesulphonyl-D-galactose using phenylhydrazine and acetate-buffered aqueous acetic acid with warming of the solution to 80° C gave a product of m.p. 203–205° C. Anal. Calc. for $C_{18}H_{20}N_4O_3$: N, 16.5. Found: N, 17.1 (lit. 3,6-*O*-anhydro-D-galactose phenylosazone, m.p. 203–204.5° C (7) and m.p. 117° C (8)).

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DETERMINATION OF RELATIVE SIGNS OF COUPLING CONSTANTS IN QUINOLINE BY NUCLEAR MAGNETIC DOUBLE RESONANCE

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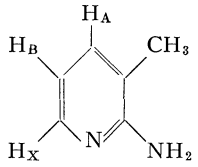
A great deal of interest has been generated recently by the discovery (1–3) that the relative signs of n.m.r. coupling constants could be determined by double-irradiation experiments. The present note describes double-resonance measurements on quinoline which yield the relative signs of the coupling constants in the heterocyclic ring. In a recent paper (4) on 2-amino-3-picoline, it was claimed that the single-resonance spectrum indicated that J_{AX} and J_{BX} were of the same sign, although details of the calculations were not given. Assuming that both coupling constants were positive, it was then shown



2-Amino-3-picoline

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