pH falls to 1). Furthermore, the capacity of the products of the prototropic reaction to add halogeno-compounds to the double bond[7] may explain the rapid decrease in the optical density. Owing to the high stability of bilirubin in chloroform, we did not examine this reaction without irradiation. This stability could be explained by the presence of hydrogen bridges in the pyrrolic ring.

Conclusions. The results presented seem to indicate that a first order reaction of a prototropic nature can occur in the transformation of bilirubin. However, it is also clear that intramolecular hydrogen bonds play an important role in the stability of this pigment.

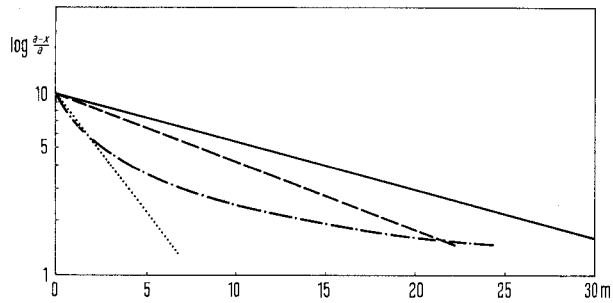

Fig. 3. Changes in relative optical density, at 450 nm, of irradiated solutions of bilirubin, plotted as a function of time measured in min. ——— = alkaline solution with EDTA (traces). - - - - = alkaline solution (5 g/dm³). – · – · – = alkaline solution with $Zn(Ac)_2$ (traces). ····· = chloroform solution.

Riassunto. Gli autori hanno studiato l'azione della luce sulla stabilità della bilirubina in soluzione alcalina e in soluzione cloroformica. Viene proposto, in via generale, un meccanismo del primo ordine per la trasformazione della bilirubina in pigmenti verdinoidi, sia per le soluzioni irradiate, sia per quelle conservate al buio.

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Structure Activity Relationships of some Centrally Active Dialkyl Substituted Propanediol Sulfites

During preliminary toxicity studies in male albino mice (Swiss Webster) of several dialkyl propanediol cyclic esters of sulfurous acid synthesized by one of us (E.R.B.) in 1957, it was noted that slight changes in the length of the alkyl chain (Table) brought about opposing effects on the central nervous system. A study of the data suggests that Compounds I (dimethyl), IV (diethyl) and XI were quite potent convulsants. In addition, Compounds II (methyl, propyl) and V (ethyl, propyl) were less potent but still effective central nervous system stimulants. Conversely, Compound VI (ethyl, *n*-butyl) was found to be a moderately potent central nervous system depressant. The activity was essentially lost when the substitution was di-*n*-butyl (Compound IX) or methyl-hexyl (Compound III).

The ability of these compounds (10 mice/dose), when administered intragastrically, to alter hexobarbital sleep times[1] was not consistent (Table). Generally, the stimulant type compounds produced a decrease in the duration of sleep (antagonism) at low doses and a lengthening (enhancement) or no effect at the upper dose tested. This type of response has not been an unusual finding in our laboratory for the central nervous system stimulant type of compound. However, the absence of an enhanced effect by the depressant type compound (VI) was unexpected.

Antagonists to central nervous system depressants such as the barbiturates might have therapeutic use. Thus, Compound IV was tested for its ability to reverse pentobarbital anesthesia in the dog[2]. Four dogs were tested and the predominant effects seen were shaking, trembling and jerks progressing to clonic-type convulsions. Two of these dogs tried unsuccessfully to get to their feet. The pattern observed resembled that observed in our laboratories for pentylenetetrazol[2,3].

The depressant compound (VI) was tested for its anticonvulsant effects in mice[4]. At relative high doses it was effective against pentylenetetrazole seizures (0.8 g/kg) and electrically induced seizures (1.6 g/kg). The other possible depressant compounds were ineffective at 0.8 g/kg by either test.

Several of the compounds (VI, VIII, IX) were evaluated for possible analgetic and antipyretic activity[5] without success. In routine cardiovascular studies[6] in the

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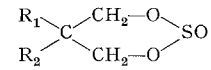
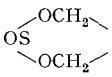
Table I. Central nervous system effects in mice



Compound	R_1	R_2	LD_{50} Route	LD_{50} mg/kg	CD_{50} Route	CD_{50} mg/kg	HD_{50} Route	HD_{50} mg/kg	Sleep time Dose mg/kg i.g.	Sleep time Ratio drug/control
I	CH_3	CH_3	i.p.	9.3 (8.8–9.9)	i.p.	< 10			10	0.63
II	CH_3	C_3H_7	i.g.	140 (100–196)	i.g.	47.0 (31.1–70.8)			25	0.67
			i.p.	52.0 (34.2–79.0)					50	1.17
III	CH_3	C_6H_{13}	i.p.	> 2000			i.p.	> 2000	100	1.00
									200	1.55
IV	C_2H_5	C_2H_5	i.p.	30.5 (27.0–35.0)	i.p.	7.3 (5.8–9.1)			25	0.61
									50	1.55
V	C_2H_5	C_3H_7	i.g.	310 (244–394)	i.p.	45 (27.1–74.7)			20	1.81
									50	0.90
									100	0.67
VI	C_2H_5	C_4H_9	i.p.	880 (746–1038)			i.p.	265 (221–318)	200	1.06
			i.g.	> 1600					400	1.50
VII	C_2H_5	C_6H_5	i.p.	~ 1100	i.p.	~ 500				
VIII	C_2H_5	C_6H_{13}	i.p.	> 1600					50	0.97
			i.g.	> 1600					100	2.53
									200	1.65
IX	C_4H_9	C_4H_9	i.p.	> 1500			i.p.	> 1500	50	1.19
									100	1.95
									200	2.65
X	CH_2OH	CH_2OH	i.p.	> 1000					200	0.66
XI			i.g.	15.2 (12.5–18.5)	i.g.	12.9 (10.3–16.1)			1	1.28
									4	0.72

All tests performed 1 h after drug administration; i.p. = intraperitoneal administration; i.g. = oral administration; LD_{50} = lethal dose for 50% mice (95% confidence limits); CD_{50} = convulsant dose for 50% mice; HD_{50} = hypnotic dose for 50% mice.

pentobarbitalized dog, all compounds were found to produce transient slight vasodepression which was unaltered by atropine.

Résumé. Une étude de 2-2-dialkyl-1-3-propanediol esters cyclique d'acide sulfureux constatait des filiations structure activité très interessantes. Avec un petit ralongant de la chaîne alkyl il est changé d'un stimulant système nerveux central (dimethyl, diethyl, et le pentaerythritol disulfite) à un dépressant système nerveux central fort modérément.

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Molecular Weight of Bovine Growth Hormone

The molecular weight of bovine growth hormone has been measured by several workers[1–6].

The results obtained at pH around 9 with different buffer solutions, vary between 39,300 and 45,000; at pH 7.4 using a Sephadex gel filtration procedure, ANDREWS and FOLLEY[6] found a molecular weight of 20,000 with a preparation obtained from the National Institutes of Health. LI and PEDERSEN[5] have carefully studied the sedimentation behaviour of the hormone prepared by LI, EVANS, and SIMPSON[1,7] under various conditions: at pH 9.93 the results suggested the presence of monomeric and dimeric forms of the hormone in solution, whereas at pH 2.32 and 11.50 it behaved like a monomeric protein. The molecular weight at these two extreme pHs differed radically: 50,000 was found at pH 2.32 and 29,000 at pH 11.50.

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