Regiospecificity in Photochemical Additions to Bilirubin. Photoinduced Reaction of 2-Vinylbiladienes-*a,c* with the Disulphide Bond

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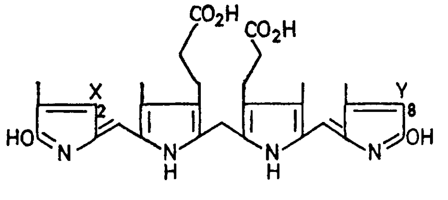
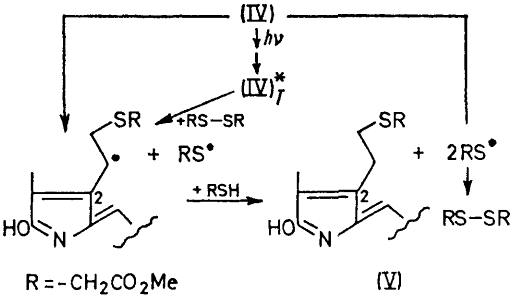
Summary Irradiation of the 2-vinylbiladiene-*a,c* (IV) in the presence of dimethyl dithiodiglycollate and methyl thioglycollate afforded an addition product (V); this reaction is of interest because of its probable relevance to the photocatabolism of bilirubin.

In connection with the studies on the mechanism by which light reduces serum bilirubin levels in animals and humans, particularly in jaundiced newborn infants,[1] much attention has been directed towards the behaviour of this bile pigment under irradiation *in vitro*. It has been recently observed that bilirubin (I) reacts under u.v. light with alcohols[2] and thiols[3] to give the adducts (II) and (III), respectively, as essentially the only products. An ionic mechanism has been suggested[2] for this *O*- and *S*-pyrryl regiospecific[4] photoaddition. We now report that the vinyl group at the 2-position of a biladiene-*a,c* skeleton can also add RSH photochemically: such an addition occurs in the presence of the corresponding disulphide and shows S–H regiospecificity.



	X	Y
(I)	$-CH=CH_2$	$-CH=CH_2$
(II)	$-CH=CH_2$	$-CH(Me)OR$
(III)	$-CH=CH_2$	$-CH(Me)SR$
(IV)	$-CH=CH_2$	$-CH(Me)S-CH_2-CO_2Me$
(V)	$-CH_2-CH_2-S-CH_2-CO_2Me$	$-CH(Me)S-CH_2-CO_2Me$

A solution of (IV)[3] ($1{\cdot}45 \times 10^{-3}$M) in chloroform containing methyl thioglycollate (0·5M) and dimethyl dithiodiglycollate ($2{\cdot}5 \times 10^{-2}$ M) was irradiated for *ca.* 8 h using a black fluorescent lamp.† A yellow photoderivative of (IV) was then isolated by preparative t.l.c. (Merck Silica Gel G, $MeOH-C_6H_6-CHCl_3$ 1·5:100:50): 25% yield (after crystallization from $MeOH-CHCl_3$ 2:1); it blackened without melting over 250°. From elemental analysis, i.r., u.v., and n.m.r. data the structure (V) was assigned to the photoproduct. Compound (V) may be formed through an induced decomposition of dimethyl dithiodiglycollate by a triplet state of (IV), as shown in the Scheme. This is in agreement with the following observations: (i) (V) is formed only if dimethyl dithiodiglycollate is present in solution; (ii) dimethyl dithiodiglycollate does not absorb light over 300 nm,[5] a fact which weighs against a direct S–S bond homolysis followed by free-radical addition; (iii) the u.v. absorption spectrum of a mixture of (IV) and dimethyl dithiodiglycollate shows no new absorption band, thus excluding the formation of a ground-state charge-transfer complex between (IV) and the disulphide; (iv) *cis*-piperylene (0·1 M, E_T 56·9 kcal mol^{-1})[6] as well as oxygen inhibits the formation of (V) completely.‡ However, a transfer of triplet excitation from (IV) to the disulphide, occurring before S–S bond scission, cannot be ruled out *a priori*.§



SCHEME

There is a possible analogy between the origin of (V) and the benzophenone-sensitized decomposition of benzoyl peroxide.[9] Furthermore, interactions like that described above might play a role in the metabolism of bile pigments[1,10a] as well as in the mechanism of bilirubin toxicity.[10]

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† OSRAM L20W/73; radiant energy 320—400 nm with a max. at 352 nm.

‡ Inhibition was verified with a disulphide concentration covering the range 0·02—0·2M.

§ In this case, triplet energy of (IV) should be greater than 70 kcal mol^{-1} considering the values of D_{S-S} in dialkyl disulphides. Further, this transfer of energy would be probably of the non-Franck–Condon type, since it appears difficult to picture a spectroscopic disulphide triplet[8] having E_T *ca.* 70—80 kcal mol^{-1}.

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