extinction coefficient) was calculated according to the equation

$$\varepsilon = \log_{10}(1/T)/bc,$$

where T is the transmittance (the ratio of the radiant power transmitted through the solution to the radiant power transmitted through the solvent), b is the length of the cell path (0.75 cm), and c is the concentration in moles per liter. We chose the wavelength of about 4100 A, at which Schönberg, Rupp, and Gumlich reported the greatest deviation from Beer's law. (Table 1.)

The limits of error in determining ε are estimated to be about ± 10 percent. The average value for ε at 100°C was 6, while Rupp reported a very considerable increase on dilution in an even smaller concentration range than the one used in the present work. The absorption curves were straight lines and did not show the peak characteristic of free organic radicals.

7) The formation and the reactions of short-life radicals of the type RS have been extensively investigated during the past 15 years. Disulfides form such radicals under the influence of irradiation, peroxides, and/or alkyl radicals. They are exceedingly reactive and initiate chain reactions, resulting in the "abnormal" addition of thiols to double bonds, polymerizations, redistributions of RS groups, and so forth. In investigating the formation of short-life radicals from disulfides, Kharasch, Nudenberg, and Meltzer (*18*) have made an important contribution to the problem of long-life sulfenyl radicals. They investigated under which conditions disulfides form short-life radicals which initiate the addition of mercaptans to double bonds and the polymerization of butadiene-styrene. They found that the disulfides, among them phenyldisulfide, had no effect in the dark. Even at 90°C, phenyldisulfide did not catalyze the addition of lauryl mercaptan to styrene, but irradiation greatly increased the rate of this addition. The emulsion copolymerization of butadiene-styrene at 50°C was not catalyzed by p-anisyldisulfide in the dark but was very much so upon irradiation. The obvious conclusion from these experiments is that up to at least 90°C phenyldisulfide does not form long-life radicals, but it does form short-life radicals on irradiation. If phenyldisulfide would reversibly dissociate at 100°C to such an extent that Beer's law would not hold, as Schönberg maintained, the C_6H_5S radicals should initiate Kharasch's reactions in the dark.

8) The present correct nomenclature of radicals RS is *sulfenyl* radicals (*23*) (derived from RSOH, sulfenic acids). Other names used by various authors, such as *thiol radicals, thiyls, mercaptide radicals, thioalkyls* and *thioaryls,* and *mercaptyls,* are awkward and incorrect.

Table 1. Phenyldisulfide in anisole.

c (10^{-2} mole/lit)	ε, Kodama, 100°C	ε, Rupp, 100°C (*4*)
0.6	5.6	
1.25		4.1
1.3	5.9	
2.5	6.4	3.2
10.0	6.4	1.6

In conclusion the experimental and theoretical evidence available at present speaks strongly against the dissociation of aryldisulfides into long-life sulfenyl radicals.

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The Isolation and Identification of "Bound" Morphine

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Gross and Thompson (*1*), for the dog, and Oberst (*2, 3*), for the human being, found that morphine was excreted in the urine, not only in the free form, but also in a combined form. Because other substances with either a phenolic or alcoholic hydroxyl group are excreted as glucuronides, it was suggested that morphine might also be excreted in this form. When the idea was tested (*3*) by measuring the concentration of glucuronic acid in hydrolyzed urine after increasing doses of morphine, the concentration was found to increase proportionally. Thus, it was concluded that probably morphine was "bound" with glucuronic acid.

Since the time of appearance of the afore-mentioned references (*1–3*), no additional specific identification of "bound" morphine has been made. This paper (*4*) reports on the isolation and identification of the conjugated morphine.

An 11-kg dog was anesthetized and infused with 4 g

of morphine sulfate during a 3-hr period. A total of 110 ml of urine was collected during this period and the succeeding 3 hr. The total urine collected was treated with urease to remove urea and then evaporated to a small volume. The concentrated urine was chromatographed on Whatman No. 1 paper, using an n-butanol, acetic acid, water solvent of 10-3-4.5 ratio. The sheets, when sprayed with Munier's alkaloid reagent (*5*), showed a spot with an Rf of 0.16 to 0.20 and a spot at an Rf of 0.55 to 0.60 [Fig. 1(2)]. This higher spot corresponds to known morphine [Fig. 1(1)]. The area with an Rf of 0.16 to 0.20 was cut from the paper, and this strip was placed in a Soxhlet apparatus. The paper was extracted by refluxing with absolute methanol to remove alcohol-soluble impurities and then eluted by refluxing with distilled water. Chromatographing of the water eluate indicated a reasonably pure substance. However, the material obtained by evaporating the water eluate was recrystallized twice from methanol-water mixture and rechromatographed [Fig. 1(3)].

Hydrolysis of the pure compound obtained from the water eluate was attempted in the following ways: with β-glucuronidase for 24 hr at 37°C at a *p*H of 5.0; and by autoclaving in 1.0*N* HCl at 15 lb for 20 min. Each of these solutions was placed on paper in duplicate, one sheet being sprayed with Munier's alkaloid reagent [Fig. 1(5, 6)] and the other being sprayed with aniline phthalate sugar spray [Fig. 2(1, 2)].

All hydrolyzed solutions treated with the alkaloid reagent gave a spot that is identical with the Rf of known morphine [Fig. 1(1, 5, 6)] and, when sprayed with the sugar reagent, gave three spots with Rf values of 0.16, 0.27, and 0.32. The spots with an Rf of 0.32 correspond to known glucuronolactone [Fig. 2(4)], and the spot with an Rf of 0.16 corresponds to known glucuronic acid [Fig. 2(3)]. The hydrolysis with β-glucuronidase carried out on a small scale gave only one spot that has the same Rf as glucuronic acid [Fig. 2(2)]. The identity of the middle spot (Rf of 0.27) is still unknown. Also, a portion of the acid hydrolyzed material gave a typical naphthoresorcinol test for uronic acids.

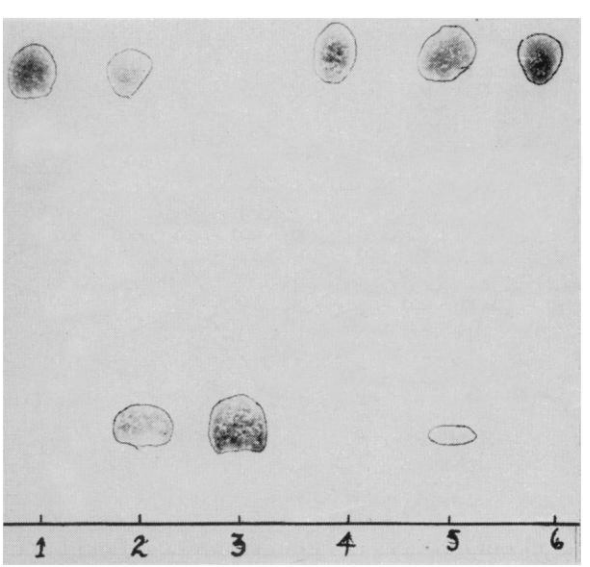

Fig. 1. (1) Known morphine. (2) Urine of morphinized dog showing spots with Rf 0.16 to 0.20 and Rf 0.55 to 0.60. (3) Low Rf spot after separation from high Rf. (4) High Rf after separation. (5) Low Rf material after hydrolysis with 1.0*N* HCl in autoclave. (6) Low Rf hydrolyzed with β-glucuronidase.

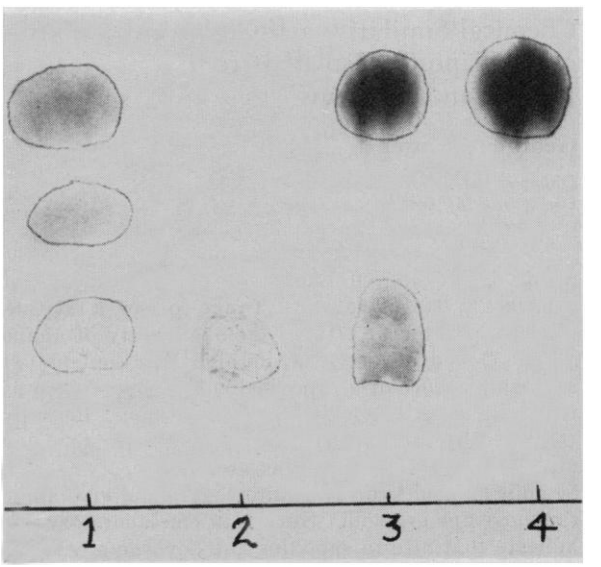

Fig. 2. (1) Low Rf substance autoclaved with 1.0*N* HCl. (2) Low Rf hydrolyzed with β-glucuronidase. (3) Known glucuronolactone heated with 0.1*N* HCl. (4) Known glucuronolactone untreated.

The free morphine that was present in the urine was characterized by its Rf value, which corresponded to that of known morphine. Also, the material with an Rf of 0.55 to 0.60 was eluted with distilled water, the water eluate was saturated with sodium bicarbonate, and the crystals were collected by filtration. Solution of these crystals and chromatographing gave Fig. 1(4). On recrystallization, the material melted at the same temperature as that of a known morphine base, and a mixed melting point proved them to be identical. Further, picrates of both morphine and the unknown substance melted at the same temperature, as did a mixture of the two picrates.

It is evident from these data that the excretion product of morphine is a glucuronide, the structure of which is now under investigation.

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