

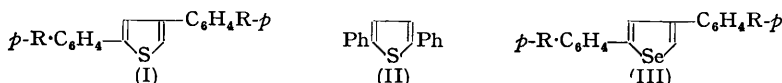
Thiophen Derivatives of Biological Interest. Part VII. The Synthesis of 2 : 4-Diarylthiophens and 2 : 4-Diarylselenophens from Anils of Alkyl Aryl Ketones.*

By P. DEMERSEMAN, NG. PH. BUU-HOÏ, R. ROYER, and ANDRÉE CHEUTIN.

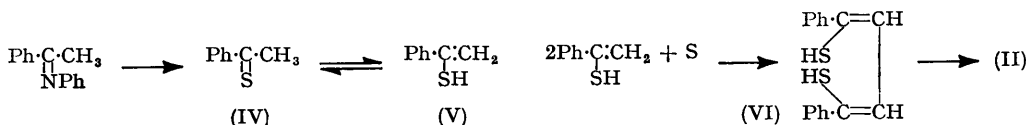
[Reprint Order No. 5276.]

The Bogert synthesis of 2 : 4-diaryl-thiophens and -selenophens by the reaction of sulphur or selenium with the anils of alkyl aryl ketones has been investigated, and, in the case of sulphur, the formation of 2 : 5-diaryl-thiophens detected both spectroscopically and chemically. A mechanism is proposed to account for the two courses of the Bogert reaction and for the difference in behaviour between sulphur and selenium.

IN connexion with another research, the preparation of 2 : 4-diphenylthiophen and its homologues was investigated. The most convenient recorded method was apparently that of Bogert and Herrera (*J. Amer. Chem. Soc.*, 1923, **45**, 238), based on the reaction of sulphur with acetophenone anil at 220—240°, which is reported to give pure 2 : 4-diphenylthiophen, to the exclusion of the 2 : 5-isomer. Repetition of this reaction gave, however, after repeated recrystallisation, a sample of 2 : 4-diphenylthiophen, m. p. 126°, which had an ultra-violet absorption spectrum differing from those of 1 : 3-diphenylbenzene and 2 : 4-diphenylselenophen (Fig. 1) in the presence of an additional band in the 3000—3200 Å



region. The fact that 2 : 5-diphenylthiophen (II) showed an absorption band in that very region (Fig. 2) suggested that Bogert and Herrera's 2 : 4-diphenylthiophen (I; R = H) contained an appreciable amount of the 2 : 5-isomer which could not be removed by crystallisation. This was proved by treating the impure 2 : 4-diphenylthiophen with an excess of *N*-methylformanilide and phosphorus oxychloride, 2 : 4-diphenylthiophen being readily converted into 3 : 5-diphenyl-2-thenaldehyde, whereas about 10% of 2 : 5-diphenylthiophen was recovered in the forerun on vacuum-distillation. A similar observation was made concerning the reaction of sulphur on *p*-methylacetophenone anil, the resulting 2 : 4-di-*p*-tolylthiophen (I; R = Me) containing some of its 2 : 5-isomer.



If one accepts the intermediate formation of thioacetophenone (IV) in the reaction of acetophenone anil with sulphur, the mechanism of the side reaction leading to 2 : 5-diphenylthiophen can be postulated as a sulphur dehydrogenation of two molecules of thioacetophenone in its thioenol form (V). The intermediate bistiophenacyl (VI) in its thioenol form would then lose one molecule of hydrogen sulphide to yield 2 : 5-diphenylthiophen. This reaction mechanism resembles the Baumann-Fromm synthesis of 2 : 5-diphenylthiophen from cinnamic acid or styrene and sulphur (*Ber.*, 1895, **28**, 890). Further it should be noted that in the Willgerodt reaction between acetophenone and ammonium sulphide a mixture of 2 : 4- and 2 : 5-diphenylthiophen is formed (Willgerodt *et al.*, *J. pr. Chem.*, 1909, **80**, 192; 1910, **81**, 74, 382).

By contrast, reaction of acetophenone anil with selenium gave pure 2 : 4-diphenylselenophen (III; R = H); so did those with the anils of *p*-methylacetophenone and *p*-methoxyacetophenone; the absorption spectra of 2 : 4-diphenyl-, 2 : 4-di-*p*-tolyl- (III;

* Part VI, *J.*, 1954, 1975.

R = Me), and 2 : 4-di-*p*-methoxyphenyl-selenophen (III; R = OMe), recorded in Fig. 3, showed no abnormality. This difference in behaviour between sulphur and selenium could be ascribed to the smaller dehydrogenating power of the latter, and, in fact, no selen-

FIG. 1.

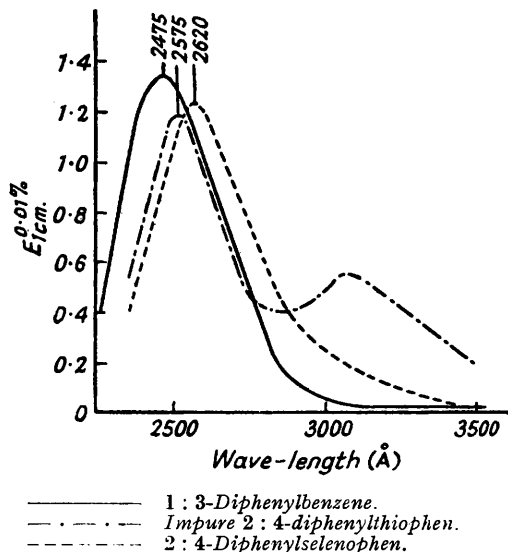


FIG. 2.

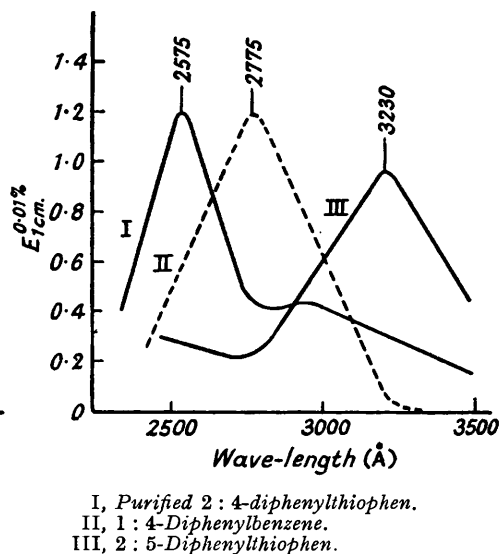


FIG. 3.

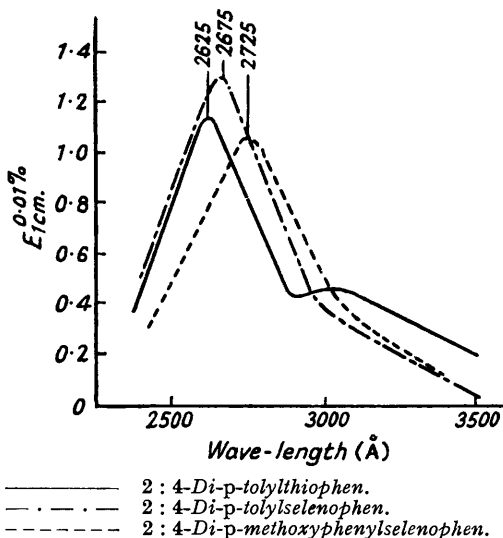
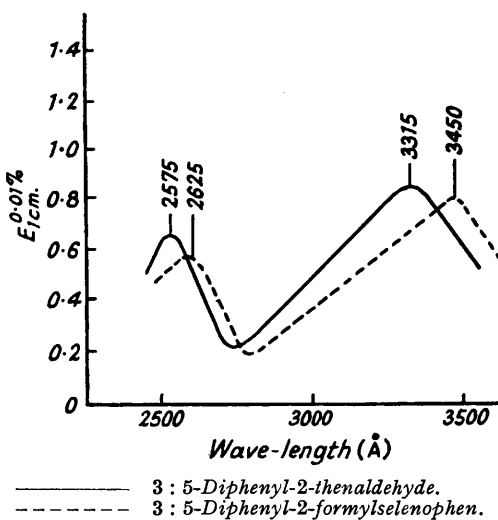


FIG. 4.



ium-containing compound could be obtained when cinnamic acid or styrene was heated with selenium. An even more pronounced lack of reactivity was displayed by tellurium, which gave no trace of 2 : 4-diphenyltellurophen from acetophenone anil. The close similarity between 2 : 4-diphenylthiophen and 2 : 4-diphenylselenophen was further shown in the analogy of the ultra-violet absorption spectra of 3 : 5-diphenyl-2-thenaldehyde and 3 : 5-diphenyl-2-formylselenophen (Fig. 4), a bathochromic effect being observed in passing from the thiophen to the selenophen series.

EXPERIMENTAL

Reaction of Sulphur with Acetophenone Anil.—Acetophenone anil [best prepared by the method used by Hansch *et al.* (*J. Amer. Chem. Soc.*, 1951, **73**, 704) for the preparation of acetophenone anil] (60 g.) and sulphur (20 g.) were heated at 185–190° for 13 hr. in a distillation apparatus, with removal of the aniline formed. The dark brown mass was fractionated in a vacuum, and the portion boiling at 265°/35 mm. (22 g.) redistilled, giving a 51% yield (20 g.) of a mixture of 2 : 4- and 2 : 5-diphenylthiophen, which crystallised as colourless leaflets, m. p. 126°, from ethanol, and gave a greenish-yellow halochromy with sulphuric acid. The m. p.s reported in the literature for 2 : 4-diphenylthiophen vary : Baumann and Fromm (*loc. cit.*) gave m. p. 119·5–120·5°; Bogert and Herrera (*loc. cit.*) reported m. p. 122·5°; and Fromm, Fantl, and Leibsohn (*Annalen*, 1927, **457**, 267), m. p. 119–124°.

Isolation of 2 : 5-diphenylthiophen. Impure 2 : 4-diphenylthiophen prepared as above (23·5 g.), *N*-methylformanilide (19 g.), and phosphorus oxychloride (22·5 g.) in toluene (100 c.c.) were refluxed for 5 hr. and, after cooling, shaken with aqueous sodium acetate. The toluene layer was washed with dilute hydrochloric acid, then with an aqueous solution of sodium carbonate, and finally with water. The residue from evaporation of the solvent gave on vacuum-fractionation 3 : 5-diphenyl-2-thenaldehyde (22 g.), crystallising as colourless prisms, m. p. 94°, from ethanol, giving a yellow colour with sulphuric acid (Found : C, 77·6; H, 4·6. Calc. for C₁₇H₁₂OS : C, 77·3; H, 4·5%). The forerun (2 g.) from the fractionation of this aldehyde gave on recrystallisation from ethanol 2 : 5-diphenylthiophen (colourless needles), m. p. 156°; Bohme, Pfeifer, and Schneider (*Ber.*, 1942, **75**, 900) gave m. p. 155–156°.

2 : 4-Di-p-tolylthiophen.—This was prepared as above with *p*-methylacetophenone anil (64 g.) and sulphur (20 g.), to give a 34% yield of 2 : 4-di-*p*-tolylthiophen, crystallising as colourless prisms, m. p. 145°, from ethanol; on formylation of the crude product, some 2 : 5-di-*p*-tolylthiophen, m. p. 171° (Willgerodt and Hambrecht, *loc. cit.*), was isolated from the forerun.

2 : 4-Di-p-tolylselenophen.—This was prepared by heating 4-methylacetophenone anil (64 g.; b. p. 200–205°/15 mm.) and selenium (48 g.) for 18 hr. at 185°; distillation (b. p. 220–225°/0·5 mm.) and recrystallisation from ethanol gave colourless leaflets (18 g.), m. p. 140°, giving a blood-red colour with sulphuric acid. Although the 40% yield recorded for this preparation was considerably higher than that reported by Bogert and Andersen (*J. Amer. Chem. Soc.*, 1926, **48**, 223), it was far less satisfactory than for 2 : 4-diphenylselenophen, the methyl groups probably undergoing dehydrogenation to afford resinous by-products.

2 : 4-Di-p-methoxyphenylthiophen (I; R = OMe).—4-Methoxyacetophenone anil (69 g.; b. p. 210–215°/17 mm., m. p. 90° after recrystallisation from benzene) and sulphur (20 g.) were heated for 13 hr. at 180°. Vacuum-fractionation yielded a thick yellow oil (5 g.) which solidified; crystallisation from ethanol gave the *thiophen* as colourless prisms, m. p. 205°, giving a brown colour with sulphuric acid, rapidly becoming green (Found : C, 72·6; H, 5·1. C₁₈H₁₆O₂S requires C, 72·9; H, 5·4%).

2 : 4-Di-p-hydroxyphenylthiophen (I; R = OH).—The foregoing compound (4 g.) and redistilled pyridine hydrochloride (10 g.) were refluxed for 20 min., and the product was treated with water after cooling. The dark brown precipitate was washed with water and dissolved in dilute aqueous sodium hydroxide; reprecipitation with hydrochloric acid gave a *product* (2·5 g.) crystallising as shiny, colourless leaflets from acetic acid (charcoal), m. p. 243°, giving a sepia halochromy with sulphuric acid (Found : C, 71·7; H, 4·5. C₁₆H₁₂O₂S requires C, 71·6; H, 4·4%).

2 : 4-Di-p-methoxyphenylselenophen (III; R = OMe).—4-Methoxyacetophenone anil (69 g.) and selenium (48 g.) were heated for 18 hr. at 185°. Working up in the usual way gave the *selenophen* (45%), a viscous oil, b. p. 260–265°/0·5 mm., which solidified. Recrystallisation from ethanol–benzene gave colourless, sublimable needles, m. p. 214°, giving a red halochromy with sulphuric acid (Found : C, 62·9; H, 4·7. C₁₈H₁₆O₂Se requires C, 62·9; H, 4·6%).

Ultra-violet Absorption Spectra.—A Beckman spectrophotometer was used, and measurements were made on solutions in pure ethanol, at a concentration of 10⁻⁵ g./c.c.

We thank Miss P. F. Boshell, M.A., for assistance.