

## Decomposition of Benzoyl Peroxide in Thiophen

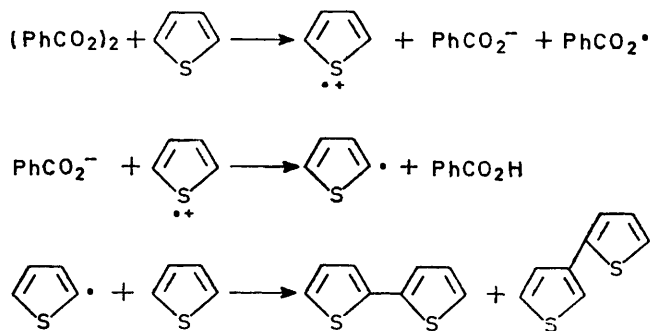
By Carlo-Maurizio Camaggi, Rino Leardini, and Antonio Tundo, Istituto di Chimica Organica dell'Università, Viale Risorgimento 4, 40136 Bologna, Italy  
Marcello Tiecco, Istituto di Chimica Organica dell'Università, Via Amendola 173, 70126 Bari, Italy

The currently accepted mechanism of the decomposition of benzoyl peroxide in thiophen is criticised on the basis of new experimental results. No free thienyl radicals are involved in the reaction, as demonstrated by scavenging experiments, and the bithienyls formed are probably derived from dimerisation of a benzoyloxythiophen radical  $\sigma$ -complex, with subsequent loss of benzoic acid.

THE anomalous behaviour of thiophen when treated with phenylazotriphenylmethane has been rationalised<sup>1</sup> as depending on the selective removal of a  $\sigma$ -complex leading to 2-phenylthiophen by stable triphenylmethyl radicals, present in high concentration in the reaction mixture. It was later shown that, on treatment with several other phenyl radical precursors, thiophen<sup>2</sup> and substituted thiophens<sup>3</sup> are phenylated in high yields giving phenylated isomers in ratios not dependent on the radical source.

The first report of the reaction of benzoyl peroxide with thiophen was by Ford and Mackay,<sup>4a</sup> who found 2-thienyl benzoate as the only product; no phenylation products were identified. A more detailed analysis was subsequently carried out by Griffin and Martin:<sup>5</sup> benzoic acid, 2-phenylthiophen, 2,2'-bithienyl, and 2,3'-bithienyl were identified as products, together with a small quantity of 2-phenylthiophen; no mention was made of 2-thienyl benzoate. The unexpected identification of bithienyls was explained<sup>5</sup> by assuming the inter-

vention of 2-thienyl radicals as intermediates (Scheme 1). This interpretation has been widely accepted<sup>6</sup> and



recently extended to explain the phenylation of thiazole and other heterocycles with benzoyl peroxide.<sup>7</sup> An alternative route to thienyl radicals in the decomposition

<sup>1</sup> C. M. Camaggi, R. Leardini, M. Tiecco, and A. Tundo, *J. Chem. Soc. (B)*, 1969, 1251.

<sup>2</sup> C. M. Camaggi, R. Leardini, M. Tiecco, and A. Tundo, *J. Chem. Soc. (B)*, 1970, 1683.

<sup>3</sup> C. M. Camaggi, G. De Luca, and A. Tundo, *J.C.S. Perkin II*, 1972, (a) 412; (b) 1594.

<sup>4</sup> (a) M. C. Ford and D. Mackay, *J. Chem. Soc.*, 1957, 4620; (b) D. Mackay, *Canad. J. Chem.*, 1966, **44**, 2881.

<sup>5</sup> C. E. Griffin and K. R. Martin, *Chem. Comm.*, 1965, 154.

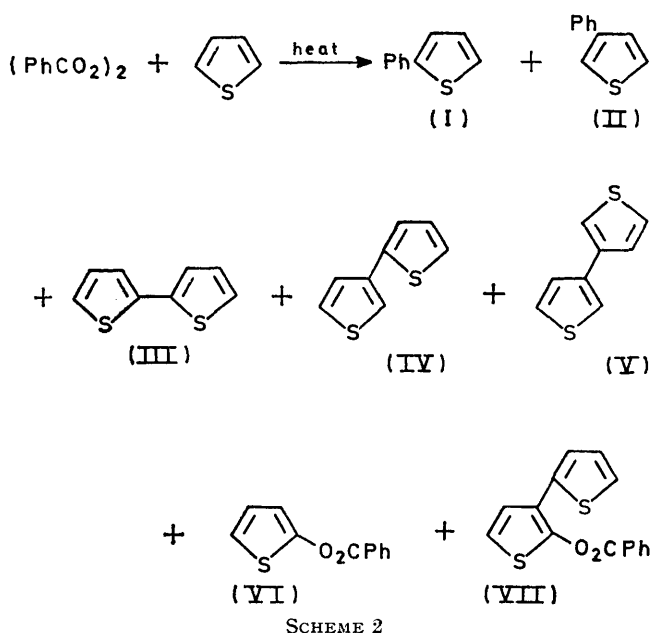
<sup>6</sup> See, e.g., K. C. Bass and P. Nababsing, *Adv. Free Radical Chem.*, 1972, **4**, 1; G. Vernin, H. J. M. Dou, and J. Metzger, *Bull. Soc. chim. France*, 1972, 1173.

<sup>7</sup> G. Vernin, H. J. M. Dou, and J. Metzger, *Bull. Soc. chim. France*, 1967, **12**, 4514.

of benzoyl peroxide in thiophen has been proposed by Mackay.<sup>4b</sup>

We report the results of investigations from which we believe it can be concluded that 2-thienyl radicals are not involved in this reaction, and that bithienyls are formed in an entirely different way.

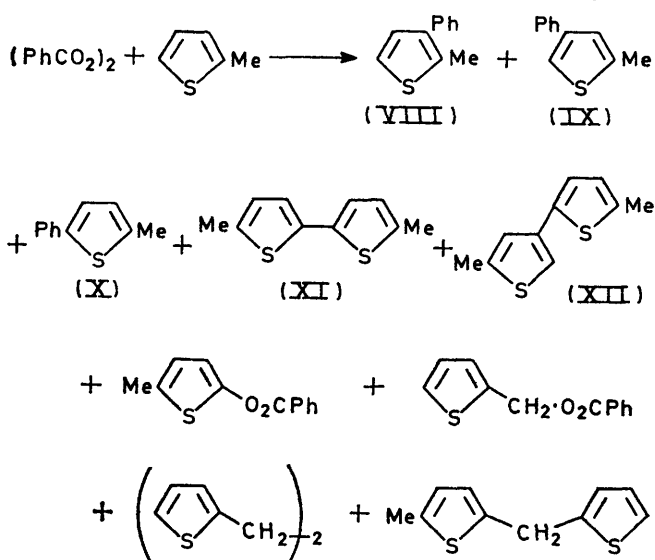
Benzoyl peroxide was allowed to decompose in thiophen at 80 °C and the reaction mixture was carefully examined by g.l.c. and column chromatography. The products reported in Scheme 2 were separated and identified. The main products were the previously reported 2-thienyl benzoate and 2,2'-bithienyl; these were, however, accompanied by 2,3'- and 3,3'-bithienyls (the latter cannot be easily explained by Griffin's mechanism) and also by 2- and 3-phenylthiophen (in the ratio 92 : 8 as



expected for a 'normal' phenylation reaction).<sup>2</sup> A further product, formed in considerable amount, was identified as 2-benzoyloxy-2',3'-bithienyl (VII) by spectroscopic methods and by comparison with the benzoyloxylation products obtained from the decomposition of benzoyl peroxide in 2,2'-, 2,3'-, and 3,3'-bithienyl. An analogous decomposition carried out in 2-methylthiophen gave interesting results: only the products shown in Scheme 3 were separated, and no 5,5'-dimethyl-2,2'-bithienyl (which, according to Griffin's mechanism should be one of the major components of the reaction mixture) was identified; the ratios of phenylation products [(VIII) : (IX) : (X) : (XI) : (XII)] are consistent with expectation.<sup>3a</sup>

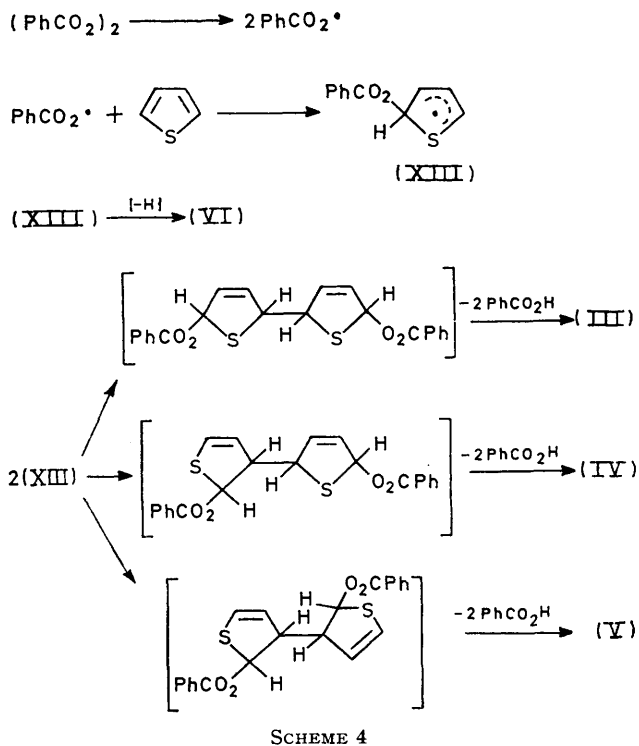
Benzoyl peroxide was then decomposed in thiophen in the presence of monosubstituted benzenes. Thienyl radicals have been proved to be quite reactive toward benzene derivatives,<sup>8</sup> behaving as aromatic free radicals like phenyl; the presence of 2-thienyl radicals in our reaction mixture should therefore have given rise, beside the products reported in Scheme 2, to a mixture of 2-aryl-

thiophens. These products were not found, and we consider this to demonstrate that 2,2'- and 2,3'-dithienyl are



not formed through substitution on thiophen by a 2-thienyl radical.

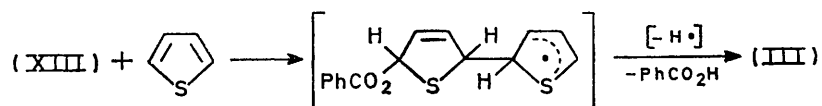
The presence of bithienyls in the reaction products can be better rationalised in terms of a process involving dimerisation of the relatively stable  $\sigma$ -complex (XIII),



followed by a non-radical fragmentation with loss of benzoic acid (Scheme 4). This process is similar to that

<sup>8</sup> L. Benati and M. Tiecco, *Boll. sci. Fac. Chim. ind. Bologna*, 1966, **24**, 225.

proposed by De Tar and his co-workers<sup>9</sup> for the formation of binaphthyls in the reaction of naphthalene with benzoyl peroxide. An alternative scheme (Scheme 5) involves homolytic substitution on thiophen by the  $\sigma$ -complex (XIII). Substitution could take place at the 2- or the 3-position of thiophen, and the reacting centre of (XIII) could be either the 5- or the 2-position. The  $\sigma$ -complex (XIII) can be considered as a cyclic allyl radical; allyl radicals do in fact substitute the thiophen nucleus, giving 2- and 3-allylthiophens in the ratio 65 : 35.<sup>10</sup>



SCHEME 5

Schemes 4 and 5 are probably both operating, though in some cases, such as the formation of the bithienyl (XII) in the reaction of 2-methylthiophen, Scheme 5 is more likely.

Indirect proof is available to support the foregoing interpretation. The low yields of phenylation products (*ca.* 3%) and the formation of considerable amounts of compounds containing benzoyloxy-groups indicate that benzoyloxy radicals are efficiently trapped before fragmentation to CO<sub>2</sub> and phenyl radicals. The role of the  $\sigma$ -complex (XIII) in the reaction was well demonstrated by experiments where benzoyl peroxide was allowed to decompose in thiophen in the presence of suitable reactants which could efficiently trap (XIII). Working in the presence of nitrosobenzene, which acts as a powerful dehydrogenating agent to give stable nitroxides,<sup>11</sup> the yield of 2-thienyl benzoate was considerably increased, and formation of bithienyls and of (VII) was strongly reduced. Similar results were obtained with other radical scavengers.

The benzoyloxy  $\sigma$ -complex (XIII) could be derived not only by scavenging of benzoyloxy radicals by thiophen (Scheme 4), but also from a one-electron transfer reaction between benzoyl peroxide and thiophen (as proposed in the first step of Scheme 1), followed by coupling between the thiophen radical cation and the benzoate anion. In order to test this possibility, diacetyl peroxide was allowed to decompose in thiophen under similar conditions. The rate of loss of CO<sub>2</sub> from acyloxy radicals is known to be nearly diffusion-controlled (rate coefficient  $1.6 \times 10^9 \text{ s}^{-1}$ );<sup>12</sup> since the homolytic substitution reaction is much slower, the formation of large quantities of

<sup>9</sup> D. F. De Tar and R. A. J. Long, *J. Amer. Chem. Soc.*, 1958, **80**, 4742.

<sup>10</sup> C. M. Camaggi and R. Leardini, in preparation.

<sup>11</sup> G. R. Chalfont, D. H. Hey, K. S. Y. Liang, and M. J. Perkins, *J. Chem. Soc. (B)*, 1971, 233.

<sup>12</sup> W. Braun, L. Rajbenback, and F. R. Eirich, *J. Phys. Chem.*, 1962, **66**, 1591.

<sup>13</sup> P. Davis, M. G. Evans, and W. C. E. Higginson, *J. Chem. Soc.*, 1951, 2563.

<sup>14</sup> J. R. Lindsay Smith and R. O. C. Norman, *J. Chem. Soc.*, 1964, 4857.

<sup>15</sup> C. D. Hurd and K. L. Krauz, *J. Amer. Chem. Soc.*, 1950, **72**, 5543.

acyloxythiophen and bithienyls would support the electron-transfer mechanism for the first step of this reaction. However, only 2-methylthiophen was formed in good yield, indicating that the formation of (XIII) takes place mainly by direct attack of the benzoyloxy radical on the thiophen nucleus.

On the basis of the new data discussed we conclude that the hypothesis of the intervention of 2-thienyl radicals in the reaction of benzoyl peroxide with thiophen must be excluded. It seems sufficiently proven that bithienyls are formed through the  $\sigma$ -complex (XIII). This kind of

dimerisation-elimination route to biaryls in homolytic substitution reactions seems to be general when the attacking radical forms a relatively weak bond with the substrate in the  $\sigma$ -complex. The formation of biaryls in the homolytic amination<sup>13</sup> and hydroxylation<sup>14</sup> of aromatic substrates might well be rationalised in this way.

#### EXPERIMENTAL

G.l.c. analyses and separations were carried out on Varian 1400 and 712 Gas Chromatographs. N.m.r. spectra were recorded on JEOL 60 and 100 MHz instruments.

The following materials were prepared according to literature methods: 2-benzoyloxythiophen,<sup>15</sup> 2-acetoxythiophen,<sup>15</sup> 2,2'-,<sup>16</sup> 2,3'-,<sup>17</sup> and 3,3'-bithienyls,<sup>18</sup> the isomeric phenylthiophens and methylphenylthiophens,<sup>3a</sup> 5,5'-dimethyl-2,2'-bithienyl,<sup>19</sup> 5,5'-dimethyl-3,3'-bithienyl,<sup>20</sup> 2-thienyl benzoate,<sup>21</sup> and 2-methyl-5-(2-thenyl)thiophen.<sup>22</sup>

**5,5'-Dimethyl-2,3'-bithienyl.**—To an ethereal solution of the Grignard reagent obtained from 2-bromo-5-methylthiophen (27 g) and magnesium (3.6 g) in dry ether was slowly added methyl propyl ketone (12.9 g). The mixture was refluxed for 1 h, then stirred overnight. After hydrolysis (10% hydrochloric acid) the ethereal layer was dried (Na<sub>2</sub>SO<sub>4</sub>) and concentrated. Distillation (77—79 °C at 3 mmHg) of the residue gave a carbinol (22 g), which was treated directly with sulphur (15 g) in an oil-bath at 200—220 °C. After 24 h the residue was chromatographed on silica to give the product (4 g), m.p. 73—75°, whose n.m.r. and mass spectra were consistent with the required structure (Found: S, 61.7; H, 5.1; S, 33.1. C<sub>10</sub>H<sub>10</sub>S<sub>2</sub> requires C, 61.85; H, 5.2; S, 33.0%).

**Decomposition of Benzoyl Peroxide in Thiophen.**—A solution of benzoyl peroxide (14 g) in thiophen (200 ml) was

<sup>16</sup> H. Winberg and A. Logothetis, *J. Amer. Chem. Soc.*, 1956, **78**, 1958.

<sup>17</sup> H. Winberg, A. Logothetis, and D. Ver Ploeg, *J. Amer. Chem. Soc.*, 1957, **79**, 1972.

<sup>18</sup> S. Gronowitz and H. O. Karlsson, *Arkiv Chemi*, 1960, **17**, 89.

<sup>19</sup> R. E. Atkinson, P. F. Curtis, and G. T. Phillips, *J. Chem. Soc. (C)*, 1967, 2011.

<sup>20</sup> S. Gronowitz and H. Frostling, *Acta Chem. Scand.*, 1962, **16**, 1127.

<sup>21</sup> T. L. Cairns and B. C. McKusick, *J. Org. Chem.*, 1950, **15**, 790.

<sup>22</sup> Ya. L. Gol'dfarb and P. A. Konstantinov, *Izvest. Akad. Nauk S.S.S.R., Otdel. Khim. Nauk*, 1956, 992.

heated in a sealed tube at 80° for 5 days. The mixture was then extracted with aqueous 5% sodium hydrogen carbonate to give benzoic acid (7.60 g) after acidification of the aqueous layer. The organic layer was concentrated and the residue was fractionated by combined column chromatography and g.l.c. The following products were separated and identified by comparison with authentic specimens: 2-phenylthiophen (0.55 g), 3-phenylthiophen (0.06 g), 2,2'- (1.85 g), 2,3'- (1.20 g), and 3,3'- (0.25 g) bithienyls, and 2-thienyl benzoate (1 g). A further product, m.p. 129—131°, was identified as 2-benzoyloxy-2',3'-bithienyl on the basis of n.m.r. data, high resolution mass spectrum, and elemental analysis (Found: C, 62.7; H, 3.8.  $C_{15}H_{10}O_2S_2$  requires C, 62.8; H, 3.5%).

*Decomposition of Benzoyl Peroxide in Thiophen in the Presence of Monosubstituted Benzenes.* Thiophen (2 ml), methyl benzoate (2 ml), and benzoyl peroxide were kept at 80 °C for 3 days. G.l.c. analysis led to the identification of compounds (I)—(VII); no methoxycarbonylphenylthiophens (prepared for comparison as reported in the literature) were detected. Analogous results were obtained in the presence of anisole or t-butylbenzene.

*Decomposition of Benzoyl Peroxide in 2-Methylthiophen.*—Benzoyl peroxide (7 g) was allowed to decompose in 2-methylthiophen (100 ml) at 80 °C for 3 days. After work-up the following products were identified by g.l.c. retention times and i.r. and/or u.v. spectra: benzoic acid (3.8 g), isomeric phenyl-2-methylthiophens (VIII), (IX), and (X) in the ratio 76 : 4 : 20, 5,5'-dimethyl-3,3'-bithienyl (XI), 5,5'-dimethyl-2,3'-bithienyl (XII), 1,2-bis(2-thienyl)ethane, 2-methyl-5-(2-thienyl)thiophen, 5-methyl-2-thienyl benzoate (1.95 g), and 2-thienyl benzoate (0.3 g). No positive identification was possible for 5,5'-dimethyl-2,2'-bithienyl. Owing to the great number of partially overlapped peaks in this g.l.c. analysis, three different columns were used: 5% FFAP (3 m), 5% LAC 728 (3 m), and (2.5% Bentone 34-2.5% FFAP) (3 m) on Varian Varaport 30 (80—100 mesh).

*Decomposition of Benzoyl Peroxide in Thiophen in the Presence of Oxidising Agents.*—Benzoyl peroxide (0.7 g) was allowed to decompose in thiophen (10 ml) at 80 °C, in the presence of nitrosobenzene (0.1 g) or copper(II) chloride (0.5 g). The mixtures were then analysed for benzoic acid (titration) and bithienyls and phenylthiophens. Results are reported in the Table.

*Decomposition of Diacetyl Peroxide in Thiophen.*—A solution of diacetyl peroxide (4 g) in thiophen (100 ml) was

refluxed for 24 h and then directly analysed by g.l.c. [5 m, 5% FFAP on Aeropak 30 (80—100) mesh]. 2-Methylthiophen (10% yield) was easily identified by its g.l.c. retention time and low resolution mass spectrum (Varian MAT III). A search for bithienyls was then made; several peaks were present at low attenuation with retention times nearly consistent with bithienyls, but the low concentration of

Effect of oxidising agents on product distribution in the decomposition of benzoyl peroxide in thiophen

Oxidising agent	Benzoyl peroxide (g)	Benzoic acid (g)	Thienyl benzoate (g)	Ratio of phenylthiophens to bithienyls
None	0.7	0.4	0.05	16 : 84
PhNO	0.7	0.55	0.15	55 : 85
CuCl <sub>2</sub>	0.7	0.5	0.20	75 : 14

these products (not more than 1 : 30 with respect to methylthiophen) did not allow positive mass spectrometric identification. No acetoxythiophen was detected by t.l.c.

*Decomposition of Benzoyl Peroxide in Bithienyls.*—(a) 2,2'-Bithienyl. Benzoyl peroxide (8 g) and 2,2'-bithienyl (8 g) were allowed to react at 80 °C for 5 days. The mixture, after extraction of benzoic acid, was chromatographed on silica and two main products were separated and identified: 5-benzoyloxy-2,2'-bithienyl, m.p. 104—107 °C, identical with an authentic specimen prepared from 5-hydroxy-2,2'-bithienyl<sup>24</sup> (Found: C, 62.35; H, 3.45. Calc. for  $C_{15}H_{10}O_2S_2$ : C, 62.9; H, 3.5%) and  $\alpha$ -quaterthienyl, m.p. 210—211°.

(b) 2,3'-Bithienyl. Benzoyl peroxide (2 g) and 2,3'-bithienyl (8 g) in ethyl acetate (10 ml) were allowed to react at 80 °C for 5 days. After work-up as above, a product of m.p. 129—131° was separated, identical with the benzoyloxybithienyl obtained in the decomposition of benzoyl peroxide in thiophen (Found: C, 62.8; H, 3.75%).

(c) 3,3'-Bithienyl. The reaction was carried out as in (b); material of m.p. 121—123°, whose i.r., n.m.r., and mass spectra were consistent with identification as 3,3'-bithienyl-2-yl benzoate, was separated (Found: C, 63.15; H, 3.3.  $C_{15}H_{10}O_2S_2$  requires C, 62.8; H, 3.5%).

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