# Nucleophile-induced Cyclisation of 2-Diazo-2'-thiocyanatoacetophenone: 2-(Cyanohydrazono)- and 2-(Triphenylphosphoranylidenehydrazono)-benzo[b]thiophen-3(2H)-one

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2-Diazo-2'-thiocyanatoacetophenone (Va) dissolves in cold dilute alkali and acidification of the solution provides 2-(cyanohydrazono)benzo[b]thiophen-3(2H)-one (IXa). The potassium salt of the latter, obtained by the interaction of the diazo-ketone and potassium cyanide. on acidic hydrolysis gives 2-semicarbazonobenzo[b]-thiophen-3(2H)-one (IXc). identical with that obtained by condensing 2.2-dibromobenzo[b]thiophen-3(2H)-one (VIIc) with semicarbazide. With triphenylphosphine the diazo-ketone gives the expected adduct. which on brief boiling with methanol suffers elimination of hydrocyanic acid to provide 2-(triphenylphosphoranylidene-hydrazono)benzo[b]thiophen-3(2H)-one (VIIIb). The potassium salt of 2-(cyanohydrazono)indane-1,3-dione (IIb) is obtained by an analogous reaction of potassium cyanide with 2-diazo-2'-(methoxycarbonyl)-acetophenone. the triphenylphosphine adduct of which, however. did not cyclise. It is suggested that these cyclisations proceed by nucleophilic attack at the terminal nitrogen atom of the diazo-function rather than by deprotonation of the diazo-carbon atom.

IT has been shown recently that 2-diazoacetophenones possessing an *ortho*-substituent susceptible to attack by a carbanion undergo cyclisation on treatment with alkali, *e.g.* (Ia) ⟶ (IIa) and (III) ⟶ (IV). Although it has been suggested that cyclisation of the ester (Ia) proceeds *via* a diazoacetyl carbanion [1] (I), and that of the nitrile (III) *via* a 1,3-dipolar reaction [2] (Scheme 1), in
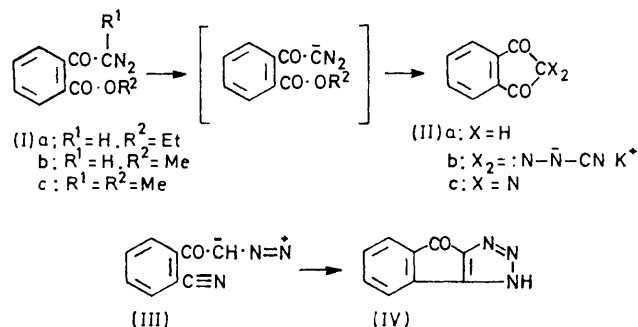
SCHEME 1

neither case is the evidence conclusive. It was therefore of interest to determine whether 2-diazo-2'-thiocyanatoacetophenone (Va) would, when treated with alkali, behave in a manner analogous to the simple cyano-derivative (III) (Scheme 1) or cyclise to a benzo-[b]thiophen derivative consequent on nucleophilic displacement of the cyano-group from the sulphur atom [(Va) ⟶ (VIa) ⟶ (VIIa)] as apparently does *o*-thiocyanatoacetophenone [3] [(Vb) ⟶ (VIb) ⟶ (VIIb)] (Scheme 2).
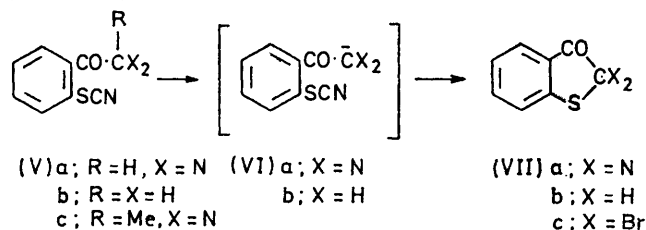
SCHEME 2

There was some tarring when the thiocyanato-diazo-ketone (Va) was treated with ice-cold dilute alkali; but the majority of it dissolved readily and acidification of the filtered solution provided the cyanohydrazone (IXa). This result might be rationalised in terms of nucleophilic attack of the diazoacetyl carbanion in (VIa) on the sulphur atom of the adjacent thiocyanato-group with concerted transfer of the cyano-group to the terminal nitrogen atom of the diazo-function [(VIa) ⟶ (VIIIa)]. An alternative process involves separation of cyanide ion from (VIa) and its subsequent addition to the intermediate α-diazo-β-keto-sulphide [(VIa) ⟶ (VIIa) ⟶ (VIIIa)]. Diazo-compounds of the type (VIIa) have not been described in the literature, but unpublished [4] work indicates that, under conditions not dissimilar to those used in the present study, they are too unstable to be isolated and that their decomposition products are complex and sometimes tarry. The modest yield and the presence of tar in our experiment with the thiocyanato-diazo-ketone (Va) prompted us to treat it with concentrated aqueous potassium cyanide,
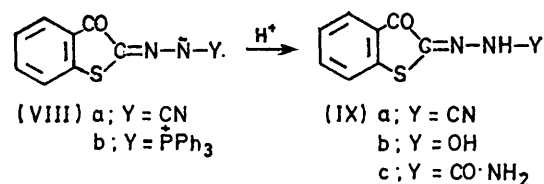
which in addition to being alkaline, would provide cyanide ion to supplement that released from the sulphur atom, and hence more effectively trap any diazo-keto-sulphide (VIIa) by converting it into cyanohydrazone anion (VIIIa). The reaction was then much cleaner and an improved yield of the cyanohydrazone (IXa) was obtained. This result does not necessarily, however, support the ionisation mechanism (VIa) ⟶ (VIIa) ⟶ (VIIIa) as opposed to the concerted mechanism (VIa) ⟶ (VIIIa), since the conditions used are precisely those described by Wolff [5] for the conversion

[1] T. L. Burkoth, *Tetrahedron Letters*, 1969, 5049, and references therein.
[2] G. Holt and D. K. Wall, *J. Chem. Soc.*, 1965, 1428.
[3] F. Arndt, A. Kirsch, and P. Nachtweg, *Ber.*, 1926, **59**, 1074.
[4] G. Heyes, Ph.D. Thesis, Manchester, 1972.
[5] L. Wolff, *Annalen*, 1902, **325**, 129.

of simple 2-diazoacetophenones into the corresponding cyanohydrazones [(XI) ⟶ (XII) ⟶ (XIII; Y = CN)], *i.e.* for cyanide ion attack on the terminal nitrogen atom of the diazo-function. If this happened with the

(X) a; R = H, Y = CN
b; R = H, Y = $\overset{+}{P}Ph_3$
c; R = H, Y = OH
d; R = Me, Y = $\overset{+}{P}Ph_3$
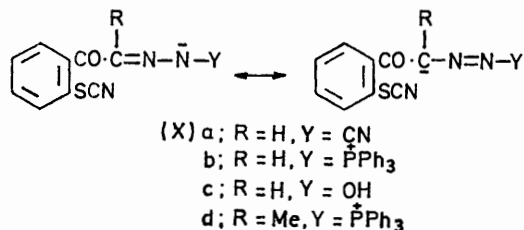
thiocyanato-diazo-ketone (Va) the first formed acyclic cyanohydrazone anion (Xa) could cyclise *via* its carb-anionic canonical form with displacement of cyanide ion

(XII)
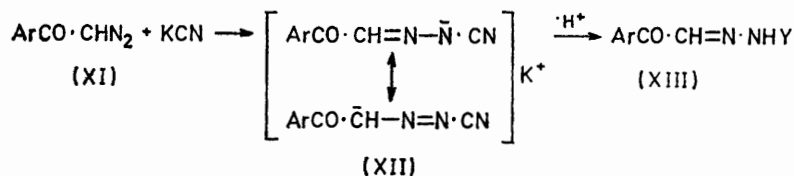
from the sulphur atom and loss of a proton to furnish the observed product (VIIIa). In terms of this mechanism, therefore, the overall process (Va) ⟶ (Xa) ⟶ (VIIIa) is catalysed by cyanide ion.

The implication that the cyclisation is induced by nucleophilic attack at the terminal nitrogen atom of the diazo-function led us to investigate the interaction of the thiocyanato-diazo-ketone (Va) and triphenylphos-phine, since the latter is known [6] to attack diazo-ketones in this way; its basicity is, however, low and it could not therefore be expected to generate the diazoacetyl carbanion (VIa). The product was the acyclic thio-cyanato-phosphoranylidenehydrazone (Xb), which, on brief boiling with methanol, underwent elimination of hydrocyanic acid and provided the cyclic phosphoranyl-idenehydrazone (VIIIb). In this instance, it is apparent that the cyclisation was initiated by attack of triphenyl-phosphine on the terminal nitrogen atom of the diazo-group, and it is difficult to avoid the conclusion that cyanide ion functions in a similar way; in the latter case the process is catalytic and it is possible that in dilute alkali also, initial attack of hydroxide ion occurs on the terminal nitrogen atom of the diazo-function to give an anion (Xc), cyclisation of which [(Xc) ⟶ (IXb)] generates cyanide ion which then continues the reaction. Anions analogous to (Xc) have been postu-lated [7] as intermediates in the decomposition of 2-diazo-acetophenone in aqueous alkali.

The addition product (XII; Ar = Ph) of 2-diazo-acetophenone (XI; Ar = Ph) and potassium cyanide was prepared and treated with very dilute acid to give the free cyanohydrazone (XIII; Ar = Ph, Y = CN) and with more concentrated acid to give the ' amide ' (XIII; Ar = Ph, Y = CONH₂).[5] Under identical con-

ditions, our potassium salt (VIIIa) also yielded the free cyanohydrazone (IXa) and the amide (IXc). The structure of the latter was confirmed by its identity with the product obtained by condensing 2,2-dibromo-benzo[b]thiophen-3(2H)-one (VIIc) with semicarbazide; the i.r. spectra of the potassium salt (VIIIa), the cyano-hydrazone (IXa), and the amide (IXc) showed satis-factory correlation with those of the corresponding derivatives (XII; Ar = Ph), (XIII; Ar = Ph, Y = CN or CO·NH₂), prepared from 2-diazoacetophenone (XI; Ar = Ph) and potassium cyanide.

The interaction of thiocyanato- and diazoacetyl groups under the influence of either potassium cyanide or triphenylphosphine is a consequence of their juxta-position, since under conditions where the intramolecular reaction proceeds readily, the addition of potassium cyanide to a mixture of 2-diazoacetophenone (XI; Ar = Ph) and phenyl thiocyanate gave a high yield of the potassium salt of 2-(cyanohydrazono)acetophenone (XII; Ar = Ph) and the thiocyanate was not in-corporated. Again, in contrast to the rapid and nearly quantitative cyclisation of the triphenylphosphoranyl-idenehydrazone (Xb), boiling a solution of phenyl thiocyanate and the triphenylphosphine adduct of 2-diazo-4'-nitroacetophenone (XI; Ar = 4'-NO₂·C₆H₄) slowly gave a complex mixture of products including methyl phenyl sulphide, triphenylphosphine oxide, and the hydrazone (XIII; Ar = 4'-NO₂·C₆H₄, Y = H).

The foregoing results prompted us to study the action of potassium cyanide and of triphenylphosphine on the ester diazo-ketone (Ib). As with the thiocyanato-derivative (Va), cyclisation proceeded very readily with potassium cyanide, and the product (IIb) was identical with that from 2-diazoindane-1,3-dione (IIc) and potassium cyanide; the yield is apparently superior to that obtained by the simple base-promoted cyclisation of the diazo-ketone (Ia). With triphenylphosphine, the diazo-ketone (Ib) readily provided the expected acyclic phosphoranylidenehydrazone which, however, resisted all attempts at cyclisation.

The 2-diazopropiophenones (Ic) and (Vc), which cannot give a formal carbanion, did not cyclise with either potassium cyanide or triphenylphosphine. This observation does not necessarily imply that such a carbanion is involved in the cyclisation of the diazo-acetophenone derivatives (Ia) and (Va), since in the potassium cyanide reaction the products (IIb) and (VIIIa) are stabilised by loss of a proton from C-2. Cyclisation of the phosphoranylidenehydrazone (Xd) would require elimination of acetonitrile, which might be

[6] H. J. Bestmann, H. Buckshewski, and H. Leube, *Chem. Ber.*, 1959, **92**, 1345.

[7] P. Yates and B. L. Shapiro, *J. Amer. Chem. Soc.*, 1959, **81**, 212.

expected to be more difficult than loss of hydrocyanic acid from the diazoacetophenone derivative (VIIIb).

Although the substitution of an SCN group in an aromatic system leads to only a small (*ca.* 0·2 p.p.m.) downfield shift in the n.m.r. signals of the *ortho*-protons, when a carbonyl function is adjacent to the SCN group, the signal of the remaining *ortho*-proton is shifted *ca.* 0·6 p.p.m. downfield; this effect is being further investigated.

In the spectra of the phosphoranylidenehydrazones having the grouping −CH=N−N=PR₃, H,P coupling of 2·3 Hz was observed.

EXPERIMENTAL

I.r. spectra were recorded on a Perkin-Elmer 257 instrument and ¹H n.m.r. spectra on Perkin-Elmer R20 and Varian HA100 spectrometers. All the known compounds gave satisfactory analytical and spectroscopic data. For products marked with an asterisk, further spectral data are available in Supplementary Publication No. SUP 21143 (6 pp.).†

Diazo-ketones.—(*a*) *o*-Thiocyanatobenzoyl chloride, m.p. 106—108° (decomp.),[8] most conveniently prepared from the acid and phosphorous pentachloride in toluene,[9] when treated with diazomethane in ether under standard [10] conditions provided 2-*diazo-2′-thiocyanatoacetophenone* * (Va) (67%) (Found: C, 53·5; H, 2·7; S, 15·6. C₉H₅N₃OS requires C, 53·3; H, 2·5; S, 15·8%), m.p. 98—102° (decomp.), ν_max. 2154m (SCN), 2122s (diazo), and 1592s (CO) cm⁻¹, τ (CDCl₃) 1·8—2·7 (4H, m, aromatic) and 3·97 (1H, s, CO·CHN₂).

With toluene-*p*-sulphonic acid in acetic anhydride,[11] the diazo-ketone gave 2′-*thiocyanato-2-(p-tolylsulphonyloxy)-acetophenone* * (28%) (Found: C, 55·4; H, 3·9; N, 3·9; S, 18·5. C₁₆H₁₃NO₄S₂ requires C, 55·3; H, 3·7; N, 4·0; S, 18·5%), m.p. 146—148° (from ethanol), ν_max. 2150m (SCN), 1688s (CO), 1352s (SO₂), and 1179 (SO₂) cm⁻¹.

(*b*) A similar reaction between the acid chloride and diazoethane provided 2-*diazo-2′-thiocyanatopropiophenone* * (Vc) (73%) (Found: C, 55·0; H, 3·1; N, 19·1. C₁₀H₇N₃OS requires C, 55·3; H, 3·2; N, 19·3%), m.p. 85—86·5° (from ether), ν_max. 2155m (SCN), 2079s (diazo), and 1603s (CO) cm⁻¹, τ (CDCl₃) 2·0—2·8 (4H, m, aromatic) and 7·85 (3H, s, CO·CMeN₂). Under standard [12] conditions this diazo-ketone with silver nitrate provided 2′-*thiocyanatoacrylo-phenone* * (68%) (Found: C, 63·6; H, 3·9; N, 7·5. C₁₀H₇NOS requires C, 63·5; H, 3·7; N, 7·4), m.p. 55—55·5° [from light petroleum (b.p. 60—80°)], which with aniline in methanol gave 3-*anilino-2′-thiocyanatopropio-phenone* * (80%) (Found: C, 68·0; H, 5·0; N, 10·0. C₁₆H₁₄N₂OS requires C, 68·0; H, 5·0; N, 9·9%), m.p. 105—106° [from light petroleum (b.p. 60—80°)].

(*c*) 2-Diazo-2′-(methoxycarbonyl)propiophenone (Ic) was obtained as an oil by the action of diazoethane on *o*-methoxycarbonylbenzoyl chloride under the conditions previously described [13] for the corresponding diazoethane reaction.

† For details of Supplementary Publications see Notice to Authors No. 7 in *J.C.S. Perkin I*, 1973, Index issue.

[8] M. Renson and I. L. Piette, *Bull. Soc. chim. belges*, 1964, **73**, 507 (*Chem. Abs.*, 1964, 10,621f).

[9] H. J. Scheifele, jun. and D. F. De Tar, *Org. Synth.*, 1952, **32**, 8.

[10] See W. E. Bachmann and N. S. Struve, *Org. Reactions*, 1942, **1**, 38 for compilation of references.

2-(*Cyanohydrazono*)*benzo*[b]*thiophen*-3(2H)-*one* (IXa).— (*a*) To a stirred suspension of 2-diazo-2′-thiocyanatoaceto-phenone (1·02 g, 5·0 mmol) in water (25 ml) at 20—21° was added 0·1M-sodium hydroxide (75 ml). The mixture immediately became dark greenish yellow and after 30 min was filtered to remove tarry material. Cautious neutralisation of the filtrate with 0·1M-hydrochloric acid, during which there was no apparent nitrogen evolution, precipitated the *hydrazone* * (IXa) (0·55 g, 54%) (Found: C, 52·5; H, 2·4; S, 16·0. C₉H₅N₃OS requires C, 53·3; H, 2·5; S, 15·8%), collapses at 156° and chars with decomposition at 180°, ν_max. 3340m (NH), 2254m (CN), and 1713s (CO) cm⁻¹, τ [(CD₃)₂SO] 2·0—2·8 (4H, m, unresolved, aromatic) and 6·0—6·1br (1H, s, NH). Attempts to purify this compound, either by recrystallisation or by chromatography, were unsuccessful.

(*b*) To a suspension of 2-diazo-2′-thiocyanatoaceto-phenone (1·02 g, 0·005 mol) in ethanol (10 ml) at 22—23° was added potassium cyanide (0·65 g, 0·01 mol) in water (2 ml). A deep green colour developed immediately, heat was evolved, and a solid began to separate. After 12 h at 0°, the product (0·78 g, 65%), m.p. 216—221° (decomp.) was separated and crystallised from water to give (with much loss) potassium *N-cyano-N′-(2,3-dihydro-3-oxobenzo-[b]thiophen-2-ylidene)hydrazinide* * (VIIIa), m.p. 220—222°, ν_max. 2140s (CN) and 1628s (CO) cm⁻¹. A suspension of the salt (1 g) in water (40 ml) was added dropwise with vigorous swirling to concentrated sulphuric acid (6 g) and water (30 ml) at 0°. The resulting solid was separated and washed with water to provide the hydrazone (IXa) (0·64 g, 96%), identical (mixed m.p. and i.r. spectra) with that described in (*a*). The above procedure applied to 2-diazo-acetophenone gave, as described by Wolff,[5] potassium *N-cyano-N′-phenacylidenehydrazinide* * (XII; Ar = Ph), ν_max. 2180m (CN), 1609s (CO) cm⁻¹, and 2-(cyanohydrazono)-acetophenone * (XIII; Ar = Ph, Y = CN), ν_max. 3220m (NH), 2228w (CN), and 1648s (CO) cm⁻¹.

2-*Semicarbazonobenzo*[b]*thiophen*-3(2H)-*one* (IXc).— (*a*) 2,2-Dibromobenzo[b]thiophen-3(2H)-one [14] (1·60 g, 5·2 mmol) was stirred for 1 h in ethanol (20 ml) and water (20 ml) containing semicarbazide hydrochloride (0·58 g, 5·2 mmol) and anhydrous sodium acetate (1·28 g, 15·6 mmol). The crude product (0·48 g), m.p. 228—231°, separated and a part of it (0·33 g) was chromatographed on silica gel (100 g; 2 × 50 cm). Elution with chloroform gave a red solid (0·21 g), m.p. 250°, whose i.r. spectrum was identical with that of thioindigo. The silica gel was extracted with chloroform–methanol (10:1) to give a yellow solid (0·10 g), m.p. 234—236° (decomp.). Recrystallisation from ethanol (charcoal) gave yellow needles of the *semicarbazone* * (IXc) (Found: C, 48·9; H, 3·3; N, 18·8; S, 14·5. C₉H₇N₃O₂S requires C, 48·9; H, 3·2; N, 19·0; S, 14·5%), m.p. 240—242° (decomp.), ν_max. 3466m (NH), 3275w and 3230w (amide NH), and 1747s and 1703s (CO) cm⁻¹.

(*b*) Potassium *N-cyano-N′-(2,3-dihydro-3-oxobenzo[b]-thiophen-2-ylidene)hydrazinide* (VIIIa) (0·50 g) in water (8 ml) was added in portions to boiling 2M-sulphuric acid (8 ml). The resultant brown solid (0·45 g), m.p. 217—222° (decomp.), was separated from the hot solution and purified

[11] A. L. Crowther and G. Holt, *J. Chem. Soc.*, 1963, 2818.

[12] P. McC. Duggleby, G. Holt, M. A. Hope, and A. Lewis, *J.C.S. Perkin I*, 1972, 3020.

[13] P. McC. Duggleby and G. Holt, *J. Chem. Soc.*, 1962, 3579.

[14] A. Bezdrik, P. Friedländer, and P. Koeniger, *Ber.*, 1908, **41**, 27.

as in (a) to provide thioindigo (0·1 g) and the product (0·33 g), m.p. 227—229°, which, after recrystallisation from ethanol, was identical (mixed m.p. and i.r. spectra) with the semicarbazone (IXc) obtained in (a). Under the same conditions, potassium N-cyano-N'-phenacylidenehydrazinide (XII; Ar = Ph) provided 2-semicarbazonoacetophenone * as described by Wolff,[5] $v_{max.}$ 3413m (NH), 3160w (amide NH), and 1694s (CO) cm⁻¹.

2-*Diazo*-2'-*(methoxycarbonyl)acetophenone and Potassium Cyanide.*—Treatment of this diazo-ketone with potassium cyanide as described in (b) gave [9] potassium N-cyano-N'-(1,3-dioxoindan-2-ylidene)hydrazinide * (IIb) identical with that obtained under similar conditions from 2-diazoindane-1,3-dione [15] and potassium cyanide. A freshly prepared sample showed the expected i.r. spectral characteristics, but in air it rapidly became oily.

Diazo-ketones and Triphenylphosphine.—(a) 2-*Diazo*-2'-*thiocyanatoacetophenone*. To this diazo-ketone (2·03 g, 10 mmol) in dry ether (50 ml), triphenylphosphine (2·62 g, 10 mmol) in dry ether (20 ml) was added all at once. The mixture was stirred for 2 h at 20—21°, filtered to remove a little tarry material, and then cooled to *ca.* −10°; there then precipitated 2'-*thiocyanato*-2-*(triphenylphosphoranylidenehydrazono)acetophenone* * (Xb) (3·3 g, 72%), m.p. 123—125°. Traces of impurities were removed by dissolution in ether at 20° and cooling the solution to −60°; the pure product (m.p. 125—127°) then separated (Found: C, 69·5; H, 4·2; N, 9·0. $C_{27}H_{20}N_3OPS$ requires C, 69·6; H, 4·3; N, 9·0), $v_{max.}$ 2160m (SCN), 1608s (CO), and 1493s cm⁻¹, τ (CDCl₃) 1·75 (1H, CO·CHN₂P) and 2·05—2·75 (19H, aromatic).

The product (Xb) (1 g) gradually (10 min) dissolved in boiling methanol or ethanol (20 ml) while the initially yellow solution became dark red-brown and hydrogen cyanide was evolved. A solid began to separate from the still hot solution, which was cooled and filtered to provide 2-*(triphenylphosphoranylidenehydrazono)benzo*[b]*thiophen*-3(2H)-*one* * (VIIIb) (92%) (Found: C, 71·7; H, 4·7; N, 6·8. $C_{26}H_{19}N_2OPS$ requires C, 71·3; H, 4·4; N, 6·4%), m.p. 196—199° (decomp.) (from ethanol), $v_{max.}$ 1660s (CO) (no SCN absorption), τ [(CD₃)₂SO] 1·8—2·8 (m, aromatic).

(b) The following phosphoranylidenehydrazones were prepared according to the general conditions of Bestmann: [6] 2'-*thiocyanato*-2-*(triphenylphosphoranylidenehydrazono)propiophenone* * (Xd) (90%), m.p. 154—156° (decomp.) (Found: C, 69·9; H, 4·6; N, 8·6. $C_{28}H_{22}N_3OPS$ requires C, 70·1; H, 4·6; N, 8·7%), $v_{max.}$ 2160s (SCN), 1605s (CO), and 1519s cm⁻¹, τ (CDCl₃) 2·2—2·7 (19H, aromatic) and 7·7 (3H, MeC·CO); 2'-*(methoxycarbonyl)*-2-*(triphenylphosphoranylidenehydrazono)acetophenone* * (92%), m.p. 140—142° (Found: C, 71·5; H, 5·0; N, 5·9. $C_{28}H_{23}N_2O_3P$ requires C, 72·1; H, 4·9; N, 6·0%), $v_{max.}$ 1718s (CO), 1634s (CO), and 1521s cm⁻¹, τ (CDCl₃) 1·15 (1H, CO·CHN₂P), 1·35—2·15 (19H, aromatic), and 6·05 (3H, OMe); 2'-*(methoxycarbonyl)*-2-*(triphenylphosphoranylidenehydrazono-propiophenone,*,* m.p. 152—155° (decomp.) (Found: 72·1; H, 5·2; N, 5·6. $C_{29}H_{25}N_2O_3P$ requires C, 72·5; H, 5·2; N, 5·8%), $v_{max.}$ 1718s (CO), 1636s (CO), and 1522m cm⁻¹, τ (CDCl₃) 1·35—2·20 (19H, aromatic), 6·0 (3H, OMe), and 7·4 (3H, CO·CMeN₂P).

[15] M. Regitz and G. Heck, *Chem. Ber.,* 1964, **97**, 1482.