3-Oxoindazolinylmethylenephosphoranes from Isatic Acids

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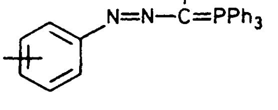
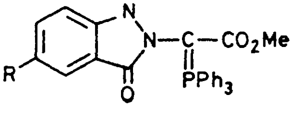
Coupling diazonium salts from isatic acids with alkoxycarbonylmethylenephosphoranes leads directly to 3-oxoindazolin-2-ylalkoxycarbonylmethylenephosphoranes.

The arylazomethylenetriphenylphosphoranes (**1**) can be prepared by coupling an aromatic diazonium salt with a stabilized phosphorus ylide.[1] It is also known that isatins, on treatment with sodium or potassium hydroxide, are easily transformed into the corresponding isatic acids, which may then be diazotized.[2] In order to prepare new arylazomethylenetriphenylphosphoranes, functionalized at the *ortho* position and suitable for the synthesis of heterocyclic compounds *via* intramolecular reactions, we decided to couple the diazonium salts from isatic acids with phosphorus ylides.†

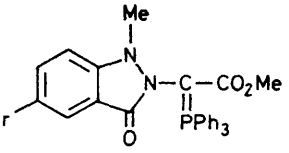
In this note we report the results obtained with isatin and 5-bromoisatin. The reaction was carried out by dropping a clear aqueous solution of the diazonium salt of the appropriate isatic acid into an alcoholic solution of methoxycarbonylmethylenetriphenylphosphorane, at 2—3 °C. The solution was then made basic with dilute NaOH solution. However, instead of the expected arylazo(methoxycarbonyl)methylenetriphenylphosphoranes we isolated the 3-oxoindazolin-2-yl(methoxycarbonyl)methylenetriphenylphosphoranes (**2a**) and (**2b**). Analytical data for compound (**2a**), m.p. 188—189 °C (from CH_2Cl_2–light petroleum) are consistent with the molecular formula $C_{28}H_{23}N_2O_3P$; ν_{max} (Nujol) 3100, 1637, and 1615 cm^{-1}; δ ($CDCl_3$ + Me_2SO) 3.25, 3.56 (3H, 2s, OMe), 6.8—8.0 (19H, m, aromatics), and 8.85, 9.01 (1H, 2s, NH). For compound (**2b**), m.p. 182—183 °C (from EtOH), analytical data are consistent with the molecular formula $C_{28}H_{22}BrN_2O_3P$; ν_{max} (Nujol) 1615 cm^{-1} (br.); δ ($CDCl_3$) 3.4, 3.6 (3H, 2s, OMe), 6.63—8.00 (18.5H, m, aromatics and NH), and 10.00 (0.5H, s, NH). The splitting of the signal for the CO_2Me methyl group observed in the ^1H n.m.r. spectra of (**2a**) and (**2b**) is in agreement with what has been reported for methoxycarbonylalkylidenephosphoranes,[3] which may also account for the NH splitting. Treatment of (**2b**) with MeI in the presence of K_2CO_3, in MeOH at room temperature, gave the 5-bromo-1-methyl-3-oxoindazolin-2-yl(methoxycarbonyl)methylenetriphenylphosphorane (**3**), m.p. 214—215 °C (from Pr^iOH). Analytical data for compound (**3**) are consistent with the molecular formula $C_{29}H_{24}BrN_2O_3P$; ν_{max} (Nujol) 1645 cm^{-1} (br.); δ ($CDCl_3$) 3.23, 3.27 (3H, 2s, NMe), 3.31, 3.55 (3H, 2s, OMe), and 6.60—7.96 (18H, m, aromatics). Compound (**3**) was obtained as well shaped crystals that were subjected to *X*-ray analysis.



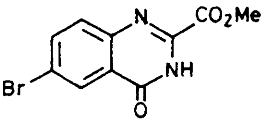
(**1**) **a**; $R^1 = o$-CHO, $R^2 = CO_2Me$



(**2**) **a**; R = H
b; R = Br



(**3**)



(**4**)

Crystal data: $C_{29}H_{24}BrN_2O_3P$, M = 559.4, orthorhombic, space group *Pbcn*, a = 30.898(10), b = 8.372(3), c = 20.455(5) Å, U = 5291.5 Å^3, Z = 8, D_c = 1.404 g cm^{-3}. The structure was solved by the heavy-atom method. Least-squares refinement of atomic positional‡ and thermal parameters (anisotropic Br, P, O, N, C; fixed H contributions) converged at R = 0.049 using 861 reflections measured on a Philips PW

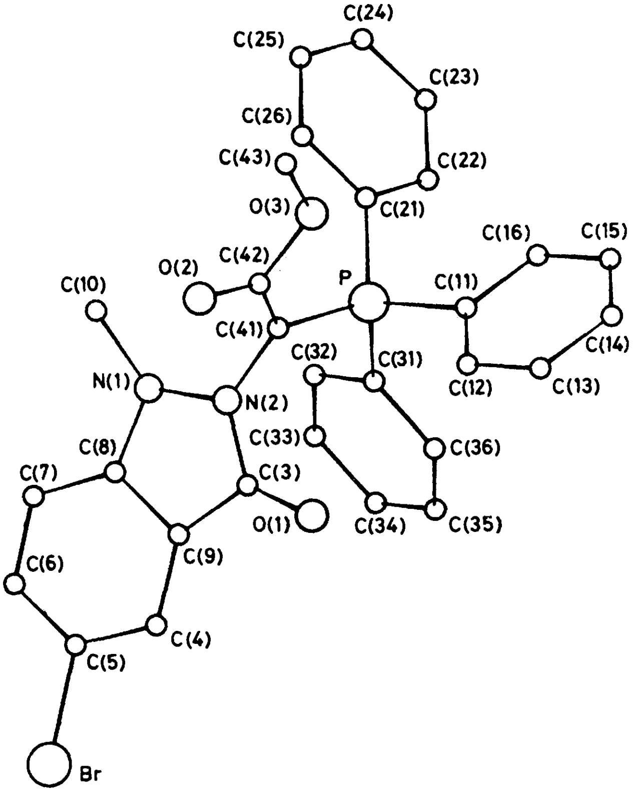


Figure 1. Projection of the structure on the (010) plane. Some pertinent bond lengths are: P–C(41) 1.71(2), C(41)–C(42) 1.37(3), and C(42)–O(2) 1.27(2) Å. All other bond distances appear to be normal.

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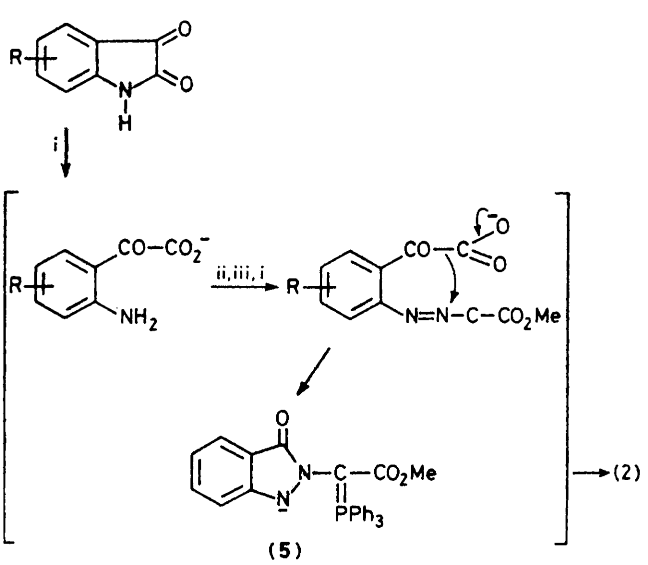
† To our knowledge coupling reactions of the diazonium salts of isatic acids have not been reported in the literature.

‡ The atomic co-ordinates for this work are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW. Any request should be accompanied by the full literature citation for this communication.

1100 four circle diffractometer (graphite monochromatized Mo-K_α radiation, $\lambda = 0.71069$ Å, ω scans, $\theta_{max} = 22.5°$). The phenyl rings of the PPh_3 group were considered to be rigid groups.

A view of the structure is shown in Figure 1. The main features of the structure of compound (**3**) from the *X*-ray analysis are: (i) the presence of an indazolinone ring which is nearly planar, as expected, apart from the C(10) atom which lies significantly out of the plane [0.60(2) Å] as a consequence of the pyramidal bonding around N(1), indicated by its displacement of 0.31(1) Å out of the plane C(8), C(9), N(2); (ii) the group of atoms P, C(41), C(42), O(2), O(3), C(43) is nearly planar. The plane formed by this group forms a dihedral angle of 102(1)° with that of indazolinone and therefore, there cannot be any conjugation between the two. The P–C(41) and C(41)–C(42) bond distances indicate some degree of π-delocalization over the P–C(41)–C(42) system. Indeed the C(41)–C(42) bond distance has considerable double bond character, and P–C(41) seems somewhat longer than a pure C=P double bond (*e.g.* 1.66 Å in $Ph_3P{=}CH_2$[4]). In the crystal the torsion angles P–C(41)–C(42)–O(2) and P–C(41)–C(42)–O(3) are −174(2)° and 9(3)°, respectively, indicating a *Z*-configuration.



Scheme 1. i, NaOH; ii, HNO_2; iii, $Ph_3P{=}CHCO_2Me$.

Compound (**2a**) is identical with the product m.p. 188—189 °C obtained by refluxing the 2-formylarylazo(methoxycarbonyl)methylenetriphenylphosphorane (**1a**) (R = *o*-CHO, $R^2 = CO_2Me$)[5] in toluene for 20 min. The structure of this product is therefore demonstrated. Interestingly, compound (**1a**) is not an intermediate in the reaction from isatic acids, as under the reaction conditions employed it is stable and its isolation, if formed, would have been quite easy.

A possible mechanism for the formation of compounds (**2**) from isatins is given in Scheme 1. The diazonium salts from isatic acids couple with the methoxycarbonyltriphenylphosphorane to give the intermediates (**5**), which cannot be isolated owing to the immediate splitting off of CO_2 and ring closure to give the products (**2**) in a concerted pathway. Compound (**2b**), heated in toluene solution at 90 °C for 3 h, gave 6-bromo-2-methoxycarbonyl-4-oxoquinazoline (**4**) and PPh_3, which is analogous to what has already been reported for (**2a**).[5]§ Analytical data for compound (**4**), m.p. 230—232 °C (from AcOH) are consistent with the molecular formula $C_{10}H_7BrN_2O_3$; ν_{max} (Nujol) 3170, 1735, 1670(br.), 1610, and 1600 cm^{-1}; δ (Me_2SO) 3.91 (3H, s, OMe), 7.72 (1H, d, 7-H), 8.00 (1H, d, 8-H), and 8.21 (1H, s, 5-H). The easy availability of the starting isatins should allow the synthesis of variously substituted oxoindazolinylmethylenephosphoranes, a new class of compounds that have already shown their usefulness in the synthesis of quinazoline derivatives.[5]

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§ This rearrangement is somewhat similar to that observed by R. Ramage for cyclic hydrazine derivatives (R. Ramage, personal communication).