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THE STAUDINGER REACTION OF *o*-AZIDOBENZALDEHYDE WITH TRIPHENYLPHOSPHINE REVISITED: INFLUENCE OF THE TEMPERATURE ON THE NATURE OF THE REACTION PRODUCTS.

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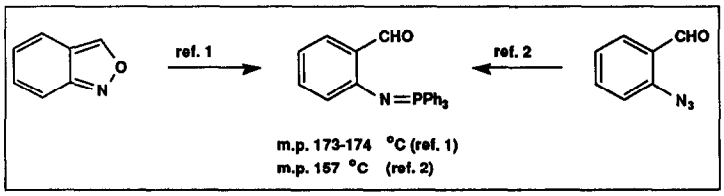
Abstract.– The reaction of *o*-azidobenzaldehyde **1** with TPP at 0°C leads to the expected iminophosphorane **2** and the indazole derivative **3** while at -20°C the phosphazide **4** was the only reaction product. The close related compounds **2** and **4** shows stricking differences in reactivity towards primary amines.

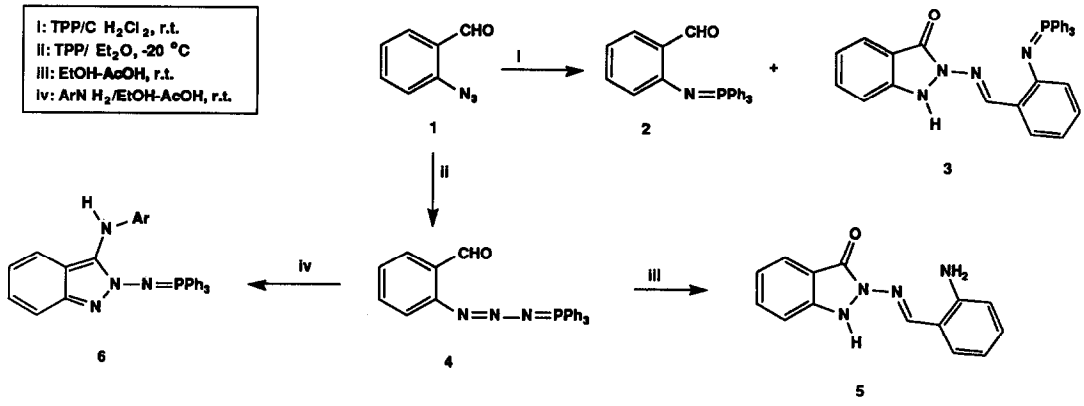
A recent work on the preparation and intramolecular aza-Wittig reaction of the iminophosphorane **2** derived from *o*-azidobenzaldehyde **1** prompts us to describe the products obtained in the Staudinger reaction between the *o*-azidobenzaldehyde and triphenylphosphine (TPP). In an earlier work[1] iminophosphorane **2** was prepared from anthranil and TPP in toluene solution at reflux temperature for 24h (m.p. 173-174°C, 42%) and recently Smalley et al[2]. claimed the preparation of **2** from **1** and TPP (m.p. 157°C, 88%).

In our hands, the reaction of *o*-azidobenzaldehyde **1** with TPP in dry dichloromethane at 0°C followed by chromatographic separation (silica gel and ethyl acetate/n-hexane as eluent) and purification gave *o*-(triphenylphosphoranyliden)amino benzaldehyde **2** (m.p. 175°C, 30%) and the iminophosphorane[3] **3** (m.p. 185°C, 25%). However, when the reaction was carried out in diethyl ether at -20°C the phosphazide **4** (m.p. 157°C, 65%) was isolated as only reaction product.[4]

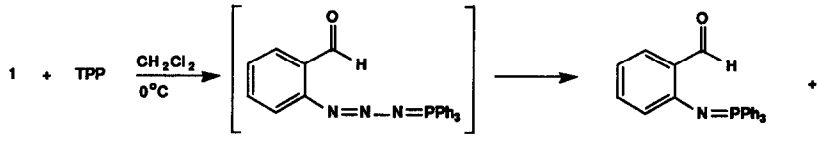
Physical and spectroscopic data of compound **2** (^{31}P n.m.r. δ 4.35 ppm) are in good agreement with the prepared from anthranil,[1] while phosphazide **4** has identical m.p. to the iminophosphorane reported by Smalley[2] for which no spectroscopic data are given. Compound **4** undergoes decomposition in chloroform solution at room temperature to give a mixture of **2** and **3**, whereas in DMSO-d_6 leads to **2** after nitrogen evolution, so n.m.r. date are not available, however, chemical evidence of structure **4** has been firmly stablished by the two following facts: *a)* compound **4** in ethanol in the presence of catalytic amounts of acetic acid at room temperature is converted into the aldimine[5] **5** (m.p. 210-211°C, 55%) and *b)* reaction with primary aromatic amines in ethanol at room temperature leads to the corresponding iminophosphorane **6** (Ar = 4-CH_3-C_6H_4, m.p. 214-

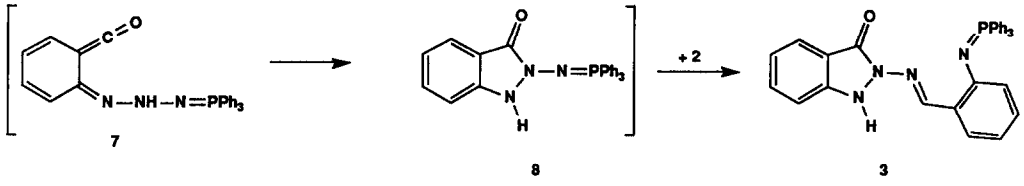


215°C, 40%) derived from 2-amino-3-arylamino-2H-indazole.[6]



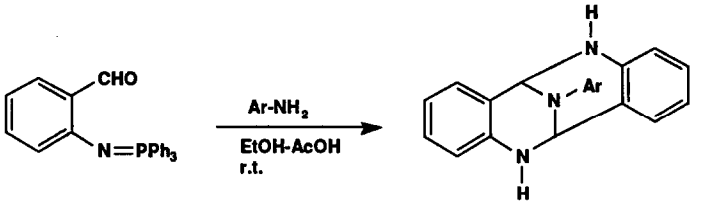
A tentative mechanisms for the conversion **1** → **2** + **3** could involve initial formation of the phosphazide **4** which after nitrogen evolution leads to **2**. Alternatively, the phosphazide **4** undergoes [1,5] proton shift to give **7** which cyclizes by nucleophilic attack of the amino group on the central carbon atom of the ketene moiety to give **8**. Finally, intermolecular aza-Wittig reaction between **2** and **8** leads to **3**. The formation of compound **5** can be understood by a similar way to **3** with hydrolytic cleavage of the iminophosphorane group at the late stage, while the formation of compound **6** involves initial condensation between the formyl and the amino groups followed by intramolecular trapping of the phosphazide moiety by the aldimine group as above is described.





Although iminophosphorane **2** contains the two reactive groups for the aza-Wittig reaction, it has been reported[2] that **2** itself made no intra- nor intermolecular aza-Wittig reaction. This stability is attibuted to the formation of a resonance-stabilized chelate-ring involving the iminophosphorane and the formyl

groups. However, we have found that iminophosphorane **2** undergoes self-condensation in the presence of aromatic amines in ethanol at room temperature to give the corresponding tricyclic compound **9** derived from the dibenzo[b,f][1,5]diazocane ring in fair yields. Presumably, the formation of **9** involves initial formation of the eight-membered ring via a double aza-Wittig reaction followed by a cross-addition of the amino group on the two aldimine bonds. In spite of the structural similarity between iminophosphorane **2** and phosphazide **4**, it is worth noticing the different behaviour showed by these compounds towards primary amines in ethanol at room temperature: the former leads to tricyclic derivatives **9** whereas the latter leads to iminophosphoranes **6** derived from the 2-amino-2H-indazole.



2 **9**

A final word about the ability of compound **3** to form inclusion compounds with several alcohol and amines is relevant. Crystals of inclusion compounds type **3·alcohol** and **3·amine**[8] are formed by addition of the corresponding guest on a solution of **3** in dry dichloromethane. The stoichiometry of the inclusion compounds has been determined by n.m.r. spectroscopy, differential scanning calorimetry (DSC) and termogravimetry (TV). In all cases the stoichiometry was host-guest 1:1.

In conclusion the results presented here show a detailed and clear picture of the Staudinger reaction between the *o*-azidobenzaldehyde **1** and TPP. Simply by changing the temperature, the reaction may driven towards the production of **2** or **4** which show a dramatic different reactivity towards primary amines, whereas compound **3** forms inclusion compounds with this kind of compounds. Thus, further detailed investigations in this area are warranted.

Acknowlegements:

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References and notes.

1. Nomura, Y.; Kikuchi, Y.; Takeuchi, Y. *Chem.Lett.*, **1974**, 575.
2. Luheshi, A-B.N.; Salem, S.M.; Smalley, R.K.; Kennewell, P.D.; Westwood, R. *Tetrahedron Lett.*, **1990**, 31, 6561.
3. Typical Procedure: To a solution of triphenylphosphine (1.78 g, 6.7 mmol) in dry dichloromethane (10 ml) at 0°C was added dropwise a solution of *o*-azidobenzaldehyde (1.0 g, 6.7 mmol) in the same

solvent (20 ml) under nitrogen and the reaction mixture was stirred at room temperature for 16h. The solvent was removed under reduced pressure and the residual material was chomatographed on a silica gel column, eluting with ethyl acetate/n-hexane (3:1) to afford **2** (0.70 g, 30%), m.p. 175°C as yellow prisms and **3** (0.87 g, 25%), m.p. 185°C as yellow crystals.

Compound **2**. ^{1}H n.m.r. (200 MHz, $CDCl_3$) δ 6.45 (d, 1H, ^3J = 8.3 Hz, H-6), 6.62 (t, 1H, ^3J = 7.5 Hz, H-4), 7.01 (ddd, 1H, ^3J = 8.3, 7.3, ^4J = 1.9 Hz, H-5), 7.39-7.58 (m, 9H, $6H_m$+$3H_p$), 7.75 (ddd, 7H, ^3J = 12.2, 8.1, ^4J = 1.7 Hz, H-3 + $6H_o$), 11.10 (s, 1H, CHO). ^{13}C n.m.r. (50 MHz, $CDCl_3$) δ 116.91 (C_4), 122.95 (^3J = 11.1 Hz), C_6), 127.91 (^4J = 2.4 Hz, C_3), 128.72 (^3J = 12.1 Hz, C_m), 129.44 (^3J = 19.6 Hz, C_2), 130.28 (^1J = 100.6 Hz, C_i).132.01 (^4J = 2.8 Hz, C_p), 132.36 (^2J = 9.9 Hz, C_o), 134.50 (C_5), 155.93 (C_1), 193.79 (CHO). Mass spectrum m/z (%) 381 (M^+, 33), 183 (100). I.r. (Nujol) 1676 cm^{-1}.

Compound **3**. ^{1}H n.m.r. (200 MHz, DMSO-d_6) δ 6.49 (d, 1H, ^3J = 8.1 Hz), 6.73 (t, 1H, ^3J = 7.4 Hz), 6.95 (td, 1H, ^3J = 7.6 Hz, ^4J = 1.4 Hz), 7.01 (d, 1H, ^3J = 8.0 Hz), 7.15 (t, 1H, ^3J = 7.5 Hz), 7.31-7.66 (m, 17H), 7.86 (d, 1H, ^3J = 7.8 Hz) 7.95 (dt, 1H, ^3J = 7.8 Hz, ^4J = 2.0 Hz), 9.50 (s, 1H, CH=N). ^{13}C n.m.r. (50 MHz, DMSO-d_6) δ 113.09 (C_7), 118.67, 119.73 (C_{3a}), 122.68 (C_5), 123.07 (^3J = 9.3 Hz), 124.29 (C_4), 127.32, 127.95 (q, ^3J = 17.8 Hz), 128.72 (^3J = 12.2 Hz, C_m), 129.95 (^1J = 100.4 Hz, C_i), 130.68, 132.02 (^4J = 2.8 Hz, C_p), 132.34 (C_6), 132.58 (^2J = 9.8 Hz, C_o), 145.76 (C_{7a}), 146.06 (CH=N), 150.73 (q), 159.19 (C=O). Mass spectrum m/z (%) 512 (M^+, 5), 134 (100). I.r. (Nujol) 1642 cm^{-1}.

4. Satisfactory elemental analysis was obtained for compound **4**. I.r. (Nujol) 1686 cm^{-1}. The mass spectrum was almost identical to the compound **2**.

5. Compound **5**. ^{1}H r.m.n. (200 MHz, DMSO-d_6) δ 6.60 (t, 1H, ^3J = 7.4 Hz), 6.79 (d, 1H, ^3J = 8.2 Hz), 6.95 (s, 2H, NH_2), 7.13 (t, 1H, ^3J = 7.7 Hz), 7.19 (t, 1H, ^3J = 7.5 Hz, H-5), 7.25 (d, 1H, ^3J = 7.2 Hz), 7.30 (d, 1H, ^3J = 8.0 Hz, H-7), 7.60 (t, 1H, ^3J = 7.6 Hz, H-6), 7.77 (d, 1H, ^3J = 7.7 Hz, H4), 8.48 (s, 1H, CH=N), 10.60 (br. s, 1H, NH). ^{13}C n.m.r. (50 MHz, DMSO-d_6) δ 112.71 (C_7), 114.37 (C_{3a}), 115.18, 115.40, 117.65 (q), 122.21 (C_5), 123.48 (C_4), 130.70, 132.48, 132.82 (C_6), 145.58 (q), 147.07 (CH=N), 147.71 (C_{7a}), 157.75 (C=O). Mass spectrum m/z (%) 252 (M^+, 25), 120 (100). I.r. (Nujol) 3426, 3313 and 1658 cm^{-1}.

6. Compound **6** (Ar = 4-CH_3-C_6H_4). ^{1}H n.m.r. (200 MHz, DMSO-d_6) δ 2.23 (s, 3H, Ar-CH_3), 6.62-6.77 (m, 3H), 6.88-7.03 (m, 3H), 7.14-7.23 (m, 2H), 7.40-7.60 (m, 9H), 7.75 (ddd, 6H, ^3J = 12.1, 7.6 Hz, ^4J = 1.5 Hz), the NH proton was not observed. ^{13}C n.m.r. (50 MHz, DMSO-d_6) δ 20.08 (CH_3), 113.14 (C_{3a}), 114.64 (C_7), 115.08, 117.33 (C_5), 118.27 (C_4), 122.79 (C_6), 127.36 (q), 128.05 (^1J = 98.4 Hz, C_i), 128.10 (^3J = 12.2 Hz, C_m), 128.82, 131.82 (^4J = 2.9, C_p), 132.81 (^2J = 9.7 Hz, C_o), 141.69 (C_{7a}), 141.80 (q). The C_3 carbon atom was not observed. ^{31}P n.m.r. δ 20.27 ppm.

7. Compound **9** (Ar = 4-CH_3-C_6H_4) (m.p. 177°C, 50%). ^{1}H n.m.r. (200 MHz, DMSO-d_6) δ 2.16 (s, 3H, CH_3Ar), 5.77 (d, 2H, ^3J = 3.3 Hz, H-6), 6.48 (d, 2H, ^3J = 7.9 Hz, H-4), 6.56 (t, 2H, ^3J = 7.3 Hz, H-2), 6.78 (d, 2H, ^3J = 3.3 Hz, NH), 6.92 (t, 2H, ^3J = 7.5 Hz, H-3), 6.98 (s, 4H, $2H_o$+$2H_m$), 7.14 (d, 2H, ^3J = 7.7 Hz, H-1). ^{13}C n.m.r. (50 MHz, DMSO-d_6) δ 20.05 (CH_3), 63.39 (C_6), 114.65 (C_4), 116.32 (C_2), 117.27 (C_o), 124.13 (C_{6a}), 127.74 (C_3), 127.98 (C_1), 128.41 (C_p), 129.29 (C_m), 142.11 (C_{4a}), 144.49 (C_i). Mass spectrum m/z (%) 314 (M^++1, 23), 313 (M^+, 100).

8. Satisfactory ^{1}H, ^{13}C, mass spectra and elemental analyses were obtained for all new compounds.

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