Tetrahedron Letters,Vol.30,No.45,pp 6237-6240,1989 0040-4039/89 $3.00 + .00
Printed in Great Britain Pergamon Press plc

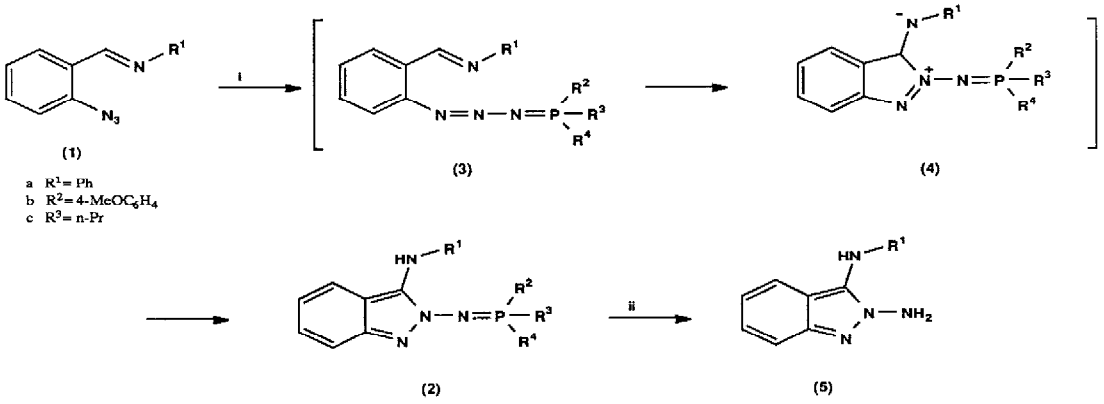
Intramolecular Trapping of a Phosphazide by an Imine: Formation of 2,3-Diamino-2H-indazole Derivatives from *o*-Azidobenzaldimines and Tertiary Phosphines.

Pedro Molina*, Antonio Arques, and María Victoria Vinader.
Departamento de Química Orgánica, Facultad de Ciencias,
Universidad de Murcia, Campus de Espinardo,
30071 Murcia, Spain

Abstract- *Treatment of o-azidobenzaldimines with tertiary phosphines in dichloromethane at 0°C gave the corresponding 2,3-diamino-2H-indazole derivatives in good yields via the Staudinger reaction followed by cyclization of the intermediate phosphazide.*

The reaction of a tertiary phosphine with an organic azide to produce an iminophosphorane after nitrogen evolution is known as the Staudinger reaction[1]. The primary imination product, phosphazides, are sometimes isolable and stable but usually they lose nitrogen at room temperature or even at lower temperature forming iminophosphoranes. In spite of the important role of iminophosphoranes in organic synthesis the chemistry of the phosphazides has been much less investigated; in fact, while relevant examples involving iminophosphoranes have been reported[2], there have been no reports dealing with synthetic applications of phosphazides, to the best of our knowledge. We report here the reactivity of *o*-azidobenzaldimines in the Staudinger reaction, thus providing an efficient and general route to 2,3-diamino-2H-indazole derivatives.

The starting *o*-azidobenzaldimines (**1**) were readily prepared as reported previously[3]. When a dichloromethane solution of (**1a**) was treated with triphenylphosphine at 0°C for 5h the indazole derivative (**2a**) was obtained in almost pure form, instead the expected *o*-(triphenylphosphoranylidene)amino benzaldimine. Reaction of the related *o*-azidobenzaldimines (**1b**) and (**1c**) also resulted in smooth formation of the 2,3-diamino-2H-indazole derivatives (**2b**) and (**2c**) respectively in *ca* 60% yields[4]. In addition, compound (**1a**) reacted with several tertiary phosphines to give the corresponding iminophosphoranes derived from 2-amino-3-phenylamino indazole (**2d-g**)[5], confirming the generality of the reaction.

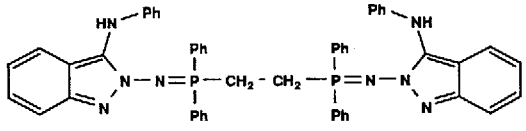


Scheme 1

Reagents and conditions: i, $R^2R^3R^4P$ in dichloromethane, 0°C 1h, room temperature 4h;
ii, HCl H_2O/dioxane, room temperature 5h

Table. Yields of indazoles† (**2**)

	R^1	R^2	R^3	R^4	%
a	Ph	Ph	Ph	Ph	75
b	4-$MeOC_6H_4$	Ph	Ph	Ph	60
c	nPr	Ph	Ph	Ph	60
d	Ph	NMe_2	NMe_2	NMe_2	74
e	Ph	Ph	Me	Me	60
f	Ph	Ph	Ph	Me	67



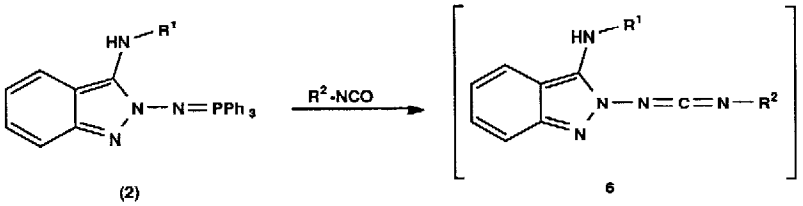
(**2g**)

† All new compounds described here had spectral and microanalytical properties in agreement with the assigned structures.

It is significant that aldimines derived from *o*-azidoformil azoles react with triphenylphosphine in a completely "normal" fashion to give the triphenylphosphoranylideneamino compounds[6], with no evidence of indazole formation. Thus, it is clear that the benzene ring play a key role in the selective formation of indazole compounds. Acid hydrolysis of (**2a**) led to 2-amino-2H-indazole (**5**, R^1=Ph) in 70% yield.

The formation of (**2**) can be rationalized in terms of a initial Staudinger reaction to give a phosphazide (**3**) as highly reactive intermediate which cleanly undergoes cyclization by nucleophilic attack of the central nitrogen atom of the phosphazide moiety on the carbon atom of the azomethine group leading to the zwitterionic intermediate (**4**). Futher transformations of (**4**) will lead to the indazoles (**2**).

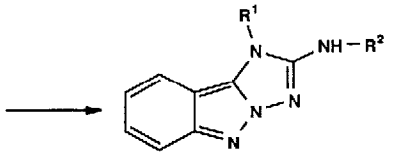
The present method demostrate that the Staudinger reaction of *o*-azidobenzaldimines affords a new and general entry to a variety of iminophosphoranes derived from 2-amino-2H-indazoles. Due to the easy access of the starting materials, good yields, mild reaction conditions and due to the simplicity of the experimental one-pot procedure, this synthetic approach compares favourably with other synthetic methods[7].



(2)

a R^1= Ph
b R^1= 4-$MeOC_6H_4$
c R^1= n-Pr

6



7

a	R^1= Ph	R^2= Et
b	R^1= Ph	R^2= 4-MeC_6H_4
c	R^1= 4-$MeOC_6H_4$	R^2= Me
d	R^1= 4-$MeOC_6H_4$	R^2= 4-FC_6H_4
e	R^1= n-Pr	R^2= Me

On the other hand, the reaction of iminophosphoranes (**2**) with aliphatic and aromatic isocyanates in dry toluene at reflux temperature for 4h gave triphenylphosphine oxide and the otherwise not readily available fused indazoles (**7**), the yield of the isolated product being higher than 60%. The carbodiimides (**6**) was indeed an intermediate in this reaction (as evidenced by IR) but was never present in high concentration. Compounds (**7**) were characterized on the basis of their spectroscopic data and mass spectrometry. The ^{1}H-NMR spectra suggest the exocyclic N-H, e.g. for (**7a**) the methylene signal appeared as a complex multiplet and for compounds (**7c**) and (**7e**) the methyl signal appeared as a doublet.

In conclusion, this work shows for the first time that easily available hetero 1,3,5-hexatrienes bearing a phosphazide moiety at one end and an azomethine group at the other, cleanly undergo heterocyclization to give directly iminophosphoranes derived from 2-amino-3-alkyl(aryl)amino indazoles, which shown to be useful precursors for the preparation of fused indazoles.

Acknowledgements:

We gratefully acknowledge the financial support of the Direccion General de Investigacion Cientifica y Tecnica (project number PB 86-0039).

References and notes.

1. H. Staudinger, J. Meyer, *Helv. Chim Acta*, **1919**, 2, 635; Yu.G. Gololobov, I.N. Zhmurova, L.F. Fasukhim, *Tetrahedron*, **1981**, 37, 437.
2. H. Takenchi, S. Yanagida, T. Ozaki, S. Hagiwara, S. Eguchi, *J. Org. Chem.*, **1989**, 54, 431; S. Eguchi, H. Takenchi, *J. Chem. Soc. Chem. Commun.*, **1989**, 602; P. Molina, M. Alajarín, C. López-Leonardo, I. Madrid, C. Foces-Foces, F.H. Cano, *Tetrahedron*, **1989**, 45, 1823 ; P. Molina, M. Alajarin, A. Vidal, *Tetrahedron Lett.*, **1989**, 2847; P. Molina, M. Alajarin, A. Vidal, *Tetrahedron* , **1989**, 45, 4263.
3. L. Krbechek, H. Takimoto, *J. Org. Chem.*, **1964**, 29, 1150.
4. Typical Procedure: A solution of triphenylphosphine (3 mmol) in dry dichloromethane (15 ml) was added dropwise under nitrogen at 0°C to a well-stirred solution of (**1c**) (3 mmol) in the same solvent (20 ml). The reaction mixture was stirred at 0°C for 1h and then was allowed to warm at room temperature for 4h. The solvent was removed under reduced pressure and the residual material was recrystallized from dichloromethane/hexane to give (**2c**) in 60% yield. ^{1}H n.m.r. (200 MHz, $CDCl_3$) δ 0.91 (t, 3 H, *J* 7.4 Hz), 1.56 (m, 2 H), 3.37 (t, 2 H, *J* 7.2), 4.65 (br, s, 1 H, NH), 6.67 (dt, 1 H, *J* 8.8 and 0.8 Hz, 5-H), 6.96 (t, 1 H, *J* 8.9 Hz, 6-H), 7.18 (d, 1 H, J 8.4 Hz, 7-H), 7.30-7.53 (m, 10 H), 7.72 (ddd, 6 H, $J_{H\text{-}P}$ 12 Hz, J_o 8.3 Hz and J_m 1.7 Hz, 3 x 2 H_o). ^{13}C n.m.r. (50 MHz, $CDCl_3$) δ 11.23 (CH_3), 23.82 (CH_2), 47.74 (CH_2-NH), 108.67 (C-3a), 114.97 (C-7), 115.91 (C-5), 118.94 (C-4), 123.28 (C-6), 128.44 (Cm J 12 Hz), 128.78 (C_i, J 98 Hz), 132.01 (C_p *J* 3 Hz), 133.13 (C_o, J 9.5 Hz), 142.62 (C-7a).
5. Compound (**2d**) ^{1}H n.m.r. (200 MHz, $CDCl_3$) δ 2.55 (d, 18 H, $J_{H\text{-}P}$ 9.3 Hz, 6 x CH_3-N), 6.53 (br, s, 1 H, NH), 6.73-6.87 (m, 4 H), 7.04-7.19 (m, 3 H), 7.32 (d, 1 H, J 8.3 Hz, 4-H), 7.46 (d, 1 H, *J* 8.7 Hz, 7-H). ^{13}C n.m.r. (50 MHz, $CDCl_3$) δ 37.19 (CH_3N, *J* 3.3 Hz), 112.58 (C-3a), 115.13 (C_o), 115.88 (C-7), 117.86 (C-5), 119.16 (C-4), 119.44 (C_p), 123.30 (C-6), 127.94 (C-3, *J* 11 Hz), 129.00 (C_m), 143.02 (C_i), 143.99 (C-7a). Values assigned by decoupling methods and 2D ^{1}H-^{13}C correlation techniques.
6. P. Molina, A. Arques, M.V. Vinader, J. Becker, K. Brondum, *Tetrahedron Lett.*, **1987**, 4451; *ibid*, *J. Org. Chem.*, **1988**, 53, 4654.
7. B.M. Adger, M. Keating, C.W. Rees, *J. Chem. Soc. Perkin Trans 1*, **1975**, 41.

(Received in UK 13 September 1989)