Tetrahedron Letters,Vol.30,No.21,pp 2847-2850,1989   0040-4039/89 $3.00 + .00
Printed in Great Britain   Pergamon Press plc

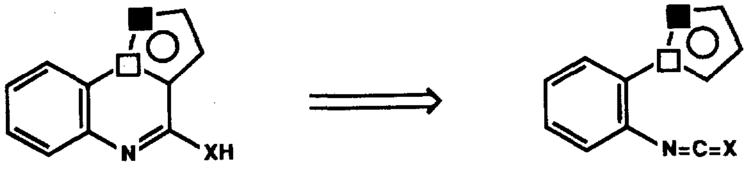
ortho-PYRROLYLPHENYL HETEROCUMULENES: PREPARATION AND CYCLIZATION TO FUSED PYRROLES

Pedro Molina*, Mateo Alajarín, and Angel Vidal
Departamento de Química Orgánica, Facultad de Ciencias Químicas
Campus de Espinardo, Universidad de Murcia, 30071 Murcia, Spain.

Summary: *The aza-Wittig reaction of iminophosphoranes derived from o-(1-pyrrolyl)phenyl azide and 2-(o-aminophenyl)indole with isocyanates, isothiocyanates, carbon dioxide or carbon disulfide, lead to functionalized pyrrolo[1,2-a]quinoxalines and 11H-indolo[3,2-c]quinolines respectively.*

Functionalized iminophosphoranes, bearing a moiety able to react with the aza-Wittig product, have shown to be useful precursors for the preparation of a wide variety of heterocyclic ring systems. In the course of our studies directed toward the iminophosphorane-mediated synthesis of heterocycles we had occasion to explore heterocyclization reactions based on a tandem aza-Wittig/heterocumulene-mediated anulation[1], intramolecular aza-Wittig reaction[2], and tandem aza-Wittig/electrocyclization strategy[3].

We now report a fundamentally new simple and apparently general method to the synthesis of fused pyrroles, namely, pyrrolo[1,2-a]quinoxalines and indolo[3,2-c]quinolines. Our approach is centered on the aza-Wittig reaction of iminophosphoranes with heterocumulenes: e.g. isocyanates, isothiocyanates, carbon dioxide and carbon disulfide to give o-pyrrolylphenyl heterocumulenes 1, which subsequently undergo ring closure to lead the fused pyrroles 2.

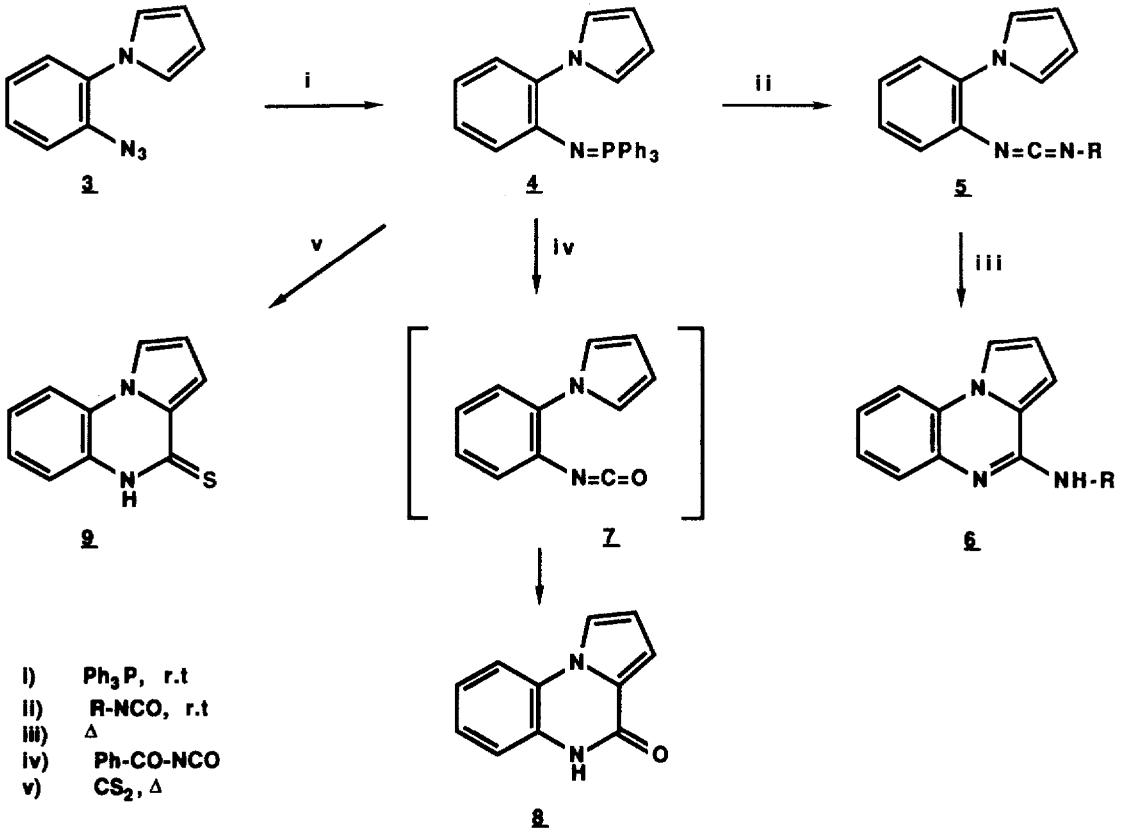


2   1

X= O, S, NR

☐= N   ■= CH
☐ = CH   ■= NH

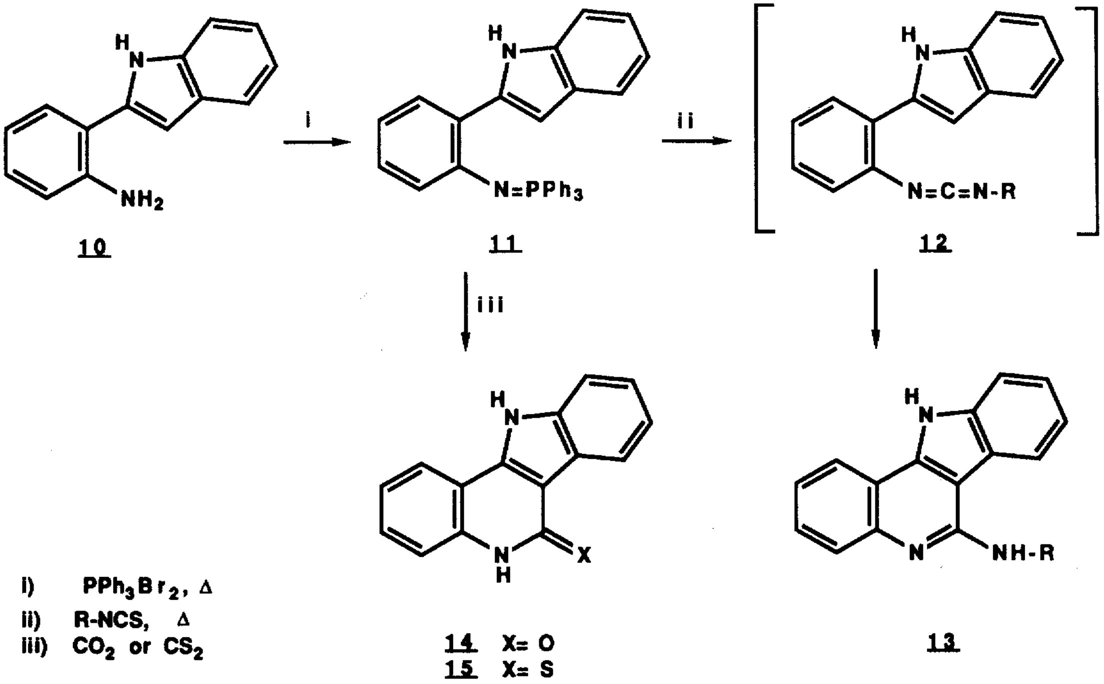
The preparation of the iminophosphorane 4 was accomplished very easily through the classical Staudinger reaction[4] of N-(o-azidophenyl)pyrrole 3, available from o-azidoaniline and 2,5-dimethoxytetrahydrofuran, with triphenylphosphine at room temperature. Aza-Wittig reaction of iminophosphorane 4 with isocyanates at room temperature afforded the corresponding carbodiimides 5, which could be isolated as viscous oils by means of short column chromatography (silica gel, n-hexane/ethyl acetate, 80:20). Upon heating at 180°C 5 undergo ring-closure to give the otherwise not readily available 4-aminopyrrolo[1,2-a]quinoxalines 6 in good yields. Despite its apparent simplicity, to our knowledge this is the first example reported of intramolecular electrophilic substitution of a pyrrole ring involving a carbodiimide group. Iminophosphorane 4 also reacts with benzoylisocyanate to give the unexpected product 8. The conversion 4 → 8 can be understood by initial abnormal aza-Wittig reaction to give N-benzoyliminophosphorane and the isocyanate 7 which undergoes ring-closure to give the fused pyrrole 8. Pyrrolo[1,2-a]quinoxaline 9 was prepared from iminophosphorane 4 and carbon disulfide. The results are summarised in the Table. Compounds 6, 8 and 9 were characterised on the basis of their spectroscopic data and mass spectrometry.



i) Ph_3P, r.t
ii) R-NCO, r.t
iii) Δ
iv) Ph-CO-NCO
v) CS_2, Δ

Electrophilic substitution of a pyrrole ring by heterocumulenes is rare. To our knowledge the reaction of phenylisocyanate with metal derivatives of pyrrole has been briefly mentioned[5]. The reaction occurs slowly to give the 1-carboxanilido compound or the thermodynamically more stable 2-isomer, depending upon the reaction temperature. Analogous reaction products are also obtained from phenylisothiocyanate. The formation of compounds 6, 8 and 9 represents the first example reported of heterocyclization based on the intramolecular electrophilic substitution of a pyrrole ring by heterocumulenes.

Our approach for the preparation of the little known indolo[3,2-c] quinolines[6] is based on the aza-Wittig reaction of iminophosphoranes with heterocumulenes to give a 2-azahexatriene moiety containing a cumulated double bond at one end and the carbon-carbon double bond belonging to the pyrrole ring at the other. Thus, iminophosphorane 11, available from 2-(o-aminophenyl)indole and triphenylphosphine dibromide, reacts with isothiocyanates in benzene at reflux temperature to give 6-amino-11H-indolo[3,2-c]quinolines 13 in excellent yields. Similarly, compound 11 reacts with carbon dioxide and carbon disulfide to give 14 and 15 respectively in high yields. We believe that the conversion 11 ⟶ 13 involves initial aza-Wittig reaction to give a carbodiimide 12 as highly reactive intermediate which undergoes electrocyclic ring-closure followed by 1,3-proton shift to give 13.



i) PPh_3Br_2, Δ
ii) R-NCS, Δ
iii) CO_2 or CS_2

Because of their simplicity, easy accesibility of starting materials, good yields, and straightforward product isolation, the investigated reactions provide a method for the preparation of pyrrolo[1,2-a]quinoxalines and indolo[3,2-c]quinolines which compares favourably with other approaches to these ring systems. Application of this annulation approach to a number of other fused pyrroles can be anticipated.

Table. Pyrrolo[1,2-a]quinoxalines [(6)-(9)] and 11H-Indolo[3,2-c] quinolines [(13)-(15)].

Compound	R	Yield (%)	m.p. (°C)
6a	Pr^i	80	124-125
6b	$4-CH_3-C_6H_4$	79	119-120
6c	C_6H_5	91	121-122
8		91	272-273
9		88	269-270
13a	$3-CH_3-C_6H_4$	78	231-232
13b	$4-CH_3O-C_6H_4$	91	275-276
14		83	280
15		94	335-337

Acknowledgements: We gratefully acknowledge the financial support of the Dirección General de Investigación Científica y Técnica (project number PB86-0039).

REFERENCES.

1. P. Molina, M. Alajarín, and A. Vidal, Tetrahedron Lett., 1988, 3849.
2. P. Molina, M. Alajarín, A. Vidal, J. Elguero, and R. M. Claramunt, Tetrahedron, 1988, 44, 2249; P. Molina, M. Alajarín, and A. Ferao, Synthesis, 1986, 843; P. Molina, M. Alajarín, C. López-Leonardo, and I.Madrid, Tetrahedron, in the press.
3. P. Molina, A. Arques, M. V. Vinader, J. Becher, and K. Brondum, Tetrahedron Lett., 1987, 4451; ibid, J.Org. Chem., 1988, 53, 4654; P. Molina, P. M. Fresneda, and P. Alarcón, Tetrahedron Lett., 1988, 379; P. Molina, P. M. Fresneda, J. Chem. Soc. Perkin Trans I, 1988, 1819.
4. Y. G. Gololobov, I. N. Zhmurova, and L. F. Kasukhin, Tetrahedron, 1981, 37, 437.
5. E. P. Papadopoulos, and H. S. Habiby, J. Org. Chem. , 1966, 31, 327; E. P. Papadopoulos, J Org. Chem., 1966, 31, 3061.
6. F. G. Mann, A. F. Prior, and T. J. Willcox, J. Chem. Soc., 1959, 3830; O. Roussel, N. P. Buu-Hoi, and P. Jacquignon, J. Chem. Soc., 1965, 5458.

(Received in UK 14 April 1989)