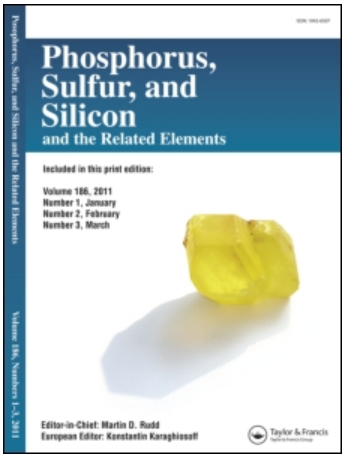


Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

REGIOCHEMICAL STEERING AND ASSIGNMENT IN CYCLOADDITIONS OF NITRONES TO DIPHENYLVINYLPHOSPHINE OXIDE

K. Michał Pietrusiewicz[a]; Alberto Brandi[b]
[a] The Polish Academy of Sciences, Centre of Molecular and Macromolecular Studies, Łódź, Poland [b] Dipartimento di Chimica Organica, Centro dei Composti Eterociclici-C.N.R., Firenze, Italy

To cite this Article Pietrusiewicz, K. Michał and Brandi, Alberto(1989) 'REGIOCHEMICAL STEERING AND ASSIGNMENT IN CYCLOADDITIONS OF NITRONES TO DIPHENYLVINYLPHOSPHINE OXIDE', Phosphorus, Sulfur, and Silicon and the Related Elements, 42: 3, 135 — 138
To link to this Article: DOI: 10.1080/10426508908054887
URL: http://dx.doi.org/10.1080/10426508908054887

Phosphorus, Sulfur, and Silicon, 1989, Vol. 42, pp. 135–138
Reprints available directly from the publisher
Photocopying permitted by license only
Printed in the United Kingdom

REGIOCHEMICAL STEERING AND ASSIGNMENT IN CYCLOADDITIONS OF NITRONES TO DIPHENYLVINYLPHOSPHINE OXIDE

K. MICHAŁ PIETRUSIEWICZ

The Polish Academy of Sciences, Centre of Molecular and Macromolecular Studies, Boczna 5, 90-362 Łódź, Poland

and

ALBERTO BRANDI[1]

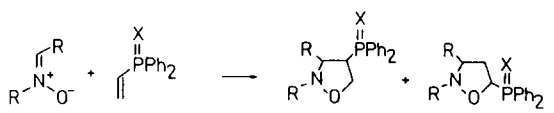
Centro dei Composti Eterociclici-C.N.R., Dipartimento di Chimica Organica, Universita' di Firenze, via G. Capponi 9, 50121 Firenze, Italy

(Received July 7, 1988)

In 1,3-dipolar cycloaddition of C,N-diphenylnitrone to diphenylvinylphosphine oxide (and also to diphenylvinylphosphine sulphide) the 4-substituted phosphinyl isoxazolidine is formed predominantly but in case of a cyclic nitrone the 5-substituted regioisomer prevails. Regiochemical distinctions between the isomeric phosphinyl isoxazolidines are best executed by means of ^{13}C NMR spectroscopy.

Key words: 1,3-Dipolar cycloaddition; diphenylvinylphosphine oxide; C,N-diphenylnitrone; phosphinylisoxazolidine; regioselective addition.

1,3-Dipolar cycloaddition of nitrones to monosubstituted alkenes is typically highly efficient in selective production of 5-substituted isoxazolidines and only some heteroatom electron-withdrawing substituents on the alkene have been found capable of steering the reaction towards the preferential formation of the corresponding 4-substituted regioisomers.[2,3] The pertinent directing ability of a phosphinyl group has however been very little recognized.[4,5] In connection with our project aimed at utilization of chiral phosphine oxides as dipolarophiles[6] we have briefly examined some model reactions involving diphenylvinylphosphine oxide and acyclic and cyclic nitrones and our preliminary results, which provide the first tenable[4] insight into the regioselectivity of such reactions, are reported herein.

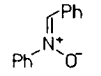
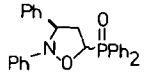
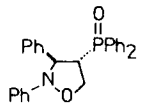
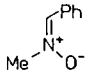
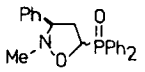
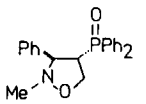
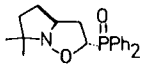
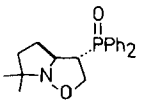


X = O,S

In all studied cases the reaction led to a mixture of isomeric isoxazolidines. As can be seen from Table I, the composition of the regioisomeric mixture depends on the structure of the nitrone and is decidedly one-sided only for the cyclic

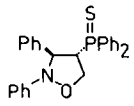
TABLE I

Cycloaddition of Nitrones to Diphenylvinylphosphine Oxide

Entry	Nitrone	Reaction conditions	Yield[a] [%]	Isoxazolidines 5-substituted	Isoxazolidines 4-substituted	Ratio[b]
1		benzene 80°C, 1.5d	82	 **1**	 **2**	40[c]:60
2		benzene 80°C, 2d	88	 **3**	 **4**	63[d]:37
3		chloroform r.t., 7d	90	 **5**	 **6**	86:14

[a] Yields are for isolated material. [b] From ^{31}P NMR spectra. [c] Cis/trans ratio 63:37 (^{31}P NMR). [d] Cis/trans ratio 82:18 (^{1}H NMR).

nitrone. For acyclic nitrones the regiochemistry seems to be more delicately balanced since the reversal of regiochemical preference can be brought about by relatively minor structural changes in the substrate (cf. entry 1 and 2, Table I).[7,9] Interestingly however, a considerable enhancement of selectivity towards the formation of the 4-substituted regioisomer can be simply attained by replacement of diphenylvinylphosphine oxide with diphenylvinylphosphine sulphide. In reaction with C,N-diphenylnitrone the latter dipolarophile afforded isoxazolidine **7** with 86% (^{31}P NMR) selectivity (overall reaction yield 90%).



7

All the isoxazolidines **1–7** were unambiguously identified by means of ^{1}H, ^{13}C and ^{31}P NMR spectroscopy and by MS, and were assigned the relative stereo-[10] and regiochemistry. The regiochemical assignment followed unequivocally from the corresponding ^{13}C NMR spectra in which positions of easily discernible signals of carbons coupled directly to phosphorus (large $^{1}J_{P-C}$) were highly diagnostic being at least 20 ppm more upfield in the 4-substituted regioisomers. The data collected in Table II typify this correlation which offers indeed a very dependable tool for distinction of regioisomers among the phosphorus substituted isoxazolidines and isoxazolines. Some of those compounds have in fact been

TABLE II

Selected ^{13}C NMR and ^{31}P NMR data of isoxazolidines **1–7**[a]

	1 cis	**1** trans	**2**	**3** cis	**3** trans	**4**	**5**	**6**	**7**
δ C-3[b]	69.38 (5.3)	69.84 (6.8)	70.12	72.00	72.00	72.47	63.75 (7.1)	64.53	71.09 (4.1)
δ C-4	40.25	41.80	53.71 (71.2)	39.76	40.30	51.45 (73.0)	38.67	51.76 (73.2)	54.18 (56.3)
δ C-5	74.57 (85.0)	75.80 (84.5)	67.39	74.20 (84.8)	74.24 (86.6)	65.91	75.16 (88.5)	66.13 (1.8)	68.30 (3.8)
δ ^{31}P	28.09	27.76	27.27	28.27	28.80	28.85	28.60	28.97	43.10

[a] Spectra recorded in $CDCl_3$ at 20 MHz (^{13}C) and 32.203 (^{31}P) respectively.
[b] In ppm. Phosphorus–carbon coupling constants are given in parentheses (Hz).

previously misassigned and the present study provides the corresponding verifications.[4,11]

In conclusion, it appears that regiochemistry of cycloadditions of nitrones to vinyl phosphine oxides (or sulphides) is very sensitive even to minor structural changes in either of the two components. This however implies, that by judicious matching of the substrates the selectivity in such additions may likely be brought to a synthetically useful level. Further investigations along this line are actively continued.

EXPERIMENTAL

Experimental conditions for individual reactions are specified in Table I or in the text. The reactions were usually monitored by ^{31}P NMR which indicated both, the end point of the additions and, the composition of the isomeric mixtures. After evaporation of the solvent, purification and separation of regiosiomers was typically accomplished by flash chromatography using mixtures of methylene chloride and ethyl acetate or, chloroform and methanol as eluents or, by crystallization from ethanol or carbon tetrachloride.

The reassignment of the preferred regiochemistry in reactions of C,N-diphenylnitrone with diphenylvinylphosphine oxide and diphenylvinylphosphine sulphide relies on the following authentication.

2: mp. 205–6°C (lit.[4] 195–6°C); IR (CCl_4) 3080, 3040, 3000, 2880, 1600, 1490, 1455, 1440, 1180, 1120, 1110 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.66 (br dq, J = 1.8, 8, 8 Hz, $^2J_{PH}$ = 8 Hz, 1H), 4.31 (t, J = 8.7 Hz, $^3J_{PH}$ = 8.7 Hz, 2H), 4.90 (dd, J = 7.2 Hz, $^3J_{PH}$ = 14.4 Hz, 1H), 6.85–7.73 (m, 20H). For ^{13}C and ^{31}P NMR data see Table II. Elemental analysis for $C_{27}H_{24}NO_2P$: calc. C 76.22; H 5.68; N 3.29. Found C 75.92; H 5.64; N 3.93. Spectral data for the corresponding 5-substituted regioisomers **1** are: ^1H NMR (300 MHz, $CDCl_3$) δ cis 2.59 (ddt, J = 5.7, 7.8, 12.5 Hz, $^3J_{PH}$ = 7.8 Hz, 1H), 3.08 (ddt, J = 8.6, 8.6, 12.5 Hz, $^3J_{PH}$ = 15.6 Hz, 1H), 4.28 (dd, J = 5.7, 8.4 Hz, 1H), 5.08 (dt, J = 7.7, 8.6 Hz, $^2J_{PH}$ = 7.7, 1H), 6.85–7.97 (m, 20H); δ trans 2.65 (m, 1H), 3.17 (m, 1H), 4.72 (t, J = 7.8, 1H), 4.99 (ddd, J = 2.7, 10.2 Hz, $^2J_{PH}$ = 6.9 Hz, 1H), 6.85–8.05 (m, 20H). IR ($CDCl_3$) 3070, 3040, 3000, 2960, 2880, 1600, 1490, 1455, 1440, 1245, 1190, 1120 cm^{-1}. Exact mass for $C_{22}H_{24}NO_2P$: calc. 425.1544. Found 425.1536. For ^{13}C and ^{31}P NMR data see Table II.

7: mp. 163–5°C (from Et_2O); IR (KBr pellet) 3070, 3030, 3010, 2930, 2875, 1600, 1490, 1450, 1435, 1105, 1100, 750, 740, 705, 690 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.97–4.06 (m, 1H), 4.26–4.42 (m, 2H), 4.98 (dd, J = 7.1 Hz, $^3J_{PH}$ = 17.1 Hz, 1H), 6.89–7.89 (m, 20H). For ^{13}C and ^{31}P NMR see Table II. Elemental analysis for $C_{27}H_{24}NOSP$: calc. C 73.44; H 5.47; N 3.17. Found C 72.93; H 5.56; N 3.82.

ACKNOWLEDGMENT

The authors thank the Consiglio Nazionale delle Ricerche–Italy and the Polish Academy of Sciences (CPBP-01.13) for financial support.

REFERENCES AND NOTES

1. Present address: Universita' della Basilicata, Istituto di Chimica, Via N. Sauro 85, 85100 Potenza, Italy.
2. D. St. C. Black, R. F. Crozier and V. C. Davies, *Synthesis*, **1975,** 205. J. J. Tufariello in 1,3-*Dipolar Cycloaddition Chemistry*, A. Padwa Ed.; Wiley-Interscience, New York, 1984, vol. 2, p. 83.
3. See also: B. A. Arbuzov, A. F. Lisin and E. N. Dianova, *Izv. Akad. Nauk SSSR, Ser. Khim.*, **1980,** 207. T. Koizumi, H. Hirai and E. Yoshii, *J. Org. Chem.*, **47,** 4004 (1982).
4. I. G. Kolokoltseva, V. N. Chistokletov, B. I. Ionin and A. A. Petrov, *Zh. Obshch. Khim.*, **38,** 1248 (1968); Engl. Edition p. 1203. This work has been later reviewed: E. Zbiral, *Synthesis*, **1974,** 775.
5. For studies related to a phosphonyl group see: B. A. Arbuzov, A. F. Lisin and E. N. Dianova, *Izv. Akad. Nauk SSSR. Ser. Khim.*, **1980,** 715. B. A. Arbuzov, Yu. Yu. Samitov, E. N. Dianova and A. F. Lisin, *ibid.*, **1976,** 2779. B. A. Arbuzov, Yu. Yu. Samitov, E. N. Dianova and A. F. Lisin, *ibid.*, **1975,** 2559. See also ref. 11.
6. A. Brandi, P. Cannavo', K. M. Pietrusiewicz, M. Zabłocka, M. Wieczorek and G. Bujacz, manuscript in preparation.
7. IP value (7.75 eV)[8] for C,N-diphenylnitrone implies that its HOMO lies somewhat higher than the HOMO of the corresponding C-phenyl-N-methylnitrone (IP = 8.01 eV)[8]; this difference might account for the observed shift in regioselectivity.
8. G. H. Armen, C. Braunstein, M. I. Weinstein and A. D. Baker, *Tetrahedron Lett.*, **1979,** 4197.
9. The replacement of Ph—P by Me—P substituent in the phosphine oxide results in similar reversal of the preferred regiochemistry. Cf. ref. 6.
10. Due to complexity of the ^{1}H NMR spectra caused by extensive proton-phosphorus coupling the stereochemical assignment should be regarded tentative. The observed formation of only one of the two possible 4-substituted stereoisomers in each studied case is most likely to originate from the preference for a transition state in which phosphinyl group and nitrone C-substituent are oriented away from each other to avoid unfavourable interactions.
11. For a relevant reinvestigation see: B. A. Arbuzov, Yu. Yu. Samitov, E. N. Dianova and A. F. Lisin, *Izv. Akad. Nauk SSSR, Ser. Khim.*, **1975,** 909.