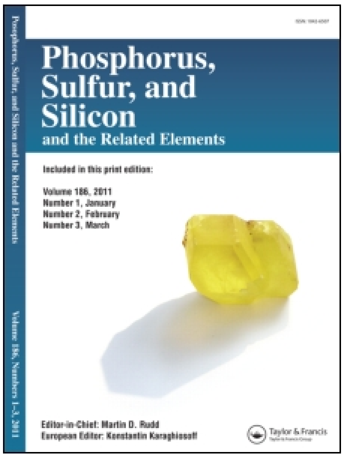

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STUDIES ON ORGANOPHOSPHORUS COMPOUNDS 90. STEREOSELECTIVE SYNTHESIS OF FUSED CARBOCYCLIC AND ISOXAZOLINE RINGS VIA INTRAMOLECULAR SILYL NITRONATE-OLEFIN CYCLOADDITIONS

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Dedicated to Professor Reinhard Schmutzler on the occasion of his sixtieth birthday

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Reactions of but-3-en-1-ylphosphonate with α-nitroalkenes followed by the addition of trimethylchlorosilane led to the stereoselective synthesis of 6-substituted 3,3a,4,5,6-pentahydrocyclopent[c]-isoxazole-5-ylphosphonates via intramolecular silyl nitronate-olefin cycloadditions by a one-pot procedure.

Key words: Stereoselective synthesis, cycloaddition, fused carbocyclic and isoxazoline rings.

In recent years intramolecular nitrile oxide-olefin cycloadditions (INOC) have been of considerable interest because of their high stereoselectivities and versatile applications in natural product synthesis.[1–4] On the other hand, while silyl nitronate can act as the synthetic equivalent of nitrile oxide in reaction with olefins,[5] intramolecular silyl nitronate-olefin cycloadditions (ISOC) have scarcely been investigated.[6,7] Recently we reported the stereoselective synthesis of fused carbocyclic and isoxazoline rings via Michael additions of alk-3-en-1-ylphosphonates to α-nitroalkenes followed by subsequent INOC reactions.[8] In our continuous investigation on the chemical behaviours of silyl nitronates,[9–12] we carried out the corresponding ISOC reactions. Herein we wish to report the reverse stereoselectivity of the ISOC reactions to that in INOC reactions.

As shown in Equation 1, condensation of **1** with α-nitroalkenes gave the corresponding nitro compounds, which led to silyl nitronate intermediates **2** on reaction

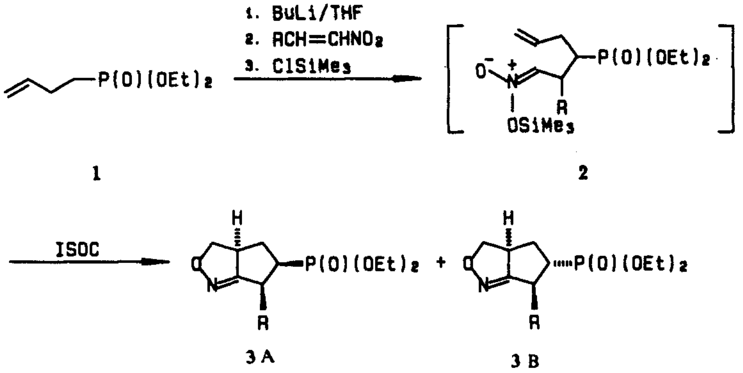


TABLE I
Compounds 3 synthesized

Entry	R	Time(h)	Yield(%)^{I}	Ratio(A/B)^{II}
a	H	4	57	50/50
b	Me	6	45	35/65
c	Et	6	50	55/45
d	Ph	10	62	>99/1
e	p-F-C_6H_4	10	66	>99/1
f	p-Cl-C_6H_4	10	60	>99/1
g	p-Me-C_6H_4	12	68	>99/1
h	p-MeO-C_6H_4	12	55	>99/1

I. Isolated yield based on phosphonate 1.

II. Determined by ^{1}H- and ^{31}P-NMR (300 MHz) spectra.

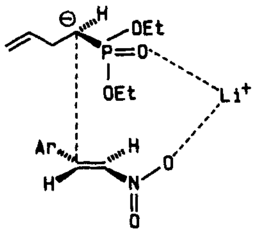
with trimethylchlorosilane. The intermediates **2** underwent ISOC reactions and product **3** with fused carbocyclic and isoxazoline rings were achieved in a one-pot procedure.

As indicated in Table I, with aryl substituted nitroalkenes, among five products studied of the eight possible configurational stereoisomers, only one, **3A**, was isolated, its spatial structure was unambiguously characterized using a Bruker AM-300 spectrometer. The ^{1}H-, ^{13}C-, ^{31}P-NMR, NOESY and ^{1}H-^{13}C COSY Spectra showed that the hydrogen at C-3 was cis to both the phosphonate group at C-5 and the aryl substituent at C-6. This result demonstrated the high diastereoselectivity of the Michael condensation reaction and high stereoselectivity in the ISOC step. The diastereoselectivity could be rationalized by transition state **4** of least steric hindrance. In the case of alkyl substituted nitroalkenes, the diastereoselectivity was not obvious probably due to their higher reactivity and the smaller steric effect of the related groups.

The high stereoselectivity of the ISOC reactions could be ascribed to transition state **5** in which the substituent R had to be trans to the bulky trimethylsilyl group. The groups R and trimethylsilyl had the predominant role on the stereoselectivity while the phosphonate substituent had little influence on it. It could be proven by the result of the reaction of nitroethylene with **1** (entry **a**, Table I). In this reaction equal amount of **3A** and **3B** was achieved as indicated by their ^{31}P NMR spectra. Thus, the stereoselectivity of ISOC reactions was opposite to that in the corresponding INOC reactions.

Compounds **3A** and **3B** should be of important use in organic synthesis. By Horner-Emmons reaction with aldehydes or ketones followed by the subsequent reductions of the C=C bond formed and the isoxazoline ring, **3A** and **3B** could be readily converted to the corresponding cis-2,3,5-trisubstituted cyclopentanone derivatives **6**, which will be published later.

As a typical procedure, BuLi (5 mmol, 1.6 M solution in hexane) was added dropwise at −68°C to THF (20 mL) solution of **1** (0.96 g, 5 mmol). After the complete addition, the solution was stirred for 30 min and 2-phenyl-1-nitroethylene



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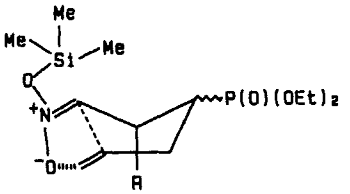

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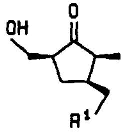

6

(0.782 g, 5 mmol) in THF (5 mL) was added dropwise. The solution was stirred for 1 h and then at r.t. for 10 h. Tri-methylchlorosilane (0.64 mL, 5 mmol) was added and the solution was stirred for 30 min. After the addition of Et_3N (10 drops), the mixture was refluxed for 10 h and then quenched by HCl (1 N). The usual work-up gave pure **3d** as a white solid. Yield: 1.00 g (62%). m.p. 70–72°C. IR (KBr) 3040, 1500, 1450, 1240, 1025. EIMS:m/z 342 (M^+ + H), 186. ^{31}P NMR ($CDCl_3$) 28.17. ^1H NMR ($CDCl_3$) 1.24, 1.26 (2 × 3H, 2t, $J = 7$, CH_3), 1.85 (1H, dddd, $J = 10.7, 11.5, 12.6, 15.7$, 4-H), 2.45 (1H, m, 4-H), 2.95 (1H, dddd, $J = 7.2, 8.0, 11.6, 17.5$, 5-H), 3.90 (2H, m, 3, 6-H), 4.10 (4H, m, CH_2O), 4.18 (1H, dd, $J = 8, 17$, **3a**-H), 4.60 (1H, dd, $J = 7, 8$, 3-H), 7.30 (5H, m, C_6H_5). Anal. Calcd for $C_{16}H_{22}NO_4P$: C, 59.44; H, 6.86; N, 4.33. Found: C, 59.53; H, 6.58; N, 4.23.

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REFERENCES

1. A. P. Kozikowski, *Acc. Chem. Res.*, **17**, 410 (1984), and references cited therein.
2. K. G. B. Torssell, "Nitrile Oxides, Nitrones, and Nitronates in Organic Synthesis," VCH Publishers, Inc., New York, 1988, pp. 129–225 and references cited therein.
3. W. Carruther, "Cycloaddition Reactions in Organic Synthesis," Pergamon Press, New York, 1990, pp. 285–297 and references cited therein.
4. J. Mulzer, H.-J. Altenbach, M. Braun, K. Krohn and H.-U. Reissig, "Organic Synthesis Highlights," VCH publishers, Inc., New York, 1991, pp. 77–95 and references cited therein.
5. K. G. B. Torssell and O. Zeuthen, *Acta Chem. Scand. Ser. B*, **B32**, 118 (1978).
6. W. Dehaen and A. Hassner, *Tetrahedron Lett.*, **31**, 743 (1990).
7. C. Li and C. Yuan, *Chin. Chem. Lett.*, (in press).
8. C. Yuan and C. Li, *Tetrahedron Lett.*, **34**, 5959 (1993).
9. C. Yuan and C. Li, *Phosphorus, Sulfur, Silicon*, **69**, 75 (1992).
10. C. Yuan and C. Li, *Phosphorus, Sulfur, Silicon*, **78**, 47 (1993).
11. C. Li, D. Zhou and C. Yuan, *Chin. Chem. Lett.*, **4**, 391 (1993).
12. C. Li and C. Yuan, *Synthesis*, 471 (1993).