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A FACILE ROUTE TO VINYL ISOCYANIDES

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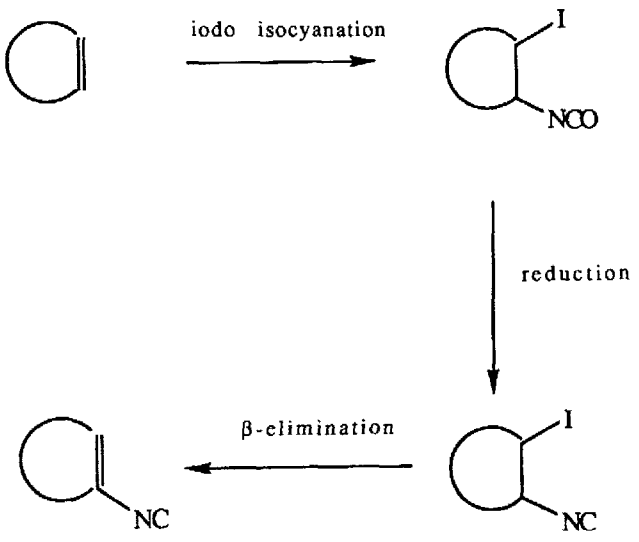
Abstract: A new procedure for the synthesis of vinyl isocyanides from olefins has been developed, which is based on the iodo isocyanation reaction of olefins followed by the conversion to a β-iodo isocyanide and a subsequent β-elimination reaction.

There has been recent attention on the isolation and synthesis of naturally occurring isocyanides,[1] in particular vinyl isocyanides some of which are active as antibacterial and antiviral agents.

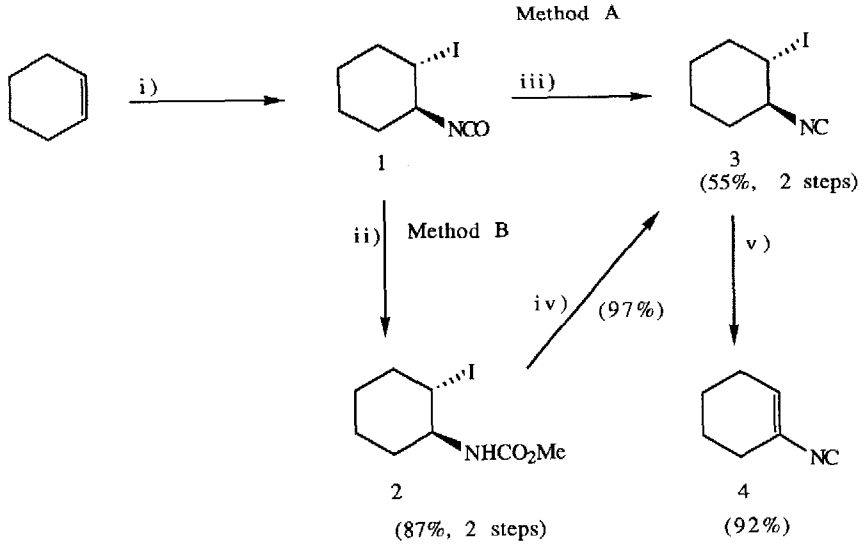
In the course of studies directed towards the synthesis of highly functionalised isocyanide antibiotics,[2] from the genus *Trichoderma*,[3] we required a simple procedure for the synthesis of vinyl isocyanides. Their synthesis has previously been achieved by, for example: the reductive formylation of oximes, followed by dehydration[4] and by reaction of a Wittig reagent containing an isocyanide moiety with carbonyl compounds.[5] Herein we describe studies on a new procedure for the preparation of vinyl isocyanides from olefins.

Our strategy consisted of three key reactions, namely, the trans addition of iodide and isocyanate to an olefin followed by the conversion to the β-iodo-isocyanide and β-elimination to give a vinyl isocyanide as shown in Scheme 1.

Scheme 1



Scheme 2



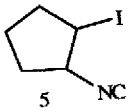
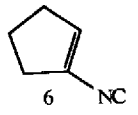
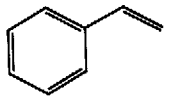
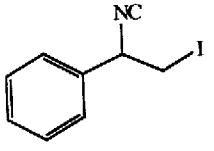
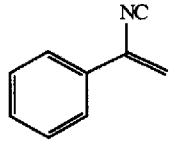
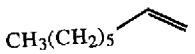
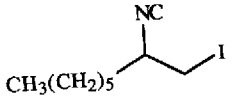
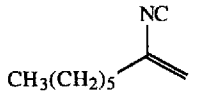
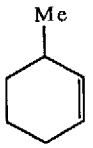
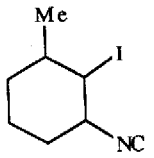
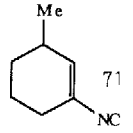
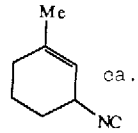
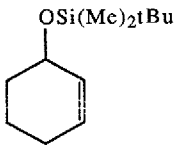
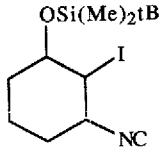
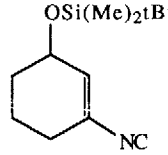
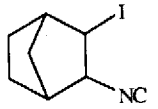
Reagents and conditions: i) olefin (0.52 mL, 5.13 mmol), AgOCN (1 g, 6.7 mmol), iodine (1.3 g, 5.13 mmol), ether (30 mL), rt, 5 h; ii) cat. LiOMe (1 drop, prepared from 25 mg of Li and 50 mL of methanol), methanol (10 mL) iii) trichlorosilane (0.77 mL, 7.7 mmol), diisopropylethylamine (2.23 mL, 12.83 mmol), dichloromethane (25 mL), 0°C, 30 min; iv) 2 (0.90 g, 3.18 mmol), trichlorosilane (0.80 mL, 7.95 mmol), diisopropylethylamine (1.39 mL, 7.95 mmol), dichloromethane (20 mL), rt, 24 h: v) 3 (570 mg, 2.43 mmol), potassium tert-butoxide (1.36 g, 12.12 mmol), tetrahydrofuran (20 mL), -78°C - rt, 3 h.

For the introduction of a suitable leaving group and a precursor of the isocyanide we used the iodo isocyanation reaction as described by Hassner[6]. Thus, for example the reaction of cyclohexene with iodine (1 equiv) and silver cyanate[7] (1.3 equiv) in ether at room temperature gave isocyanate (1).[8] In order to convert isocyanate (1) into iodo isocyanide (3), two routes were investigated: one was the direct reduction of (1) (Method A) and the other was via carbamate (2) (Method B). Thus treatment of (1) with a catalytic amount of lithium methoxide in methanol afforded carbamate (2)[6] in 87% yield (from olefin). Next, isocyanate (1) and carbamate (2) were converted to isocyanide (3)[10] using methodology previously developed in this laboratory[9] [1: trichlorosilane (1.5 equiv), diisopropylethylamine (2.5 equiv), dichloromethane, 0°C, 30 min, 55% (from olefin)], [2: trichlorosilane (2.5 equiv), diisopropylethylamine (2.5 equiv), dichloromethane, room temperature, 24 h, 97%]. Finally, the treatment of iodo isocyanide (3) with 5 equiv of potassium t-butoxide in tetrahydrofuran (at -78°C to room temperature) gave vinyl isocyanide (4) in 92% yield after silica gel chromatography (Scheme 2). In spite of the disfavoured cis-elimination[11], this reaction proceeded smoothly. These routes were extended to several olefins as illustrated in the Table.

These routes provide a relatively simple method for synthesis of vinyl isonitriles from olefins on laboratory scale.

We thank the Uehara Memorial Foundation for a Postdoctoral Fellowship (to Y.Y.).

TABLE

ENTRY	SUBSTRATE	METHOD[a]	IODO ISOCYANIDE	YIELD (%)[bc]	VINYL ISOCYANIDE	YIELD (%)[c]
1		A	 5	24	 6	73
		B		32		
2		A	 7	--[d]	 8	66[b]
		B		--		72[b]
3	$CH_3(CH_2)_5$ 	A	 9	25	 10	66
4		A	 11	60[e]	 12	71
		B		61[e]	 13	ca.5[f]
5		A	 14	37[e]	 15	80
6		A	 16	21[e]		0[g]
		B		20[e]		

a) A: via reduction of isocyanates
B: via reduction of carbamates

b) Overall yield from olefin

c) Isolated yield after the silica gel chromatography (Petrol/diethyl ether)

d) The reaction with Cl_3SiH and diisopropylethylamine gave the vinyl isonitrile directly.

e) Diastereomixtures.

f) 13 was isolated as a mixture of 12 and 13.
Yield of 13 was estimated by ^1H-NMR spectrum.

g) The corresponding vinyl isocyanide was not detected.

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7. We used AgOCN produced by Aldrich Co., without further purification.

8. After filtration of silver salts and evaporation of solvent, all isocyanates were used without further purification for the next step.

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10. All new compounds gave appropriate spectral data. Selected data are as follows. 3: δ_H (200 MHz, $CDCl_3$) 4.22 - 4.11 (m, 1H), 3.77 - 3.69 (m, 1H), 2.45 - 1.27 (m, 8H); ν_{max} ($CHCl_3$) 2150 (-NC). 4: δ_H (200 MHz, $CDCl_3$) 6.02 (bs, 1H), 2.20 - 2.08 (m, 4H), 1.73 - 1.50 (m, 4H); δ_C (50 MHz, $CDCl_3$) 129.13(d), 125.10(s), 28.24(t), 23.92(t), 21.50(t), 20.64(t); ν_{max} ($CHCl_3$) 2120 (-NC). 5: δ_H (200 MHz, $CDCl_3$) 4.25 - 4.19 (m, 1H), 4.09 - 4.04 (m, 1H), 2.56 - 1.67 (m, 6H); δ_C (50 MHz, $CDCl_3$) 63.48(d), 63.23(d), 36.59(t), 31.50(t), 22.32(t); ν_{max} ($CHCl_3$ 2145 (-NC). 6: δ_H (200 MHz, $CDCl_3$) 6.97 (bs, 1H), 2.60 - 2.38 (m, 4H), 1.99 - 1.91 (m, 2H); ν_{max} ($CHCl_3$) 2115 (-NC). 8: δ_H (200 MHz, $CDCl_3$) 7.66 - 7.61 (m, 2H), 7.46 - 7.42 (m, 3H), 5.85 - 5.80 (m, 1H), 5.63 (bs, 1H), ν_{max} (neat) 2120 (-NC). 9: δ_H (200 MHz, $CDCl_3$) 3.93 - 3.85 (m, 1H), 3.39 - 3.25 (m, 2H), 1.82 - 0.86 (m, 13H); ν_{max} (neat) 2140 (-NC). 10: δ_H (200 MHz, $CDCl_3$) 5.26 (bs, 1H), 5.06 (bs, 1H), 2.31 - 0.81 (m, 13H); ν_{max} (neat) 2115 (-NC). 12: 5.89 (bs, 1H), 2.31 - 1.12 (m, 7H), 1.03 (d, J = 7 Hz, 3H); ν_{max} (neat) 2110 (-NC). 15: δ_H (200 MHz, $CDCl_3$) 5.92 (bs, 1H), 4.35 - 4.23 (m, 1H), 2.33 - 2.08 (m, 2H), 1.95 - 1.48 (m, 4H), 0.90 (s, 9H) 0.08 (s, 6H); ν_{max} (neat) 2120 (-NC).

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