

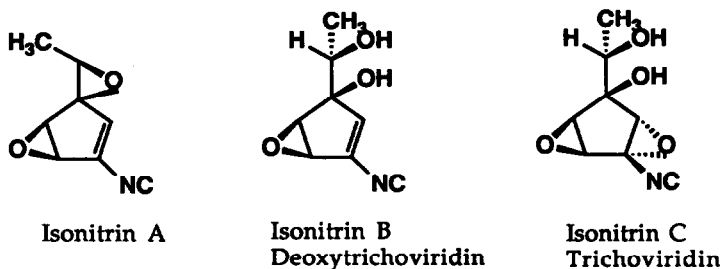
A New And Mild Procedure For The Preparation Of Vinyl Formamides From Thiooximes

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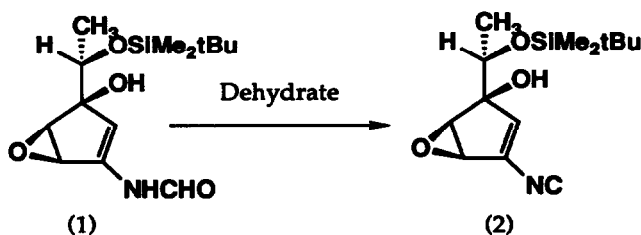
Summary: Treatment of thiooximes with triphenylphosphine and acetic formic anhydride in dichloromethane at room temperature gives good yields of vinyl formamides under essentially neutral conditions.

Isonitrins A,B and C are isonitrile containing natural products isolated from fungi of the genus trichoderma¹. Their unusual and complex molecular structure coupled with their anti-microbial activity prompted us to undertake their total synthesis².



In our approach to the total synthesis of deoxytrichoviridin we planned to prepare and dehydrate the vinyl formamide (1) as the key step. (scheme 1) We anticipated that the vinyl

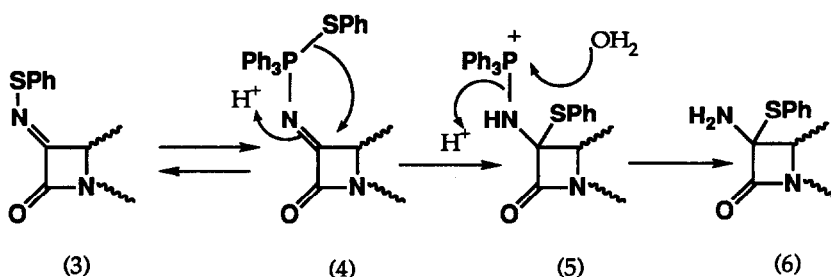
Scheme 1



formamide (1) would be extremely sensitive to acid³ and as there were no methods for the

preparation of vinyl formamides under mild conditions at the outset of this work⁴ we decided to investigate alternative procedures for their synthesis. We noted that in a related synthetic problem, Gordon and co-workers⁵ had converted the cephalosporin thiooxime (3) to an α -thioamine (6) by treatment with PPh_3 and silica gel. He proposed the intermediacy of (4) which underwent migration of the thiophenyl to the imine carbon followed by protonation and loss of triphenylphosphine oxide to give the product (6). (scheme 2)

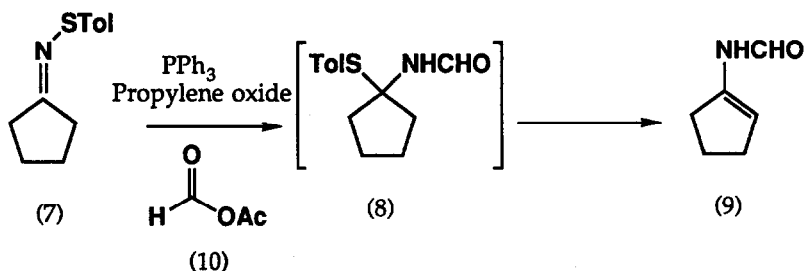
Scheme 2



We speculated that by replacing the silica gel with a formyl source that the product

would be an α -thioformamide, which would undergo loss of thiotolyl to give the vinyl formamide (scheme 3)

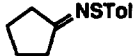
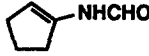
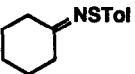
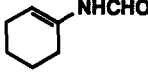
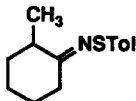
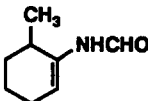
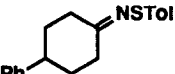
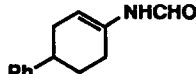
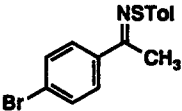
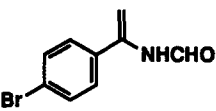
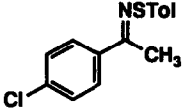
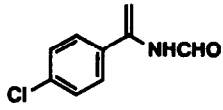
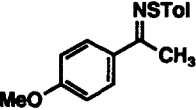
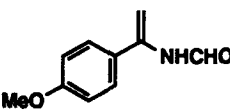
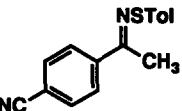
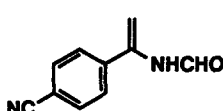
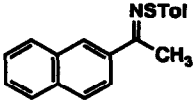
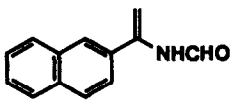
Scheme 3



We tested our conjecture and found that vinyl formamides are isolated using this modified procedure. Experimentally the reaction consists of treating the cyclopentanone thiooxime (7) with PPh_3 (3eq.), acetic formic anhydride⁶ (3eq.) and propylene oxide (5eq.) (as an acid scavenger), and stirring at room temperature under an atmosphere of argon for 18 hours. The crude reaction mixture is washed with 5% aq. NaHCO_3 , dried (Na_2SO_4) and then purified by chromatography on basic alumina to give the vinyl formamide (9) in 68%. We have assumed that the α -thioformamide (8) is formed, although alternative intermediates are possible. This methodology has been applied to a variety of thiooximes and we have found it to be a very general procedure for the preparation of vinyl formamides under mild conditions. (see table). The precursor thiooximes are conveniently available from either the corresponding ketones⁷ or amines⁸ in one step transformations using readily available starting materials. The isolation of the less substituted

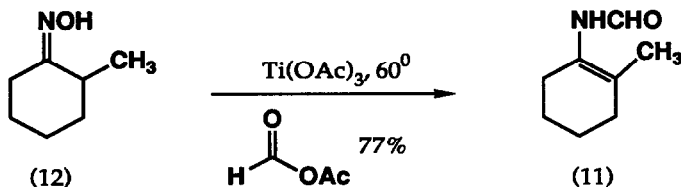
Table

a) Purified by recrystallization from pentane at -30° . b) Purified by chromatography on flash silica.

	THIOOXIME	% YIELD THIOOXIME	VINYL FORMAMIDE	% YIELD VINYL FORMAMIDE
1		89 ^a		68
2		88 ^a		76
3		94 ^b		58
4		89 ^a		80
5		89 ^a		81
6		92 ^a		86
7		96 ^a		85
8		66 ^b		68
9		69 ^a		86

vinyl formamide in case 3 is noteworthy, giving a complimentary result to a recently published route to vinyl formamides⁴ in which only the more thermodynamically stable vinyl formamide (11) was isolated on treating oxime (12) with $Ti(OAc)_3$ and acetic formic anhydride. (scheme 4) We are currently investigating this unusual result further.

Scheme 4



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