Structural Requirements in Chiral Diphosphinerhodium Complexes. Part 9.[1] ^{1}H Nuclear Magnetic Resonance Determination of *E,Z*-Configuration and *cis,trans*-Amide Conformations in Prochiral Substrates used in Asymmetric Hydrogenation Reactions: Methyl and Ethyl α-Formamido-β-substituted Acrylates

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By ^{1}H n.m.r. spectroscopy, *E*-methyl or -ethyl α-formamido-β-substituted acrylates may be characterized by the relatively large difference in chemical shift values ($\Delta\delta$ = 0.75—1.25 p.p.m. in $CDCl_3$) of the two H_β (vinylic) proton signals exhibited by the *cis*- and *trans*-amide conformers. Change of solvent from $CDCl_3$ to CF_3CO_2H causes this difference in H_β chemical shift values to be considerably reduced, and also results in an increase in the quantity of the minor *cis*-amide conformer. *Z*-Methyl or -ethyl α-formamido-β-alkylacrylates may be characterized by a much smaller difference in chemical shift values ($\Delta\delta$ = 0.05—0.10 p.p.m. in $CDCl_3$) for the corresponding H_β signals. Change of solvent from $CDCl_3$ to CF_3CO_2H causes the H_β proton signals (for the *cis*- and *trans*-amide conformers) to both undergo similar downfield shifts, but did not result in an increase in the quantity of the minor *cis*-amide conformer [in the series of compounds studied]. *E*-Methyl or -ethyl α-formamido-β-arylacrylates may be further characterized by the anisotropy of the aromatic ring causing an upfield shifting of the proton signals within the ester moiety as compared to the corresponding signals in olefins having the *Z*-configuration or to non-aromatic substituted α,β-unsaturated esters in general.

For the past three years, considerable work has been devoted in the Beersheva laboratory to the study of the asymmetric hydrogenation of *N*-acyl-α,β-dehydroamino-acids and esters catalysed by homogeneous chiral diphosphinerhodium(I) complexes.[1,2] These prochiral olefins act as subtle probes in the systematic investigation of the intimate 'lock' and 'key'-type interactions between the chiral transition-metal catalyst and the prochiral substrate. In order to gain insight into the steric and electronic requirements within the active catalytic species, it is imperative that the geometry of the prochiral olefins be unambiguously characterized. This paper reports the ^{1}H n.m.r. determination of the *E,Z*-configuration and the *cis,trans*-amide conformations of methyl and ethyl α-formamido-β-substituted acrylates used as prochiral substrates in the above-mentioned reaction.

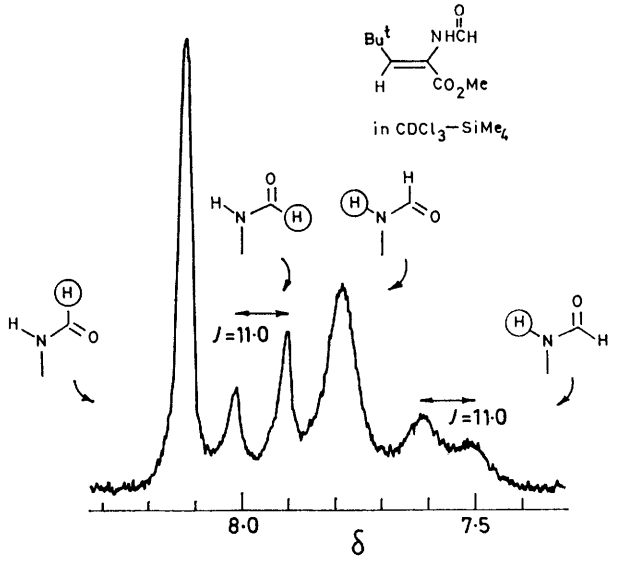

FIGURE 1 ^{1}H N.m.r. partial spectrum of *Z*-methyl α-formamido-β-t-butylacrylate (4a): *J* values in Hz

RESULTS AND DISCUSSION

α-Formamido-β-substituted acrylate esters are readily prepared by condensation of the appropriate isocyanoacetic acid ester with an aldehyde or ketone in the presence of base.[3] Thus, acetaldehyde, propionaldehyde, isobutyraldehyde, pivalaldehyde, and benzaldehyde were treated with methyl or ethyl isocyanoacetate to give the corresponding condensation products as a mixture of *Z*- and *E*-olefins.[3] Characteristic signals from the ^{1}H n.m.r. spectra of the *Z,E*-methyl α-formamido-β-substituted acrylates are listed in Table 1. The ethyl ester analogues exhibited very similar spectra.

Restricted rotation within the amide moiety due to partial double-bond character between the nitrogen and carbon atoms therein results in one conformational isomer having the nitrogen bound proton (amide proton) *trans* to the carbonyl oxygen atom (a *trans*-amide), while the other isomer is the *cis*-conformer.[4] It should be remembered that for the case of formamides, the *trans*-amide conformation (A) results in a *cis*-relationship between the amide proton and the aldehydic proton (formyl proton). Similarly, the *cis*-amide conformation (B) shows a *trans*-relationship between these two protons (see Figure 2).

FIGURE 2

TABLE 1

^{1}H N.m.r. data of *Z,E*-methyl α-formamido-β-substituted acrylates, RCH=C(NHCHO)COOCH$_3$[a]

Compd.	R	Config.	Amide comform.[b]	Formyl-H	Amide-H	Hβ Vinylic	Hγ and other
(1a)	Me	*Z*	*trans*	8.12 (s)	*c*	6.73 (q, *J* = 7)	1.77 (d, *J* = 7) [d]
				[8.34 (d, *J* = 2)]	[8.41 (broad s)]	[7.20 (q, *J* = 7.5)]	1.90 (d, *J* = 7.5) [d]
(1a)	Me	*Z*	*cis*	*c*	*c*	6.66 (q, *J* = 7)	1.90 (d, *J* = 7) [d]
				[8.18 (d, *J* = 12)]	[8.67, (broad d, *J* = 12)]	[7.17 (q, *J* = 7.5)]	2.00 (d, *J* = 7.5) [d]
(1b)	Me	*E*	*trans*	8.19 (s)	*c*	7.17 (q, *J* = 7.5)	2.07 (d, *J* = 7.5) [d]
				c	*c*	[6.92 (q, *J* = 7.5)]	[2.15 (d, *J* = 7.5] [d]
(1b)	Me	*E*	*cis*	*c*	*c*	6.08 (q, *J* = 7.5)	2.09 (d, *J* = 7.5) [d]
				c	*c*	[6.48 (q, *J* = 7.5)]	[2.18 (d, *J* = 7.5)] [d]
(2a)	Et	*Z*	*trans*	8.13 (s)	*c*	6.66 (t, *J* = 7.5)	2.2 (m) [e]
				[8.26 (d, *J* = 2)]	*c*	[6.93 (t, *J* = 7.5)]	[2.3 (m)] [e]
(2a)	Et	*Z*	*cis*	*c*	*c*	6.54 (t, *J* = 7.5)	2.2 (m) [e]
				c	*c*	[6.93 (t, *J* = 7.5)]	[2.3 (m)] [e]
(2b)	Et	*E*	*trans*	*c*	*c*	6.74 (t, *J* = 7.5)	2.5 (m) [e]
				c	*c*	[6.83 (t, *J* = 7.5)]	[2.6 (m)] [e]
(2b)	Et	*E*	*cis*	*c*	*c*	6.01 (t, *J* = 7.5)]	2.5 (m) [e]
				c	*c*	[6.32 (t, *J* = 7.5)]	[2.6 (m)] [e]
(3a)	Pr^i	*Z*	*trans*	8.12 (s)	*c*	6.46 (d, *J* = 10)]	2.6 (m) [f]
				[8.35 (s)]	[8.33 (broad s)]	[6.94 (d, *J* = 10)]	[2.7 (m)] [f]
(3a)	Pr^i	*Z*	*cis*	*c*	*c*	6.41 (d, *J* = 10)]	2.6 (m) [f]
				[8.18 (d, *J* = 12)]	[8.70 (broad d, *J* = 12)]	[6.90 (d, *J* = 10)]	[2.7 (m)] [f]
(3b)	Pr^i	*E*	*trans*	8.15 (s)	*c*	6.75 (d, *J* = 10)]	3.3 (m) [f]
				c	*c*	[6.61 (d, *J* = 10)]	[3.4 (m)] [f]
(3b)	Pr^i	*E*	*cis*	*c*	*c*	5.77 (d, *J* = 10)]	3.3 (m) [f]
				c	*c*	[6.20 (d, *J* = 10)]	[3.4 (m)] [f]
(4a)	Bu^t	*Z*	*trans*	8.09 (s)	7.75 (s)	6.63 (s)	
				[8.33 (s)]	*c*	[7.12 (s)]	
(4a)	Bu^t	*Z*	*cis*	7.92 (d, *J* = 11)	7.52 (d, *J* = 11)	6.67 (s)	
				[8.10 (d, *J* = 12)]	[8.55 (d, *J* = 12)]	[7.15 (s)]	
(5a)	Ph	*Z*	*trans*	*c*	*c*	*c*	3.78 (s) [g]
				[8.30 (s)]	[8.47 (broad s)]	[7.70 (s)]	[3.99 (s)] [g]
(5a)	Ph	*Z*	*cis*	*c*	*c*	*c*	3.78 (s) [g]
				[8.10 (d, *J* = 11)]	[8.66 (broad d, *J* = 11)]	*c*	[3.97 (s)] [g]
(5b)	Ph	*E*	*trans*	*c*	*c*	7.97 (s)	3.58 (s) [g]
				[8.33 (s)]	[8.64 (broad s)]	[7.54 (s)]	[3.78 (s)] [g]
(5b)	Ph	*E*	*cis*	*c*	*c*	6.75 (s)	3.58 (s) [g]
				c	[9.13 (broad d, *J* = 12)]	*c*	[3.81 (s)] [g]
(6a)	*m,p*-OMe$_2$Ph	*Z*	*trans*	*c*	*c*	7.00 (s)	*c*
				[8.43 (s)]	[8.62 (broad s)]	[7.72 (s)]	*c*
(6a)	*m,p*-OMe$_2$Ph	*Z*	*cis*	*c*	*c*	*c*	*c*
				[8.20 (d, *J* = 12)]	[8.70 (broad d, *J* = 12)]	*c*	*c*

The formyl protons in compounds (1)—(6) all show ^{1}H n.m.r. signals indicating the presence of these two *cis,trans*-amide conformations in unequal proportions in $CDCl_3$. The ^{1}H n.m.r. partial spectrum ($CDCl_3$; $SiMe_4$; 100 MHz) of compound (4a) (Figure 1) provides a good illustration of this phenomenon. The presence of two amide conformers is clearly indicated by the two sets of signals for each of the formyl and amide protons in the ratio of 2 : 1 for each set. Thus, the minor conformer shows a doublet at δ 7.92 (J = 11 Hz) and a slightly broadened doublet at δ 7.52 (J = 11 Hz) for the formyl and amide protons, respectively. The major conformer shows a singlet at δ 8.09 and a slightly broadened singlet at δ 7.75 for these same two protons. With formamide

TABLE 2

^{1}H N.m.r. data of *Z,E*-methyl α-acylamino-β-substituted-acrylates, R^{1}CH=C(NHCOR^2)COOCH$_3$[a]

Compd.	R^1	R^2	Config.	Amide conform.[b]	Hβ vinyl	Hγ	Acetyl-H
(7a)	Me	Me	*Z*	*trans*	6.72 (q, *J* = 7.5)	1.73 (d, *J* = 7.5) [d]	2.07 (s)
					[7.23 (q, *J* = 7.5)]	[1.93 (d, *J* = 7.5)] [d]	[2.42 (s)]
(7a)	Me	Me	*Z*	*cis*			
					c	[2.02 (d, *J* = 7.5)] [d]	[2.20 (s)]
(7b) [h]	Me	Me	*E*	*trans*	6.90 (q)	2.02 (d) [d]	2.00 (s)
(8a)	Pr^i	Me	*Z*	*trans*	6.45 (d, *J* = 10)	2.63 (m) [f]	2.10 (s)
					[6.93 (d, *J* = 10)]	[2.72 (m)] [f]	[2.41 (s)]
(8a)	Pr^i	Me	*Z*	*cis*	*c*	*c*	*c*
					c	*c*	[2.20 (s)]
(9a)	Ph	Me	*Z*	*trans*	*c*	*c*	2.03 (s)
					[7.72 (s)]	*c*	[2.36 (s)]
(9a)	Ph	Me	*Z*	*cis*	*c*	*c*	*c*
					[7.87 (s)]	*c*	[2.02 (s)]
(10a)	Ph	Bu^t	*Z*	*trans*	*c*	*c*	
					[7.73 (s)]	*c*	
(10a)	Ph	Bu^t	*Z*	*cis*			
(11a)	*m,p*-OMe$_2$Ph	Me	*Z*	*trans*	*c*	*c*	2.03 (s)
					[7.70 (s)]	*c*	[2.43 (s)]
(11a)	*m,p*-OMe$_2$Ph	Me	*Z*	*cis*	*c*	*c*	2.03 (s)
					[7.85 (s)]	*c*	[2.10 (s)]

itself, it has been shown that the vicinal *trans* protons have a coupling constant of 12.9 Hz, while the vicinal *cis*-protons have a coupling constant of 2.1 Hz.[5] It is, therefore, reasonable to assign the coupling constant of 11 Hz exhibited by the minor conformer to be that arising from an interaction between two vicinal protons that are *trans* to each other (*i.e.* the *cis*-amide). The major conformer in (4a) thus can now be assigned the *trans*-amide structure. These assignments of amide conformation are in agreement with the ^{1}H n.m.r. data for *N*-methylformamide, *N*-ethylformamide, *N*-isopropylformamide, and *N*-t-butylformamide.[6] All exist in both the *cis*- and *trans*-amide conformations, with the *trans*-amide predominating (although the *cis*-isomer increases as the alkyl group becomes bulky).[6]

E,Z-Configurational assignment in the methyl α-formamidocrotonates (1a, b) can be made by comparison with the ^{1}H n.m.r. spectra in Table 2 of the corresponding α-acetamido-analogues (7a, b) of known *Z*- and *E*-configuration. Olsen *et al.*[7,8] have prepared the *Z*- and *E*-methyl α-acetamidocrotonates [(7a) and (7b) respectively] *via* elimination reactions [using DABCO] upon the *N*-acetyl-*O*-tosyl-(*R,S*)-threonine methyl ester or the *erythro*-α-acetamido-β-chloro-(*R,S*)-butyric acid methyl ester. Olsen *et al.*[7] stated that the H_β vinyl proton signals of various α-acylaminocrotonates [formamides were not studied] suffered downfield or upfield shifts from $SiMe_4$ upon change of solvent from $CDCl_3$ to trifluoroacetic acid (TFA) when the olefin was of *Z*- or *E*-configuration, respectively. We prepared the *Z*-methyl α-acetamidocrotonate (7a) from *N*-acetyl-*O*-benzoyl-(*R,S*)-threonine methyl ester and studied the ^{1}H n.m.r. in two solvents, $CDCl_3$ and TFA. In TFA, the ^{1}H n.m.r. spectrum showed the appearance of two amide conformers in the ratio of 5 : 1 for the *Z*-olefin (7a), while in $CDCl_3$ only evidence for one amide conformation was found. Thus, it was decided to determine the ^{1}H n.m.r. spectra in two solvents ($CDCl_3$ and TFA) for all the *N*-acyldehydroamino-esters of interest.

Comparison of the data for the formamides (1a, b) and acetamides (7a, b) shown in Tables 1 and 2 readily allows us to assign the *Z* and *E*-configuration to formamides (1a) and (1b), respectively. As is seen there is a very satisfactory agreement in the chemical shift values for the corresponding protons for each type of amide. The magnitude of the vicinal coupling constant for the amide and formyl protons [in TFA as solvent] allows us to assign the *trans*- and *cis*-amide conformations to the major and minor formamide conformers, respectively. Finally, the good correlation between the chemical shifts of the vinyl and β-methyl protons in each of the conformers of the acetamides (7a, b) *vs.* those in the corresponding formamides (1a, b) now allows us to assign the *trans*- and *cis*-amide conformations to the major and minor acetamide conformers, respectively (in TFA).

For example, the major conformers of methyl α-formamidocrotonate (1a) and *Z*-methyl α-acetamidocrotonate (7a) show vinyl proton signals of δ 6.73 *vs.* 6.72, respectively, and β-methyl proton signals of δ 1.77 *vs.* 1.73, respectively (in $CDCl_3$). In addition, the major and minor *Z*-formamide conformers show amide vicinal coupling constants of 2 and 12 Hz, respectively (in TFA). Thus, the two major conformers of *Z*-methyl α-formamido- or acetamido-crotonate are assigned the *trans*-amide conformation, while the minor conformers are the corresponding *cis*-amides.

In a similar manner, the major conformer of the methyl α-formamidocrotonate isomer (1b) can be shown to be the *E-trans*-amide. Since the corresponding ethyl ester analogues (12a, b) show almost identical ^{1}H n.m.r. chemical shifts for the respective vinyl and β-methyl proton signals (see Table 3), it is clear that the original configurational assignment of the ethyl α-formamidocrotonates (12a, b) must now be reversed.[3]

Attention is brought to the fact that in the *Z*-methyl α-formamidocrotonate (1a), the β-methyl protons are somewhat sensitive to the *cis,trans*-amide conformations (δ 1.77 and 1.90 for the *trans*- and *cis*-amide conformers in $CDCl_3$ as solvent), while the vinyl protons are less sensitive (δ 6.73 and 6.66). In the *E*-methyl α-formamidocrotonate (1b) now the vinyl protons are extremely sensitive to the two formamide conformations in $CDCl_3$ (δ 7.17 *vs.* 6.08 for the vinyl protons in the major *trans*-amide conformer *vs.* the minor *cis*-amide conformer, respectively), while the β-methyl protons are now insensitive (δ 2.07 *vs.* 2.09). This appears reasonable since in the *Z*-configurational isomer (1a) it is the β-

TABLE 3

^{1}H N.m.r. data of *Z,E*-ethyl α-acylamino-β-substituted acrylates (*trans*-amide conformer), $R^1R^2C{=}C(NHCOR^3)$-$COOCH_2CH_3$ [a]

Compd.	R^1	R^2	R^3	Config.	H_β vinyl	H_γ	OCH_2CH_3	OCH_2CH_3
(12a) [i]	Me	H	H	*Z*	6.68 (q)	1.73 (d) [d]	4.19 (q)	1.29 (t)
(12b) [i]	H	Me	H	*E*	7.17 (q)	2.05 (d) [d]	4.29 (q)	1.33 (t)
(13a)	Ph	H	H	*Z*	*c*	*c*	4.25 (q)	1.31 (t)
(13b)	H	Ph	H	*E*	7.84 (s)	*c*	4.02 (q)	0.98 (t)
(14a) [i]	Ph	Me	H	*Z*		2.25 (s) [d]	4.20 (q)	1.29 (t)
(14b) [i]	Me	Ph	H	*E*		2.10 (s) [d]	3.85 (q)	0.80 (t)
(15a) [j]	Ph	H	Ph	*Z*	*c*	*c*	4.33 (q)	1.38 (t)
(15b) [j]	H	Ph	Ph	*E*	8.10 (s)	*c*	4.20 (q)	1.05 (t)

[a] Spectra were measured with a Varian XL–100–15 at 100 MHz, ambient probe temperature, and the chemical shifts are expressed in δ values relative to internal $SiMe_4$. *J* values are in Hz. Solvent is $CDCl_3$, chemical shift values in brackets are for trifluoroacetic acid as solvent. [b] [*trans*-amide conformer]/[*cis*-amide conformer] > 1. [c] Signal overlaps with neighbouring signal(s). [d] β-Methyl protons. [e] β-Methylene protons. [f] β-Methine protons. [g] OCH_3 protons. [h] Data taken from refs. 7 and 8. [i] Solvent is CCl_4. [j] Data taken from ref. 12.

methyl protons that are *cis* to the amide group while in the *E*-configurational isomer (1b) it is the vinyl protons that are now *cis* to the amide.

Change of solvent from $CDCl_3$ to TFA resulted in a change of the *trans*/*cis*-amide ratio from 3 : 1 to 3 : 2 for the *E*-configurational isomer (1b). An increase in the amount of *cis*-amide was shown when monosubstituted formamides were studied in conc. H_2SO_4 *vs.* the neat liquid.[6] This was explained in terms of larger steric interactions between the *N*-alkyl group and the protonated oxygen atom [which are *cis* to each other in the *trans*-amide] as compared to the case when the oxygen atom is unprotonated. This also explains the observation that the *Z*-methyl α-acetamidocrotonate (7a) exhibits ^1H n.m.r. signals corresponding to only the *trans*-amide conformer in $CDCl_3$ while in TFA two amide conformations can be readily seen in the *trans*/*cis*-amide ratio of 5 : 1. *N*-Monosubstituted aliphatic amides with the carbonyl substituent larger than hydrogen (*i.e.* acetamides, propionamides, and isobutyramides, for example) show the presence of only the *trans*-amide conformation in the ^1H n.m.r. of the neat liquids, while the formamides show both the *cis*- and *trans*-amide forms.[6]

Change of solvent from $CDCl_3$ to TFA did not result in a change in the *trans*/*cis*-amide ratio of 2 : 1 for the *Z*-configurational isomer (1a). Further, the *trans*/*cis*-amide ratio of the other *Z*-methyl α-formamido-β-alkylacrylates (1)—(4) listed in Table 1 did not vary appreciably upon change of solvent from $CDCl_3$ to TFA, while this ratio in the other *E*-olefins listed in Table 1 showed an appreciable increase in the amount of the *cis*-amide in TFA. Examination of C.P.K. space filling models shows strong steric interactions between β-substituents and the amide proton (*cis* to each other in the *Z*-olefin) which would necessarily be absent when the β-substituent is a proton (as is the case for the olefins of *E*-configuration). Thus, one might speculate that there might be a connection between the torsional angle between the nitrogen and α-carbon *vis-à-vis* the sensitivity of the *trans*/*cis*-amide ratio to change when the solvent is changed. However, this is only a hypothesis which awaits verification *via* a more complete and detailed investigation of this phenomenon.

Table 1 shows that change of solvent from $CDCl_3$ to TFA causes the H_β proton signals corresponding to the *Z-trans*-amide and *Z-cis*-amide conformers to both undergo similar downfield shifts from $SiMe_4$. However, for the H_β proton signals corresponding to the *E-trans*-amide and *E-cis*-amide conformers, such a solvent change causes a decrease in the very large difference between their respective chemical shift values shown in $CDCl_3$. Thus, the H_β proton signal at smaller δ value (for the *E-cis*-amide conformer) undergoes a downfield shift for all cases studied, but the H_β proton signal at larger δ value (for the *E-trans*-amide conformer) shows variable behaviour. For the *E*-α-formamido-β-substituted acrylate esters, the H_β proton signal for the *E-trans*-amide conformer moves upfield towards $SiMe_4$ when the β-substituent is methyl, isopropyl, or phenyl. However, when the β-substituent is an ethyl group this particular proton signal underwent a slight downfield shift upon solvent change from $CDCl_3$ to TFA.

On the basis of these arguments, we can now assign the olefinic configuration and amide conformation to the other α-formamido-β-substituted acrylate esters (2)—(5) listed in Table 1. Comparison of the ^1H n.m.r. data for the *Z*-methyl α-formamido-β-isopropylacrylate (3a) with that of the methyl α-acetamido-β-isopropylacrylate (8a) [obtained *via* methanolysis of the azlactone produced from *N*-chloroacetyl-(*R*,*S*)-leucine according to the method of Doherty *et al.*[9]] shows that the α-acetamido-analogue (8a) is also of *Z*-configuration.

Z-Methyl α-formamido-β-t-butylacrylate (4a) was selected for ^1H n.m.r. variable-temperature study in $CDCl_3$. While coalescence of the formyl proton singlet and doublet signals to form one singlet is not well defined (as is generally accepted for the case of coalescence of two singlet signals), the range in which the shape of the ^1H n.m.r. signals exhibited the greatest sensitivity to temperature change was found to be 50 ± 3 °C.

The *Z*-configuration of *Z*-methyl α-acetamidocinnamate (9a) has been ascertained by ^1H n.m.r.[10] The *Z*-configuration of *Z*-methyl α-pivaloylamidocinnamate (10a) has been determined by correlation with that of the acetamido-analogue (9a) *via* the fact that the ^1H n.m.r. spectra of both parent azlactones show a singlet at δ 7.02 for the H_β proton. However, in $CDCl_3$ the H_β vinyl protons of methyl α-formamidocinnamate (5a), *Z*-methyl α-acetamidocinnamate (9a), and *Z*-methyl α-pivaloylamidocinnamate (10a) cannot be used for structural assignment since they fall within the multiplet for the aromatic protons. Fortunately, change of solvent to TFA shifts these vinyl protons downfield out of the aromatic multiplet to δ 7.70, 7.72, and 7.73, respectively. Thus, it now appears quite reasonable to assign the *Z*-configuration to the methyl α-formamidocinnamate (5a). *Z*-Methyl α-formamidocinnamate (5a) was also prepared from the ethyl α-formamidocinnamate (13a) *via* mild saponification to the free acid followed by reaction with diazomethane. Therefore, the ethyl ester analogue (13a) is also of *Z*-configuration. The α-acetamido- and α-pivaloylamido-methyl esters (9a) and (10a) show ^1H n.m.r. signals in $CDCl_3$ of only the *trans*-amide conformer, as opposed to the α-formamido-analogue (5a). Change of solvent to TFA shows the percent *trans*-amide conformer to be 51, 80, and 100% in this solvent for the formamido-, acetamido-, and pivaloylamido-esters, respectively. This is quite reasonable, since as the group attached to the carbonyl carbon atom becomes more sterically bulky, the interactions between it and the olefinic residue attached to the nitrogen [located *cis* to each other in the *cis*-amide] should become more and more severe.

The H_β vinyl proton of *E*-methyl α-formamidocinnamate (5b) shows ^1H n.m.r. signals at δ 7.97 and 6.75 in $CDCl_3$, corresponding to the *E-trans*-amide and *E-cis*-

amide conformers, respectively. Change of solvent to TFA results in an upfield shift of the H_β *E-trans*-amide proton signal to δ 7.54, and a downfield shift of the H_β *E-cis*-amide proton signal to within the δ 7.30 ± 0.10 multiplet of the aromatic protons. Thus, the *Z,E*-configurational assignment of the methyl α-formamidocinnamates (5a, b) is consistent with all the points mentioned thus far.

In addition, the anisotropy of the β-phenyl ring can be utilized to further characterize the *E*-methyl or -ethyl α-formamidocinnamates in particular. C.P.K. space filling models show a severe steric interaction between the β-phenyl group and the ester moiety [*cis* to each other in the *E*-olefin] such that the β-phenyl group is skew to the olefinic bond. The ethoxycarbonyl or methoxycarbonyl groups can assume a conformation such that the CH_3 protons therein fall in the middle of the phenyl ring shielding cone. Thus, the chemical shifts in $CDCl_3$ of the methylene and methyl protons of the ethoxycarbonyl group in the *trans*-amide conformers of the *E vs.* the *Z*-olefin [(13b) *vs.* (13a)] are δ 4.02 (quartet) and δ 0.98 (triplet) *vs.* δ 4.25 (quartet) and δ 1.31 (triplet), respectively. Similarly, the chemical shifts in $CDCl_3$ of the methyl protons in the methoxycarbonyl group in the *E vs.* the *Z*-olefins [(5b) *vs.* (5a)] are δ 3.58 and 3.78, respectively. These values can be compared to those of the *trans*-amide conformers of *Z*- and *E*-ethyl α-formamidocrotonate esters (12a, b) (where there can be no phenyl group anisotropy) in which the methyl protons within the ethoxycarbonyl moiety appear in $CDCl_3$ at δ 1.29 and 1.33, respectively.

The phenyl ring anisotropy effect upon the protons of the neighbouring ethoxycarbonyl group is also seen in the *trans*-amide conformer of *E*-ethyl α-formamido-β-methylcinnamate (14b) as well as in the corresponding *E*-ethyl α-benzamidocinnamate (15b) analogue. The question of *E,Z*-configuration in the 4-benzylidene-2-phenyl-2-oxazolin-5-one azlactones has been unambiguously resolved by X-ray determination of the ring-opened acid [from the 166—167 °C melting point *Z*-azlactone].[11] The ^1H n.m.r. of the *Z*- and *E*-ethyl α-benzamidocinnamates obtained *via* ethanolysis of the *Z* and *E*-azlactones showed triplet (OCH_2CH_3) signals at δ 1.37 and 1.05, respectively.[12]

Thus, the use of ^1H n.m.r. has been demonstrated to be quite effective as a tool in the unambiguous assignment of *Z* and *E*-configuration for a wide group of prochiral α-formamido-α,β-unsaturated esters.

EXPERIMENTAL

All ^1H n.m.r. spectra were performed in the continuous wave mode using a Varian XL-100-15 spectrometer at 100.1 MHz (unless otherwise noted), and ambient probe temperature. Sample concentration was 40—50 mg dissolved in 0.25—0.30 ml of solvent. The solvents utilized were primarily deuteriochloroform or trifluoroacetic acid and are so noted. All chemical shift values are given in p.p.m. relative to internal $SiMe_4$.

The *Z,E*-methyl or ethyl α-formamido-β-substituted-acrylates were synthesized according to the method of Schöllkopf *et al.*[3] *via* condensation of methyl or ethyl isocyanoacetate and the appropriate aldehyde (or ketone) in the presence of base. With the exception of *Z*-methyl α-formamidocrotonate, the *Z*-methyl or -ethyl α-formamido-β-substituted acrylates were isolated *via* crystallization from the *Z,E*-olefinic mixture in benzene–light petroleum. In this manner, *Z*-methyl α-formamido-β-ethylacrylate, m.p. 42 °C; *Z*-methyl α-formamido-β-isopropylacrylate, m.p. 78 °C; *Z*-methyl α-formamido-β-t-butylacrylate, m.p. 58—59 °C; *Z*-methyl α-formamidocinnamate, m.p. 88—89 °C; *Z*-ethyl α-formamidocinnamate, m.p. 68—69 °C; and *Z*-methyl α-formamido-3′,4′-dimethoxycinnamate, m.p. 134—136°, were all isolated. The corresponding *E*-isomers were obtained *via* distillation *in vacuo* of the appropriate mother liquors to yield an *E,Z*-mixture of olefins enriched in the *E*-isomers. The *Z*-methyl α-formamidocrotonate, b.p. 113 °C/1 Torr, was obtained *via* silica-gel chromatography of the *Z,E*-olefinic mixture followed by distillation *in vacuo*. All new compounds that were crystalline plus the liquid *Z*-methyl α-formamidocrotonate gave satisfactory elemental analysis for C, H, and N to within 0.3% of the calculated values. Elemental analyses were performed at the Hebrew University of Jerusalem.

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