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Synthesis of β,γ-unsaturated primary amides from α,β-unsaturated acids and investigation of the mechanism

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ABSTRACT

α,β-Unsaturated acids, through their acid chlorides, react with tritylamine in the presence of triethylamine under mild conditions, to afford in high yield and high regioselectivity the corresponding β,γ-unsaturated tritylamides. Detritylation with TFA generates quantitatively β,γ-unsaturated primary amides. An investigation of this deconjugative isomerization was performed.

1. Introduction

The development of efficient methods for the synthesis of amides remains a great challenge because of their importance in chemistry and biology, as valuable intermediates in organic synthesis and with a wide range of applications in industry.

In the course of our ongoing interest in tritylamine reactions and their synthetic uses,[1] we have designed the synthesis of primary amines and primary amides by aminotritylation of the corresponding halides or acid chlorides and subsequent detritylation with TFA, under mild conditions. A wide range of carboxylic acids and derivatives were successfully converted to their corresponding primary amides.[1d] During this study it has been observed that the described procedure, applied on an *E*-2-unsaturated acid, did not gave the expected *E*-2-unsaturated amide, but a deconjugative isomerization occurred and the corresponding 3-unsaturated amide was obtained in high yield.

Although the β,γ-unsaturated primary amides are synthetically important key intermediates and useful precursors for various important and biologically active compounds,[2] there is no extensive literature on their synthesis. In general, traditional methods are suggested for the conversion of β,γ-unsaturated carboxylic acids (3-alkenoic acids) and their derivatives to the corresponding amides,[3] as, for example, the reaction of the corresponding acyl chlorides with ammonia[3a,3c] and the hydration of β,γ-unsaturated nitriles.[2g,3b] However the above precursors are not always readily accessible. Ragoussis et al. prepared (*E*)-3-alkenoic acids, in good yields, by a modified Knoevenagel condensation.[4] In addition, starting from allylic compounds, β,γ-unsaturated amides were obtained by rhodium carbonyl-catalyzed azacarbonylation of allyl phosphates[5] and by treatment of allylic alcohols with *N*,*N*-dimethylformamide acetals, giving β,γ-unsaturated *N*,*N*-dimethylamides.[6] Aminolysis of β-dialkylphosphoryl-γ-lactones, provided preferentially (*E*)-β,γ-unsaturated amides.[7] Moreover, several palladium-catalyzed methods for the synthesis of important β,γ-unsaturated amides have been reported.[8]

The present work was undertaken in order to establish an efficient procedure to β,γ-unsaturated primary amides by the reaction of tritylamine with α,β-unsaturated acid halides and subsequent detritylation by TFA, under mild conditions. Moreover, an investigation of the deconjugative isomerization of the α,β-unsaturated acid derivatives, during the tritylation process, was performed in our laboratory.

2. Results and discussion

The reaction of α,β-unsaturated acyl chlorides with tritylamine and the subsequent detritylation of the *N*-tritylamides[1d] was

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further investigated to explore the optimal reaction conditions, in order to finally obtain the desired unsaturated primary amides. In a typical procedure the α,β-unsaturated acyl chlorides, derived from the corresponding *E*-2-alkenoic acids, were treated with triethylamine in dichloromethane at 0 °C, followed by the addition of tritylamine. The *N*-tritylamides were isolated in high yield after work-up. Surprisingly it has been observed that, in almost all the cases, the expected α,β-unsaturated *N*-tritylamide was not obtained, but the β,γ-unsaturated tritylamide, regioselectively and in high yield. Detritylation of these *N*-tritylamides by TFA in DCM at rt, followed by the addition of triisopropylsilane $^{i}Pr_3SiH$, gave almost quantitatively the primary β,γ-unsaturated amides, as mixtures of their geometrical isomers. The results are summarized in Table 1.

In a similar way, under the same reaction conditions, we treated two different α,β-unsaturated acyl chlorides (crotonic chloride and 2-hexenoic chloride) with a series of several amines, in the presence or not of Et_3N, in order to study the possible deconjugation of the double bond in the corresponding substituted amides. The results are summarized in Table 2. The ratio of the substituted amides, appearing in the Table 2, is deduced from the ^1H NMR spectra.

The isomerization appeared to be dependent on the steric hindrance of the amine-reagent as well on the size and the basicity of the amine present in the medium of the reaction. Thus, only in the case of the bulky tritylamine in the presence of Et_3N, was the β,γ-unsaturated *N*-tritylamide the sole product. In all the other cases, either mixtures of conjugated and deconjugated products, or only the conjugated products were obtained. As confirmed from the ^1H

Table 1
Synthesis of β,γ-unsaturated primary amides from α,β-unsaturated acyl chlorides, using tritylamine and triethylamine

Substrate	*N*-Tritylamide[a]	Amide[b]	Ref.
$CH_3CH{=}CHCOCl$	$CH_2{=}CHCH_2CONHTr$	$CH_2{=}CHCH_2CONH_2$	3a,c
$CH_3CH_2CH{=}C(CH_3)COCl$	$CH_3CH{=}CHCH(CH_3)CONHTr$ (22%) +$CH_3CH_2CH{=}C(CH_3)CONHTr$ (78%)	—	—
$CH_3(CH_2)_2CH{=}CHCOCl$	$CH_3CH_2CH{=}CHCH_2CONHTr$	$CH_3CH_2CH{=}CHCH_2CONH_2$	2g
$CH_3(CH_2)_3CH{=}CHCOCl$	$CH_3(CH_2)_2CH{=}CHCH_2CONHTr$	$CH_3(CH_2)_2CH{=}CHCH_2CONH_2$	5
$CH_3(CH_2)_4CH{=}CHCOCl$	$CH_3(CH_2)_3CH{=}CHCH_2CONHTr$	$CH_3(CH_2)_3CH{=}CHCH_2CONH_2$	—
$CH_3(CH_2)_5CH{=}CHCOCl$	$CH_3(CH_2)_4CH{=}CHCH_2CONHTr$	$CH_3(CH_2)_4CH{=}CHCH_2CONH_2$	5
$CH_3(CH_2)_6CH{=}CHCOCl$	$CH_3(CH_2)_5CH{=}CHCH_2CONHTr$	$CH_3(CH_2)_5CH{=}CHCH_2CONH_2$	—

[a] Yields, based on 2-alkenoic acids, are ~80–90%.
[b] Detritylation is almost quantitative (≥85%).

The obtained products were easily separated or purified by column chromatography on silica gel. Some of the final products are already known compounds and their spectroscopic data are consistent with the literature values. The identity of the intermediate *N*-tritylamides and of the final products was determined by ^1H NMR and IR spectroscopy.

The deconjugation of a carbon–carbon double bond of unsaturated carbonyl compounds, by the use of a strong base,[9] such as LDA, *t*-BuOK, *n*-BuLi, disilazide, etc., is an interesting reaction that has been described several times in the past. The γ-deprotonation of α,β-unsaturated salts of carboxylic acids or esters, afforded the corresponding β,γ-unsaturated derivatives in a mixture of *Z*/*E* isomers in variable ratios.[9] Deconjugation of α,β-unsaturated chlorides has been observed during their esterification in the presence of benzyl alcohol and triethylamine, affording β,γ-unsaturated benzyl esters.[10]

Our results (Table 1) may be ascribed to the formation of an intermediate ketene, as it is known that, when an acyl halide is treated with a tertiary amine (Et_3N), the corresponding ketene (R–CH=C=O) is generated.[11,12] The fact that α,β-unsaturated acyl chlorides disposing hydrogen atoms on the γ-carbon, in the presence of tertiary amines, are precursors to vinyl ketenes, strongly indicates that a vinyl ketene is the active acylating agent. This transformation is a base-induced elimination of hydrogen chloride from an acid chloride.[12] In the present work, the ketenes, formed from the α,β-unsaturated acid chlorides (RCH=CH–CH=C=O), are supposed to be trapped by the bulky tritylamine to afford the *N*-tritylamides, which are, later, detritylated with TFA (Fig. 1).

Table 2
Formation of *N*-substituted amides from α,β-unsaturated acyl chlorides

Substrate	Amine (RNH_2)	Base	*N*-Tritylamides (according to the ^1H NMR spectra) (yield)
$CH_3CH{=}CHCOCl$	$TrNH_2$	Et_3N	$CH_2{=}CHCH_2CONHTr$
		Pyr	$CH_3CH{=}CHCONHTr$
		$TrNH_2$	$CH_3CH{=}CHCONHTr$
	$BnNH_2$	$BnNH_2$	$CH_3CH{=}CHCONHBn$
		Et_3N	$CH_3CH{=}CHCONHBn$
	$MeNH_2$	$MeNH_2$	$CH_3CH{=}CHCONHMe$
	Ph_2CHNH_2	Et_3N	$CH_2{=}CHCH_2CONHCHPh_2$ (30%)+ $CH_3CH{=}CHCONHCHPh_2$ (70%)
	$PhNH_2$	Et_3N	$CH_2{=}CHCH_2CONHPh$ (38%)+ $CH_3CH{=}CHCONHPh$ (62%)
	$ArNH_2$[a]	Et_3N	$CH_2{=}CHCH_2CONHAr$ (45%)+ $CH_3CH{=}CHCONHAr$ (55%)
$CH_3(CH_2)_2$ CH=CHCOCl	$TrNH_2$	Et_3N	CH_3 $CH_2CH{=}CHCH_2CONHTr$
		Pyr	$CH_3(CH_2)_2CH{=}CHCONHTr$
	n-$BuNH_2$	n-$BuNH_2$	$CH_3(CH_2)_2CH{=}CHCONHBu$
		Et_3N	$CH_3(CH_2)_2CH{=}CHCONHBu$
	$MeNH_2$	$MeNH_2$	$CH_3(CH_2)_2CH{=}CHCONHMe$
	$BnNH_2$	$BnNH_2$	$CH_3(CH_2)_2CH{=}CHCONHBn$
		Et_3N	$CH_3(CH_2)_2CH{=}CHCONHBn$
	Ph_2CHNH_2	Et_3N	$CH_3CH_2CH{=}CH$ $CH_2CONHCHPh_2$ (40%)+ $CH_3(CH_2)_2CH{=}CHCONHCHPh_2$(60%)
	$PhNH_2$	Et_3N	$CH_3CH_2CH{=}CH$ $CH_2CONHPh$ (48%)+ $CH_3(CH_2)_2CH{=}CHCONHPh$ (52%)
	$ArNH_2$	Et_3N	$CH_3CH_2CH{=}CH$ $CH_2CONHAr$ (58%)+ CH_3 $(CH_2)_2CH{=}CHCONHAr$ (42%)

[a] Where $ArNH_2$ is the 2-methyl-6-nitroaniline.

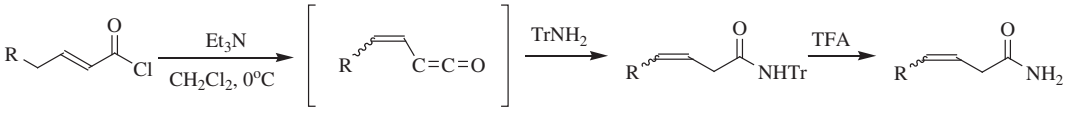


Fig. 1. Synthesis of β,γ-unsaturated primary amides from α,β-unsaturated acid chlorides.

NMR spectra, highly reactive and unhindered amines (*n*-butylamine, benzylamine and methylamine) produced the conjugated products, with or without Et_3N in the medium. When the steric effects become more significant and the nucleophilicity is weaker (diphenylmethylamine, aniline or 2-methyl-6-nitroaniline), poor selectivity was obtained and mixtures of the above two isomers were formed. It is noteworthy that, in the synthesis of tritylamides, when pyridine was used in the place of Et_3N, or when tritylamine was used in excess without Et_3N, the sole product was the conjugated isomer in all the cases.

Taking into account the fact of the formation of an intermediate ketene, when an acyl halide is treated with a tertiary amine,[11] we can reasonably assume, now, that the above described isomerization takes place during the amidation of the acyl halide by a weak and bulky amine, as follows (Fig. 2, A).

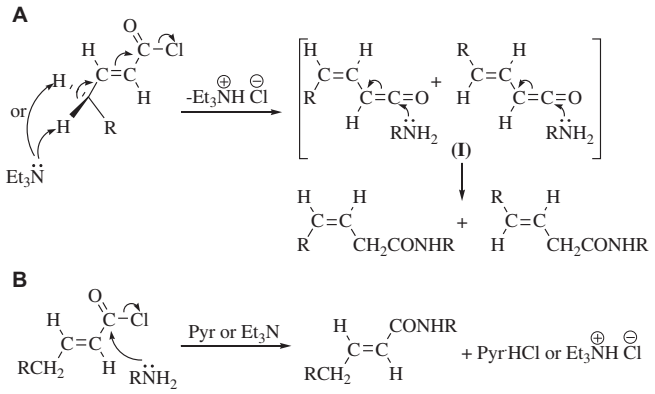


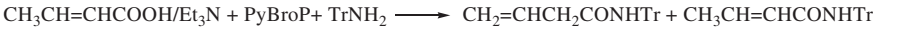
Fig. 2. (A) Plausible mechanism for the bulky amine RNH_2/Et_3N acylation and isomerization; (B) Mechanism for the bulky amine RNH_2/Pyr acylation, or for the unhindered amine RNH_2/Et_3N acylation.

It seems that the isomerized products arise from the intermediate β,γ-unsaturated ketene, which reacts with tritylamine, a weak nucleophile. The strong tertiary base triethylamine abstracts the γ-methylene proton ($RCH_2CH{=}CHCOCl$) and causes the carbon–carbon double bond migration. Subsequent reaction of the tritylamine with the intermediate ketene produced variable ratios of *Z* and *E* isomers of β,γ- products, the *Z*-configuration slightly predominating. The observed *Z*/*E* distributions must arise in the proton abstraction and the double bond migration step, and could be explained starting from different conformations of the RCH_2 group of the acyl chloride (Fig. 2, A). The *Z* and *E* isomers could be separated by column chromatography or preparative TLC, according to the literature.[9e]

Under the same reaction conditions, as mentioned above, the weaker tertiary base pyridine can not abstract the γ-methylene proton and cause the double bond migration. In this case a nucleophilic acyl substitution takes place by the amine and pure α,β-unsaturated products are isolated. The conjugated amides arise, in any case, via the direct acylation of the amine with the acid chloride, as the nucleophile reacts rapidly attacking the carbonyl group, before the generation of a ketene (Fig. 2, B).

It should also be noted that a steric effect on the reaction of an α-substituted acid halide was observed. In the case of the $CH_3CH_2CH{=}C(CH_3)COCl$ (*E*-2-methyl-2-pentenoyl chloride), the main reaction product, 78%, was the *E*-α,β-unsaturated tritylamide $CH_3CH_2CH{=}C(CH_3)CONHTr$ and only 22% of the *Z*-β,γ-unsaturated product $CH_3CH{=}CHCH(CH_3)CONHTr$ was obtained. The above ratio of the two substituted amides, appearing in the Table 1, is deduced from the ^1H NMR spectrum of the isolated product. Obviously, the replacement of hydrogen by a methyl group produces significant steric hindrance[10] in the abstraction of a γ-hydrogen by the bulky Et_3N to form the corresponding ketene.

As an alternative synthetic method, in order to better elucidate the proposed mechanism, we tried to couple crotonic acid with tritylamine by the use of bromotripyrrolidinophosphonium hexafluorophosphate (PyBroP), an effective peptide coupling reagent suggested for sterically hindered reactants, in the presence of Et_3N,[1d,13] through the preparation of an active ester (Scheme 1). In this case, the isomerized β,γ-unsaturated compound was obtained as the main product (~75%). With aniline, the isomerized amide was only 8%, while with benzylamine the product was exclusively the α,β-unsaturated amide. Similar results were obtained with the coupling of 2-hexenoic acid (~80% isomerization with $TrNH_2$ and ~10% with $PhNH_2$).



Scheme 1.

It is not evident that the intermediate activated ester liberates the unsaturated ketene, directly or after a speculated in situ formation[13b] of the acyl bromide, which may react in accord to the same above described mechanism. At least, it seems reasonable that the intermediate activated species undergoes aminolysis by two paths, depending on the bulkiness and the nucleophilicity of the amine. A possible proposed mechanism is as follows (Fig. 3).

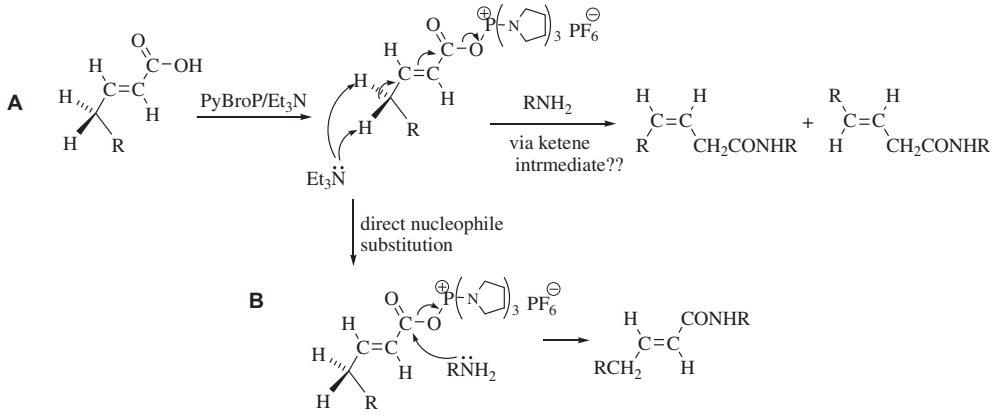


Fig. 3. Proposed possible mechanism for the coupling of 2-alkenoic acids with RNH_2 by the use of $PyBroP/Et_3N$.

Inspection of the ^{1}H NMR spectra of all the β,γ-unsaturated amides reveals a useful feature, which is in accordance with the literature:[5,6,9e] the α-protons of the *Z*- and *E*-β,γ-unsaturated amides are observed as two very characteristic-diagnostic doublets at $\delta = \sim 3.0$ ppm (=CHCH_2CO–), with different integrals (*Z*,*E*). The signal of the *Z* isomer ($J = \sim 7$ Hz) is located at slightly lower field (~ 0.04–0.09 ppm) than the *E* isomer ($J = \sim 6$ Hz), as expected.[3d,5,9e] The IR spectra of *N*-tritylamides revealed the N–H absorbance at 3260 cm^{-1}, which was replaced, after TFA deprotection and conversion to primary amides, by two N–H absorptions at 3360 and 3185 cm^{-1}.

The structures of α,β-unsaturated amides, obtained, e.g., in the presence of pyridine or otherwise, are readily deduced from their ^{1}H NMR spectra. The chemical shifts of all the conjugated amides are consistent with the expected ones for the α,β-unsaturated isomers, with the entire absence of the characteristic, for the β,γ-isomer, doublet at $\delta = \sim 3.0$ ppm.[9e,14]

3. Conclusions

We report in this paper a novel, easy and efficient method for the conversion of linear α,β-unsaturated carboxylic acids to the β,γ-unsaturated primary amides, in good yields and high regioselectivity, by tritylation of the corresponding acid chlorides with tritylamine and subsequent detritylation in mild conditions. It is reasonably assumed that the deconjugated tritylamides arise by the acylation of the amine through the intermediate ketene and not via direct acylation of the amine with the acid chloride. The experimental process and the reagents are readily available.

4. Experimental

4.1. General

^{1}H NMR spectra were obtained at 250 MHz using a Bruker AMX-250 spectrometer, in $CDCl_3$ solutions. Chemical shifts are given in δ units parts per million (ppm) relative to TMS as internal standard. Infrared spectra were obtained on a Perkin–Elmer GX FT spectrometer, using KBr disks (4000–400 cm^{-1}). Column chromatography was carried out over silica gel 60 (70–200 mesh). Thin layer chromatography (TLC) was performed using Merck Silica gel 60 F_{254} plates. Commercially available reagents were used without further purification. Tritylamine was prepared according to the literature.[1a] All solvents were dried by standard methods and distilled before use.

4.2. Typical procedure for the preparation of *N*-trityl-3-alkenamides from α,β-unsaturated acids

(a) To a solution of the 2-alkenoic acid (1 mmol) in dry dichloromethane (DCM, 3 mL), oxalyl chloride $(COCl)_2$ (3.5 mmol, 0.3 mL) and two drops of DMF were added at 0 °C. The mixture was allowed to stir for 15 min at 0 °C and then for ~2 h at rt, until no gas was observed. The solvent and the excess of oxalyl chloride were distilled off to dryness. The obtained acyl chloride was used in the next step without further purification.

(b) The above obtained chloride was dissolved in dry DCM (5 mL) under argon and cooled at 0 °C. Et_3N (5 mmol) was added, followed by addition of $TrNH_2$ or other RNH_2 (1 mmol) in DCM (3 mL) at 0 °C under stirring for 5 min. The resulting mixture was allowed to stir at rt until complete conversion, as indicated by TLC. The solvent was removed, the residue was redissolved in DCM, washed with water, an aqueous solution of 5% potassium hydrogen sulfate ($KHSO_4$) and brine, dried over anhydrous Na_2SO_4, concentrated in vacuo and purified by column chromatography on silica gel (methanol/dichloromethane, 1:20). The products, *N*-trityl-3-alkenamides, are white solids, mixtures of geometrical isomers *E* and *Z*, except of *N*-trityl-3-butenamide, as revealed from their ^{1}H NMR spectra. Yield: 80–90%.

4.2.1. N-Trityl-3-butenamide. ^{1}H NMR: δ 3.01 (d, 2H, J=7.20 Hz, CH_2), 5.26–5.28 (m, 2H, CH_2=), 6.01 (m, 1H, =C*H*) 6.88 (s, 1H, N*H*), 7.20–7.40 (m, 15H, Ar*H*); IR (KBr) 3241, 3026, 2855, 1654, 1633, 970 cm^{-1}.

4.2.2. N-Trityl-2-methyl-2-pentenamide (E, 78%). ^{1}H NMR: δ 1.11 (t, 3H, J=7.50 Hz, CH_3), 1.95 (s, 3H, CH_3), 2.24 (q, 2H, J=7.25 Hz, CH_2), 6.40 (dt, 1H, J=7.25, 1.25 Hz, C*H*=), 6.97 (s, 1H, N*H*), 7.20–7.60 (m, 15H, Ar*H*), and *N-Trityl-2-methyl-3-pentenamide* (*Z*, 22%); ^{1}H NMR: δ 1.31 (d, 3H, J=7.00 Hz, CH_3), 1.80 (d, J=7.00 Hz, 3H, CH_3), 3.08 (q, 1H, J=7.00 Hz, C*H*(CH_3)), 5.65–5.75 (m, 2H, C*H*=C*H*), 6.93 (s, 1H, N*H*), 7.20–7.60 (m, 15H, Ar*H*).

4.2.3. N-Trityl-3-hexenamide. ^{1}H NMR: δ 1.08 (two overlapping t, 3H, CH_3), 2.10–2.30 (m, 2H, CH_2), 3.08 and 3.18 (two d, 2H, J=6.25 Hz, CH_2 for (*E*) ~35% and J=7.00 Hz, CH_2 for (*Z*) ~65%), 5.60–5.90 (m, 2H, C*H*=C*H*), 7.02 (br s, 1H, N*H*), 7.20–7.46 (m, 15H, Ar*H*); IR (KBr) 3261, 3022, 2962, 2933, 2873, 1651, 967 cm^{-1}.

4.2.4. N-Trityl-3-heptenamide. ^{1}H NMR: δ 0.98 (t, 3H, J=7.50 Hz, CH_3), 1.38–1.54 (m, 2H, CH_2), 2.11 (m, 2H, CH_2), 3.08 and 3.16 (two d, 2H, J=6.25 Hz, CH_2 for (*E*) ~45% and J=7.00 Hz, CH_2 for (*Z*) ~55%), 5.65–5.86 (m, 2H, C*H*=C*H*), 6.96 and 6.98 (two s, 1H, N*H*, for (*E*) 45% and for (*Z*) 55%), 7.15–7.42 (m, 15H, Ar*H*); IR (KBr) 3260, 3023, 2959, 2928, 2871, 1650, 967 cm^{-1}.

4.2.5. N-Trityl-3-octenamide. ^{1}H NMR: δ 0.82 (two overlapping t, 3H, CH_3), 1.18–1.30 (m, 4H, (CH_2)$_2$), 2.05 (m, 2H, CH_2), 2.97 and 3.05 (two d, 2H, J=6.00 Hz, CH_2 for (*E*) ~48% and J=7.00 Hz, CH_2 for (*Z*) ~52%), 5.55–5.74 (m, 2H, C*H*=C*H*), 6.85 and 6.87 (two s, 1H, N*H*, for (*E*) and for (*Z*)), 7.10–7.35 (m, 15H, Ar*H*); IR (KBr) 3260, 3022, 2956, 2856, 1650, 968 cm^{-1}.

4.2.6. N-Trityl-3-nonenamide. ^{1}H NMR: δ 0.97 (t, 3H, J=7.50 Hz, CH_3), 1.25–1.54 (m, 6H, (CH_2)$_3$), 2.17 (m, 2H, CH_2), 3.09 and 3.18 (two d, 2H, J=6.00 Hz, CH_2 for (*E*) ~43% and J=6.75 Hz, CH_2 for (*Z*) ~57%), 5.76 (m, 2H, C*H*=C*H*), 7.01–7.03 (two overlapping s, 1H, N*H* for (*Z*) and for (*E*)), 7.20–7.44 (m, 15H, Ar*H*); IR (KBr) 3260, 3020, 2924, 2855, 1651, 970 cm^{-1}.

4.2.7. N-Trityl-3-decenamide. ^{1}H NMR: δ 0.89 (t, 3H, J=7.50 Hz, CH_3), 1.18–1.42 (m, 8H, (CH_2)$_4$), 2.08 (m, 2H, CH_2), 3.01 and 3.09 (two d, 2H, J=6.50 Hz, CH_2 for (*E*) ~47% and J=7.25 Hz, CH_2 for (*Z*) ~53%), 5.56–5.84 (m, 2H, C*H*=C*H*), 6.89 and 6.92 (two s, 1H, N*H*, for (*E*) and for (*Z*)), 7.15–7.35 (m, 15H, Ar*H*); IR (KBr) 3259, 3029, 2957, 2924, 2853, 1650 cm^{-1}.

4.3. Typical procedure for the preparation of (*E*)-*N*-trityl-2-alkenamides from α,β-unsaturated acids

These compounds were prepared and purified according to the general procedure described above for the synthesis of *N*-trityl-3-alkenamides, using pyridine instead of triethylamine. The pure products were identified only by their ^{1}H NMR spectra.

4.3.1. N-Trityl-2-butenamide (E). A white solid, mp 190–191 °C; ^{1}H NMR: δ 1.84 (dd, 3H, J=8.00, 2.00 Hz, CH_3), 5.94 (dd, 1H, J=15.50, 2.00 Hz, C*H*=), 6.56 (s, 1H, N*H*), 6.81 (m, 1H, C*H*=), 7.15–7.43 (m, 15H, Ar*H*).

4.3.2. N-Trityl-2-hexenamide (E). A white solid, mp 199–201 °C; ^{1}H NMR: δ 0.98 (t, 3H, J=7.25 Hz, CH_3), 1.48 (m, 2H, J=7.25 Hz, CH_2),

2.25 (m, 2H, CH_2), 5.98 (d, 1H, J=15.25 Hz, CH=), 6.63 (s, 1H, NH), 6.89 (dt, 1H, J=15.25, 7.25 Hz, CH=), 7.20–7.42 (m, 15H, ArH).

4.3.3. N-Trityl-2-octenamide (E). A white solid, mp 203–205 °C; ^{1}H NMR: δ 0.91 (t, 3H, J=7.00 Hz, CH_3), 1.20–1.45 (m, 6H, (CH_2)$_3$), 2.18 (m, 2H, CH_2), 5.77 (d, 1H, J=15.50 Hz, CH=), 6.68 (s, 1H, NH), 6.90 (dt, 1H, J=15.50, 7.00 Hz, CH=), 7.08–7.40 (m, 15H, ArH).

4.4. Typical procedure for the preparation of *N*-tritylamides from α,β-unsaturated acids with PyBroP as coupling reagent

To a solution of the carboxylic acid (1 mmol) in dry DCM (3 mL), TrNH$_2$ (1 mmol), PyBroP (1 mmol) and Et$_3$N (3 mmol) in DCM (2 mL) were added and the mixture was allowed to stir at 0 °C for 5 min and at rt overnight, until completion of the reaction. The mixture was then diluted with AcOEt (25 mL), washed with water, 5% KHSO$_4$, dried over anhydrous Na$_2$SO$_4$, concentrated in vacuo and purified by column chromatography on silica gel. The obtained *N*-tritylamides were mixtures of α,β- and β,γ-unsaturated compounds, as identified by ^{1}H NMR spectroscopy.

4.5. Typical procedure for the detritylation of the *N*-trityl-3-alkenamides

To a solution of the tritylamide (1 mmol) in DCM (2 mL), TFA (6 mL) was added and the reaction mixture was allowed to stand at rt for 0.5–3 h, until completion of the reaction. Triisopropylsilane (~3 mmol) was added and the produced bright yellow colour of the solution was disappeared in a few minutes. After 30 min the colourless solution was diluted with CCl$_4$ and evaporated to dryness. The residue was redissolved in diethyl ether (2 mL) and hexane was added for the precipitation of the deprotected amide as white amorphous solid. The resulting triphenylmethane remains soluble in hexane. If necessary, the amide was purified by column chromatography on silica gel (methanol/dichloromethane, 1:20 to 1:4). The obtained 3-alkenamides were, as expected, mixtures of *E* and *Z* isomers, except of 3-butenamide, and the yield was ≥85%.

4.5.1. 3-Butenamide. A white solid, mp 71–72 °C (lit.[3a] 74–75 °C; lit.[15] 72 °C); [Found: C, 56.70; H, 8.13; N, 16.52. C$_4$H$_7$NO requires C, 56.45; H, 8.29; N, 16.46%]; ^{1}H NMR: δ 2.98 (d, 2H, J=7.20 Hz, CH_2), 5.40–5.75 (m, 2H, =CH_2), 6.00 (br m, 2H: 1H, =CH and 1H, NH, NH$_2$); 6.20 (br s, 1H, NH, NH$_2$); IR (KBr): 3353, 3186, 2815, 1671, 962 cm^{-1}.

4.5.2. 3-Hexenamide. A white solid; [Found: C, 63.81; H, 9.73; N, 12.51. C$_6$H$_{11}$NO requires C, 63.68; H, 9.80; N, 12.38%]; ^{1}H NMR: δ 0.95 (two overlapping t, 3H, CH_3), 2.03 (m, 2H, CH_2), 2.90 and 2.95 (two d, 2H, J=6.25 Hz, CH_2 for (*E*) ~35% and J=7.00 Hz, CH_2 for (*Z*) ~65%), 5.40–5.75 (m, 2H, CH=CH), 5.82 and 6.35 (two br s, 2H, NH_2); IR (KBr) 3354, 3191, 2964, 2870, 1667, 969 cm^{-1}.

4.5.3. 3-Heptenamide. A white solid; [Found: C, 66.01; H, 10.43; N, 11.24. C$_7$H$_{13}$NO requires C, 66.10; H, 10.30; N, 11.01%]; ^{1}H NMR: δ 0.89 (m, 3H, CH_3), 1.27–1.54 (m, 2H, CH_2), 2.02 (m, 2H, CH_2), 2.93 and 3.01 (two d, 2H, J=6.00 Hz, CH_2 for (*E*) ~40% and J=6.75 Hz, CH_2 for (*Z*) ~60%), 5.40–5.90 (br m, 4H: 2H, CH=CH and 2H, NH_2); IR (KBr) 3353, 3200, 2961, 2872, 1665, 970 cm^{-1}.

4.5.4. 3-Octenamide. A white solid; [Found: C, 67.91; H, 10.93; N, 10.14. C$_8$H$_{15}$NO requires C, 68.04; H, 10.71; N, 9.92%]; ^{1}H NMR: δ 0.84 (m, 3H, CH_3), 1.20–1.40 (m, 4H, (CH_2)$_2$), 2.01 (m, 2H, CH_2), 2.92 and 3.00 (two d, 2H, J=6.25 Hz, CH_2 for (*E*) ~50% and J=7.25 Hz, CH_2 for (*Z*) ~50%), 5.40–5.75 (m, 2H, CH=CH), 5.82 and 6.34 (two br s, 2H, NH_2); IR (KBr) 3360, 3195, 2938, 2927, 2850, 1653 cm^{-1}.

4.5.5. 3-Nonenamide. A white solid; [Found: C, 69.89; H, 10.83; N, 9.24. C$_9$H$_{17}$NO requires C, 69.63; H, 11.04; N, 9.02%]; ^{1}H NMR: δ 0.86 (t, 3H, J=7.5 Hz, CH_3), 1.15–1.40 (m, 6H, (CH_2)$_3$), 2.02 (m, 2H, CH_2), 2.93 and 3.00 (two d, 2H, J=6.50 Hz, CH_2 for (*E*) ~44% and J=7.25 Hz, CH_2 for (*Z*) ~56%), 5.45–5.70 (m, 2H, CH=CH), 5.70–6.10 (br d, 2H, NH$_2$); IR (KBr) 3364, 3185, 2958, 2924, 2856, 1651, 969 cm^{-1}.

4.5.6. 3-Decenamide. A white solid; [Found: C, 70.69; H, 11.48; N, 8.51. C$_{10}$H$_{19}$NO requires C, 70.96; H, 11.31; N, 8.28%]; ^{1}H NMR: δ 0.82 (t, 3H, J=7.5 Hz, CH_3), 1.12–1.36 (m, 8H, (CH_2)$_4$), 2.00 (m, 2H, CH_2), 2.88 and 2.95 (two d, 2H, J=6.50 Hz, CH_2 for (*E*) ~46% and J=7.25 Hz, CH_2 for (*Z*) ~54%), 5.40–5.70 (m, 2H, CH=CH), 5.90 and 6.50 (two br s, 2H, NH_2); IR (KBr) 3354, 3186, 2926, 2856, 1667, 969 cm^{-1}.

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