

SYNTHESIS AND REACTIONS OF ALLENIC AMIDES

ALLENES-XXXI¹

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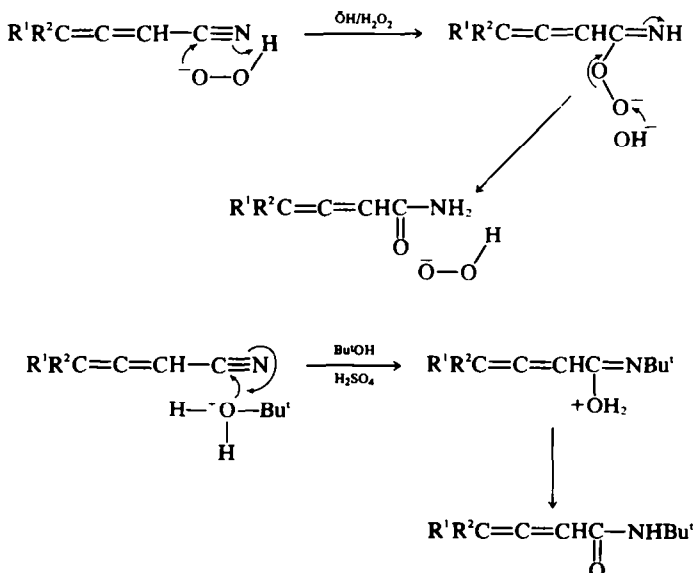
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Abstract—Allenic amides are prepared from allenic nitriles using alkaline hydrogen peroxide and by a Ritter reaction with t-butyl alcohol, when N-t-butylamides are obtained. Strong nucleophiles attack the central carbon of the allene system to give α,β -unsaturated addition products.

Very few allenic amides have been described in the literature,² and no general method for their preparation has been reported. We now give details³ of two such methods, the reaction of the readily available allenic nitriles⁴ with alkaline hydrogen peroxide and the Ritter reaction⁵ using t-butyl alcohol and concentrated sulphuric acid, when in each case a concerted addition to the nitrile group occurs rather than attack at the central carbon of the allene system (Scheme 1).

a standard procedure the reaction mixture is heated at 80° for 1 h. On cooling, the amide crystallizes from the solution. However, low molecular weight nitriles are best reacted at 0° to avoid dimerisation.⁶

Similarly, in the Ritter reaction, the addition with cooling of an allenic nitrile and t-butyl alcohol to a 20% solution of sulphuric acid in glacial acetic acid, and keeping overnight, gave a crystalline, allenic t-butylamide. Both types of amide showed an NH stretch band near 3400 cm⁻¹ (CONH₂ showed a



SCHEME 1

The addition of hydrogen peroxide (100 vol) to a solution of an alka-2,3-dienitrile in alcoholic sodium hydroxide usually causes an exothermic reaction which is complete in a few minutes, but as

second NH stretch near 3200 cm⁻¹), an allene band at 1945–1975 cm⁻¹ and twin amide bands about 1670 and 1600 cm⁻¹. In the UV region allenic amides gave λ_{max} about 210 nm and allenic t-butylamides λ_{max} 213–214 nm, whereas the NMR spectra showed a signal near τ 4.5 for the allenic hydrogen.

Normal hydrolytic procedures for nitriles under

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acid or basic conditions give none of the required allenic amides but cause Michael addition at the central carbon of the allene system. Thus, on attempting to hydrolyse 4-methylhexa-2,3-dienitrile **1** with ethanolic sodium hydroxide, nucleophilic attack of ethoxyl lead to a variety of products (Scheme 2) but no allenic carboxylic acid or amide was obtained. Compounds **2**, **3**, **4** and **5** were isolated by chromatography of acidic and neutral fractions and identified by means of IR, UV and NMR spectra and by comparison with authentic samples.

As expected the amides were found to be less prone to nucleophilic attack at the Michael position than the nitriles and did not react spontaneously at room temperature with strong nucleophiles which is characteristic of allenic nitriles.⁷ However on heating for 1 h with an amine the Michael adduct could be isolated in near quantitative yield. Surprisingly the conversion of the amide to the allenic acid proved difficult both by standard hydrolytic procedures and with nitrous acid. Apparently Michael addition tends to be the preferred mode of reaction even with the relatively less electron attracting amide group and only in cases of highly sterically hindered allenes (e.g. $\text{Bu}^t\text{MeC}=\text{C}=\text{CHCONH}_2$) could any allenic acid be isolated. Recently⁸ allenic esters, in which the allene group was tetrasubsti-

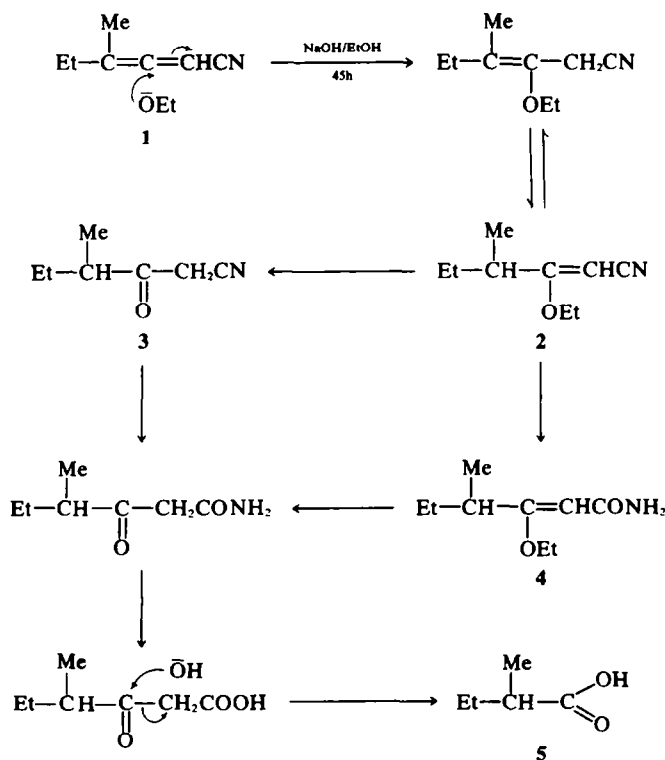
tuted and contained at least one phenyl substituent were hydrolysed in good yield to the corresponding acids under the standard conditions of ethanolic sodium hydroxide. Both steric and electronic factors may account for the absence of Michael addition in this case.

EXPERIMENTAL

IR spectra were determined on Nujol mulls or 5% solutions in chloroform with a Perkin-Elmer 137 or 257 spectrometer. UV spectra were obtained for ethanolic solutions with a Bausch and Lomb spectronic 505 or a Pye-Unicam SP 1800 spectrometer. NMR spectra were determined with a Varian T60 or a Perkin-Elmer RIO spectrometer for solutions in deuteriochloroform, with tetramethylsilane as internal standard.

Alka-2,3-dienamides. Hydrogen peroxide (30% w/v 100 volume; 12 ml) was added dropwise, with vigorous stirring, to the alka-2,3-dienitrile* (0.03 mole) dissolved in absolute ethanol (12 ml) containing 6N sodium hydroxide (1 ml). When the initial exothermic reaction had subsided the temperature was maintained at 80° for 1 h (for exceptions see Table 1). The allenic amide generally tallised out on cooling or, for amides of low molecular weight, was extracted into chloroform and recrystallised. Physical and spectroscopic data re given in Tables 1 and 2.

N-t-butylalka-2,3-dienamides. The alka-2,3-dienitrile* (0.05 mole), dry tert butyl alcohol (0.1 mole), concentrated sulphuric acid (10.2 g) and glacial acetic acid



SCHEME 2

Table 1. Preparation and physical data for allenic amides (R¹R²C=C=CHCONHR³)

R ¹	R ²	R ³	Temp (°C)	Time (h)	m.p. (°C)	Yield (%)	Found (%)			Required (%)		
							C	H	N	C	H	N
Me	Me	H	0	1.0 ^a	131 ^b	35	64.7	8.2	12.5	64.8	8.2	12.6
Me	Et	H	0	1.0 ^a	102 ^c	71	67.0	8.7	11.1	67.2	8.9	11.2
Et	Et	H	80 ^d	1.0	139 ^e	57	68.9	9.4	10.2	69.0	9.4	11.5
Bu ^f	Me	H	80 ^d	1.0	172 ^b	73	70.4	9.7	9.0	70.5	9.9	9.1
Pr ^f	Pr ^f	H	80 ^d	1.0	113	65	71.9	10.4	8.3	71.8	10.2	8.4
Bu ^f	Bu ^f	H	80 ^d	1.0	94	61	73.4	10.5	7.0	73.8	10.8	7.2
Bu ^f	Bu ^f	H	80	2.0	96 ^e	70	73.3	10.7	6.8	73.8	10.8	7.2
Me	Et	Bu ^f	0 ^h	16	140 ^f	60	72.9	10.1	8.1	72.9	10.6	7.7
Et	Et	Bu ^f	20	16	105 ^g	59	74.1	10.5	7.1	73.8	10.8	7.2
Bu ^f	Me	Bu ^f	50 ^h	16	121 ^f	61	74.8	10.8	6.8	74.6	11.1	6.7
Pr	H	Bu ^f	20	16	73 ^f	61	72.7	10.6	7.8	72.9	10.6	7.7

^a Also 0.25 h at 20°.^b Recryst. CHCl₃/isohexane.^c Purified by column chromatography on alumina (Woelm acid, activity II).^d Initially at 20°, exothermic reaction.^e Recryst aq EtOH.^f Recryst isohexane/benzene.^g Recryst hexane.^h Exothermic reaction, temperature controlled by external cooling.

Table 2. Spectroscopic data

R ¹	R ²	R ³	(NH stretch)		ν_{\max}	(cm ⁻¹)	λ_{\max}	ϵ	τ
					(C=C=C)	(C=O)	(NH def.)		
Me	Me	H	3360,	3180	1970	1660	1610 209	11,200	8.12 (6H, d, Me ₂), 4.55 (1H, m, C=C=CH), 4.30 br (2H, s, NH ₂). ^a
Me	Et	H	3360,	3170	1965	br1660	- 1610 210	14,800	8.95 (3H, t, CH ₃ CH ₂), 8.18 (3H, d, CH ₃ C=), 7.90 (2H, m, CH ₂ CH ₂), 4.47 (1H, m, C=C=H), 4.27 br (2H, s, NH ₂). ^a
Et	Et	H	3360,	3180	1955	1650	1620 208	14,600	8.95 (6H, t, CH ₃ CH ₂), 7.87 (4H, qd, CH ₂ CH ₂), 4.33 (1H, m, C=C=CH), 4.08 br (2H, s, NH ₂). ^a
Bu ^f	Me	H	3400,	3200	1975	1670	1625 209	13,000	8.85 (9H, s, Me ₃ C), 8.15 (3H, d, CH ₃ C=) 4.50 (1H, m, C=C=CH), 4.3 br (2H, s, NH ₂). ^a
Pr ^f	Pr ^f	H	3400,	3210	1955	1655	1630 210	15,000	
Bu ^f	Bu ^f	H	3410,	3210	1960	1655	1625 211	10,100	
Bu ^f	Bu ^f	H	3410,	3200	1945	1675	1600 208	8 8,200	
Me	Et	Bu ^f	3,400		1955	1655	1510 213	14,700	8.97 (3H, t, CH ₃ CH ₂), 8.63 (9H, s, Me ₃ C) 8.18 (3H, d, CH ₃ C=), 8.00 (2H, m, CH ₂ CH ₂), 4.50 (1H, m, C=C=CH), 4.45 br (1H, s, NH) ^a
Et	Et	Bu ^f	3,400		1950	1655	1510 214	14,600	8.93 (6H, t, CH ₃ CH ₂), 8.62 (9H, s, Me ₃ C), 7.87 (4H, qd, CH ₂ CH ₂), 4.43 (1H, m, C=C=CH), 4.37 br (1H, s, NH). ^a
Bu ^f	Me	Bu ^f	3,420		1950	1650	1510 214	13,800	8.90 (9H, s, Me ₃ C-C=), 8.60 (9H, s, NHCMe ₃), 8.20 (3H, d, CH ₃ C=), 4.50 (1H, m, C=C=CH), 4.40 br (1H, s, NH) ^a
Pr	H	Bu ^f	3,240		1965	1635	1565 213	9,900	9.03 (3H, t, CH ₃ CH ₂) 8.92 (9H, s, Me ₃ C) 8.48-7.45 (4H, m, CH ₂ CH ₂), 4.33 (3H, m, CHCH=, =CHCO, -NH). ^a

^a Disappears on deuteration.^b 1H disappears on deuteration.

(50 ml) were mixed and the exothermic reaction controlled by occasional cooling. The reaction mixture was set aside overnight and then poured into water. The *N*-t-butylamide crystallised out or was extracted into chloroform, washed with dilute sodium bicarbonate, water, dried (MgSO_4), the solvent removed and the solid twice recrystallised; final drying was carried out under vacuum at 20° to avoid sublimation. Physical and spectroscopic data are given in Tables 1 and 2.

Hydrolysis of 4-methylhexa-2,3-dienitrile 1. Sodium hydroxide solution (30%, 50 ml) was added to 4-methylhexa-2,3-dienitrile⁴ (3.21 g, 0.03 mol) in absolute ethanol (50 ml) and the mixture heated under reflux for 45 h. The product was poured into water (50 ml) and the neutral material extracted into ether. The aqueous layer was acidified with 2*N* hydrochloric acid and the acidic material extracted into ether, dried (MgSO_4) and the solvent evaporated to give a product (0.46 g) which was chromatographed on a silica gel column (50 g). Elution with isohexane/ether (4:1) gave 2-methylbutanoic acid **5** (0.28 g, 9%), ν_{max} 1710 cm^{-1} (C=O), τ (CDCl_3) 9.02 (3H, t, CH_2CH_3), 8.78 (3H, d, CH_3CH), 8.35 (2H, m, CH_2CH_2), 7.76 (1H, m, $\text{Me}(\text{Et})\text{CH}$) and -0.9 (1H, s, COOH). Elution with isohexane/ether (3:2) gave 4-methyl-3-oxohexanenitrile **3** (0.07 g, 2%), IR, UV and NMR spectra were identical with those of a previously characterised sample prepared by hydrolysis of the corresponding enamine.⁷

The neutral component (1.31 g) was chromatographed on alumina (120 g, type 'H', Laporte Industries Ltd deactivated by 10% of 10% acetic acid) and elution with isohexane/ether (9:1) gave 3-ethoxy-4-methylhex-2-enitrile **2** (0.81 g, 18%), ν_{max} 2220 cm^{-1} (C=N), 1610 cm^{-1} (C=C), λ_{max} 225 nm (ϵ 13,700), τ (CDCl_3) 9.25-8.27 (11H, m, $\text{CH}_2\text{CH}_2\text{C}=\text{C}$, CH_3CH , OCH_2CH_3), 7.10 (1H, m, $\text{CH}-\text{C}=\text{C}$), 6.15 (2H, q, CH_2CH_3) and 5.65 (1H, s, =CHCN), identical with an authentic sample prepared from the nitrile and NaOEt/EtOH . Elution with isohexane/ether (1:1) gave 3-ethoxy-4-methylhex-2-enamide **4** (0.30 g, 6%), m.p. 94-95° (Found: C, 63.0; H, 9.9; N, 8.3. $\text{C}_9\text{H}_{17}\text{O}_2\text{N}$ requires C, 63.1; H, 10.0; N, 8.2%), ν_{max} 3410, 3140 (NH stretch), 1660 (C=O) and 1600 (NH def.) cm^{-1} , λ_{max} 235 (ϵ 19,000), τ (CDCl_3) 9.25-8.27 (11H, m, $\text{CH}_2\text{CH}_2\text{C}=\text{C}$, CH_3CH , OCH_2CH_3), 6.10 (3H, m, $\text{CH}-\text{C}=\text{C}$ and OCH_2CH_3), 5.10 (1H, s, =CHCO), 4.63 br (2H, s, NH_2 , disappears on deuteration).

3-(*n*-Butylamino)-4-methylhex-2-enamide. 4-Methylhexa-2,3-dienamide (0.63 g, 0.0015 mol) was added to redistilled butylamine (2 g, 0.03 mol) at room tempera-

ture. No reaction took place as shown by IR and UV spectra; the mixture was heated under reflux for 1 h. Excess amine was removed by rotary evaporation under reduced pressure (0.5 mmHg) yielding 3-(*n*-butylamino)-4-methylhex-2-enamide in quantitative yield, m.p. 57° (Found: C, 66.2; H, 10.8; N, 13.8; $\text{C}_{11}\text{H}_{22}\text{N}_2\text{O}$ requires C, 66.7; H, 11.1; N, 14.1%), λ_{max} 294 nm, ϵ 23,700, λ_{max} 3400 3300 (NH_2), 1650, 1610 (CONH_2) cm^{-1} τ (CDCl_3) 9.08-8.87 (9H, m, (CH_2CH_2- and CH_3CH)), 8.80-8.17 (7H, m, CH_2 and CH) 7.07-6.67 (2H, m, CH_2NH), 5.80 (1H, s, =CH) 5.46 (1H, s, CH_2NH), 0.5 (2H, s, CONH_2).

***N*-t-Butyl-3-(*n*-butylamino)-hept-2-enamide** (with Z. T. Fomum). *N*-t-Butylhepta-2,3-dienamide (0.5 g, 0.003 mol) was added to redistilled *n*-butylamine (2 g, 0.03 mol) at room temperature. After 10 min. IR and UV spectra of the mixture showed that no detectable reaction had taken place. The mixture was refluxed for 1 h and excess amine removed by rotary evaporation under reduced pressure (0.5 mmHg) to give crude *N*-t-butyl-3-(*n*-butylamino)-hept-2-enamide in quantitative yield, m.p. 48-50°, (Found: C, 70.6; H, 11.3; N, 10.4; $\text{C}_{15}\text{H}_{30}\text{N}_2\text{O}$ requires C, 70.9; H, 11.8; N, 11.0%). ν_{max} 3310 (NH), 1640, 1600 (CONH) cm^{-1} , λ_{max} 289 nm, ϵ 16,200 τ (CDCl_3) 9.08 (3H, t, CH_3), 8.80-8.17 (2OH, m, $\text{NH}-\text{CH}_2$), $\text{CH}_3(\text{CH}_2)_2\text{C}$, $\text{CH}_3(\text{CH}_2)_2\text{CH}_2\text{C}$, $\text{CH}_3(\text{CH}_2)_2$ CH_2N); 8.10-7.67 (2H, m, $\text{CH}_2\text{C}=\text{C}$); 7.07-6.67 (2H, m, CH_2N), 5.80 (1H, s, =CH), 5.33-5.07 (1H, s, $\text{CH}_3(\text{CH}_2)_2\text{NH}$); 0.01 (1H, s, NHCM_2).

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