

Elimination and Addition Reactions. Part XXVII.¹ Addition of Amides to Electrophilic Alkenes

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Treatment of amides from primary amines with strong bases and electrophilic alkenes (acrylonitrile or *p*-tolyl vinyl sulphone) gives products derived from *N*-alkylation of the amide. When amides without an N-H bond are used, no reaction occurs unless the amide gives a stabilised carbanion on proton abstraction; *C*-alkylation then occurs. When *N*- and *C*-alkylation can compete, *N*-alkylation is preferred. Dialkylation of diamides occurs readily, and evidence for alkylation of a low molecular weight polyamide has been obtained. Alkylation of Nylon 6 and Nylon 66, however, does not occur to an appreciable extent under the conditions used for the other amides.

NUCLEOPHILIC addition to electrophilic alkenes is an important and versatile reaction^{2,3} and is particularly successful when the alkene bears a cyano-² or sulphonyl^{4,5} group. Addition of amides to electrophilic alkenes has, however, received only scant attention⁶⁻⁸ and we now report on the reactivity of simple mono-, di-, and polyamides towards *p*-tolyl vinyl sulphone and acrylonitrile.

Neutral amides show only very restricted nucleophilicity; the site of protonation is variable⁹ and in inter-¹⁰ and intra-molecular¹¹ nucleophilic displacements in which the neutral amido-group is the nucleophilic centre, oxygen is the nucleophilic site.

Simple amides which possess an ionisable N-H bond are weak acids¹² with pK_a values in the region of 15. Under suitable basic conditions, nitrogen anions derived

¹ Part XXVI, M. J. van der Sluijs and C. J. M. Stirling, *J.C.S. Perkin II*, 1974, 1268.

² P. F. Butskus, *Russ. Chem. Rev.*, 1961, **30**, 583; H. A. Bruson, *Org. Reactions*, 1949, **5**, 79.

³ H. O. House, 'Modern Synthetic Reactions,' 2nd edn., Benjamin, New York, 1972.

⁴ A. T. Kader and C. J. M. Stirling, *J. Chem. Soc.*, 1962, 3686, and references cited therein.

⁵ S. M. McDowell and C. J. M. Stirling, *J. Chem. Soc. (B)*, 1967, 343.

⁶ R. P. Mariella and R. J. Johauskas, *J. Org. Chem.*, 1958, **23**, 923.

⁷ B. P. 875,135 (*Chem. Abs.*, 1963, **59**, 6420).

⁸ B. P. 920,213 (*Chem. Abs.*, 1962, **58**, 14148).

⁹ M. Liler, *Adv. Phys. Org. Chem.*, 1975, **11**, 267.

¹⁰ M. G. Ahmed, R. W. Alder, G. H. James, M. L. Sinnott, and M. C. Whiting, *Chem. Comm.*, 1968, 1533.

¹¹ C. J. M. Stirling, *J. Chem. Soc.*, 1960, 255.

¹² S. Kaae and A. Senning, *Acta Chem. Scand.*, 1968, **22**, 2400.

from amides can take part in intra-^{11,13} or intermolecular¹⁴ nucleophilic displacements with halides. Addition of simple amides of aromatic carboxylic acids to acrylonitrile under catalysis by Triton B has been accomplished,⁶ and alkoxide-catalysed addition of lactams to several electrophilic alkenes has been claimed.⁷ In base-catalysed nucleophilic addition of amides to electrophilic alkenes, the base used to generate the anion must not itself compete in the addition process. In the present work we have mainly employed potassium *t*-butoxide in *t*-butyl alcohol as the solvent-base system. This medium is sufficiently basic to give significant equilibrium concentrations of ions derived from the amides used, and *t*-butoxide ion is feebly nucleophilic towards electrophilic alkenes.

Yields of adducts obtained from simple mono-amides and either *p*-tolyl vinyl sulphone or acrylonitrile are given in Table I. In several reactions, separation of the

In all amides which possess an N-H bond, alkylation occurs at nitrogen. The acyl groups are clearly not sufficiently acidic to allow competitive reaction *via* a carbonyl-stabilised carbanion. This is true even of *N*-methylphenylacetamide (4), in which the carbanion would be additionally stabilised by the phenyl group; the products are solely derived from *N*-alkylation. In an *NN*-dialkylamide, such as dimethylacetamide (6) no reaction occurs under conditions in which *N*-mono-substituted amides are alkylated. In *NN*-dimethylphenylacetamide (5), however, *C*-alkylation occurs readily. Recently, *C*-alkylation of dimethylacetamide by β -nitrostyrene in the presence of lithium amides has been accomplished.¹⁵

Yields of *N*-alkylated product in all reactions are modest. In recent work,¹⁶ reactivity of amido-groups as leaving groups in activated β -eliminations has been determined. The amide (8) reacts slowly with ethanolic

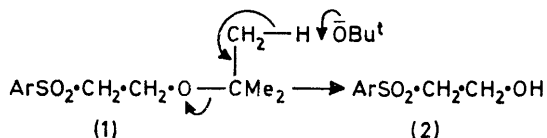
TABLE I

Addition of amides to alkenes

Amide	Alkene ^a	Catalyst ^b	Solvent	Yield of adduct (%)	Other products (%)
AcNHBu (3)	ArSO ₂ ·CH=CH ₂ ^c	Bu ^t OK (0.2)	Bu ^t OH	38 ^d	
AcNHBu (3)	ArSO ₂ ·CH=CH ₂ ^c	Bu ^t OK (1.0)	Bu ^t OH	42 ^d	Ether ^e (28), alcohol ^f (20), amide (59)
AcNHBu (3)	ArSO ₂ ·CH=CH ₂ ^c	Bu ^t OK (1.5)	Bu ^t OH	37 ^d	
AcNHBu (3)	ArSO ₂ ·CH=CH ₂ ^c	NaOH (0.8)	PhH	56 ^d	
AcNHBu (3)	NC·CH=CH ₂ ^g	NaOH (1.0)	PhH	40 ^h	Amide (43)
AcNHBu (3)	NC·CH=CH ₂ ^g	Bu ^t OK (0.5)	Bu ^t OH	31 ^h	Amide (48)
AcNHBu (3)	ArSO ₂ ·CH=CH ₂ ^c	Bu ^t OK (0.26)	DMA ^j	11 ^{h,k}	
AcNHBu (3)	ArSO ₂ ·CH=CH ₂ ^c	Bu ^t OK (0.26)	DMA-Bu ^t OH(1) ^b	29	
(AcNH·CH ₂) ₂ (7)	NC·CH=CH ₂ ^g	Bu ^t OK (0.15)	Bu ^t OH	37	Amide (57)
(AcNH·CH ₂) ₂ (7)	ArSO ₂ ·CH=CH ^{e,g}	Bu ^t OK (0.25)	Bu ^t OH	43	Amide (57), alcohol (35), ether (16)
PhCH ₂ ·CO·NHMe (4)	ArSO ₂ ·CH=CH ₂ ^c	Bu ^t OK (0.5)	Bu ^t OH	43 ⁱ	
PhCH ₂ ·CO·NMe ₂ (5)	ArSO ₂ ·CH=CH ₂ ^c	Bu ^t OK (0.8)	Bu ^t OH	65 ^m	
AcNMe ₂ (6)	ArSO ₂ ·CH=CH ₂ ^c	Bu ^t OK (0.8)	Bu ^t OH	0	Alcohol (61), ether (30) [+amide (77)]

^a Molar proportions (amide : alkene) 1 : 1 unless otherwise stated. ^b Molar proportions in parentheses. ^c Ar = *p*-tolyl. ^d ¹H N.m.r. analysis of adduct-alcohol mixture. ^e ArSO₂·CH₂·CH₂·OBu^t. ^f ArSO₂·CH₂·CH₂·OH. ^g 2 mol per mol of amide. ^h ¹H N.m.r. analysis of amide-adduct mixture. ^j Dimethylacetamide. ^k No proton donor. ⁱ ¹H N.m.r. analysis of adduct-ether mixture. ^m *C*-Alkylated product.

amide-alkene adduct either from *t*-butoxide-alkene adducts or from unchanged amide was not attempted; such product mixtures were analysed by ¹H n.m.r. spectroscopy. In reactions with *p*-tolyl vinyl sulphone, the ether (1) and the alcohol (2) were usually formed. The alcohol (2) presumably arises by β -elimination in the ether (1) derived from the addition of *t*-butoxide ion to the alkene.



The structures of alkene-amide adducts were authenticated by syntheses involving acylation of the readily formed amine-alkene adducts.⁵

¹³ M. S. Manahas and S. J. Jeng, *J. Org. Chem.*, 1967, **32**, 1246.

¹⁴ J. D. Park, R. D. Englert, and J. S. Meek, *J. Amer. Chem. Soc.*, 1952, **74**, 1010.

sodium ethoxide ($k_{\text{elim}} = 2.3 \times 10^{-5} \text{ l mol}^{-1} \text{ s}^{-1}$ at 40 °C) to give the products (9) and (10) derived from initial elimination of the corresponding amide anion. In the amide alkylation reactions, therefore, equilibration probably occurs between adduct and free amide, and part of the electrophilic alkene is diverted to addition reactions with the base-solvent system. Support for this view is found in the observation that when *C*-alkylation occurs, yields are substantially higher than in the *N*-alkylation reactions (Table I). Elimination of carbon leaving groups in activated β -eliminations occurs only slowly, and diversion of the electrophilic alkene to other products is therefore disfavoured.

Alkylation of the diamide (7) (Table I) occurs at both nitrogen atoms, but surprisingly yields of dialkylated product were not sensitive to the alkene-amide ratio when this was varied from 2 : 1 to 1 : 1.

¹⁵ D. Seebach and H. F. Leitz, *Angew. Chem. Internat. Edn.*, 1971, **7**, 501.

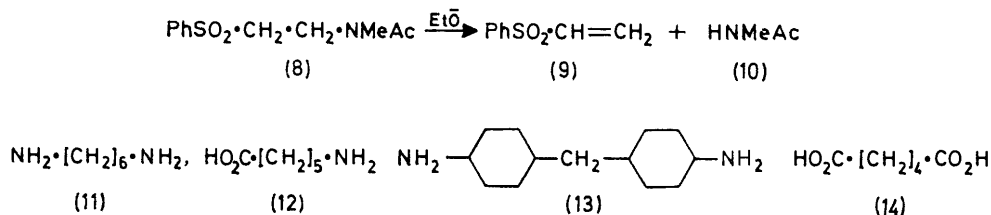
¹⁶ D. R. Marshall, P. J. Thomas, and C. J. M. Stirling, *J.C.S. Chem. Comm.*, 1975, 940.

Formation of a stable addition product in these reactions requires the presence of a proton donor. Thus alkylation of *N*-butylacetamide in dimethylacetamide with *t*-butoxide as base but without added proton donor gives a yield of alkylated product only one-third of that obtained in the presence of an equimolar proportion of *t*-butyl alcohol.

Reactions with Polymeric Amides.—Reactions with commercial polymers, even to very limited extents, may produce technologically valuable changes such as modification of surface properties. We were interested to discover whether such changes could be effected by

decomposition. The importance of a proton donor is clearly seen in reactions with polymers also; in the absence of *t*-butyl alcohol, the degree of sulphur incorporation in *t*-butoxide-catalysed reactions is reduced by 90%.

Reactions with polyamides of much higher molecular weight (Nylon 6 and Nylon 66) were not successful. Calculated values for complete sulphonylethylolation are higher but extents of incorporation were small as on sublimation most of the sulphur incorporated was lost, suggesting that little alkylation occurs. Mutual solubilisation of the reagents under conditions in which a proton



N-alkylation of polymeric amides with electrophilic alkenes. The only reported example of this type of reaction is the cyanoethylation of Nylon 6 catalysed by sodium hydroxide in dioxan.⁸ No proof of chemical incorporation was given. Two difficulties arise in reactions with polymers; mutual solubilisation of the reagents and proof of chemical rather than purely physical incorporation of the reagent.

Preliminary work was carried out with a simple polyamide, Ultramid IC, which contains the four components (11)—(14) in a polymer of molecular weight *ca.* 20 000.

donor is present constitutes a severe problem and the tightly hydrogen-bonded structure of the polymers probably contributes to their low reactivity.

EXPERIMENTAL

Reagents.—*p*-Tolyl vinyl sulphone had m.p. 64° (lit.,¹⁷ 63—66°), *N*-butylacetamide had b.p. 118° at 10 Torr., *n*_D¹⁷ 1.4417 (lit.,¹⁸ b.p. 135° at 18 Torr., *n*_D²⁰ 1.4412); *NN'*-ethylenediacetamide had m.p. 173° (lit.,¹⁹ 173°); *N*-methyl- α -phenylacetamide had m.p. 57° (lit.,²⁰ 57°); *NN*-dimethyl- α -phenylacetamide had m.p. 42—43° (lit.,²¹ 43.5°).

TABLE 2

p-Tolylsulphonylethylolation^a of polyamides

Polymer	Solvent	Proton donor	Base	%S Incorporated
Ultramid IC	DMA <i>t</i> -Bu ^t OH (10 : 1)	Bu ^t OH	KOBu ^t	2.2, 2.6, 1.5 ^d
	DMA <i>t</i> -Bu ^t OH (4 : 1)	Bu ^t OH	KOBu ^t	2.9
	DMA		Et ₃ N	0.0
Nylon 66	Bu ^t OH	Bu ^t OH	KOBu ^t	0.2
	Bu ^t OH-DMSO	Bu ^t OH	KOBu ^t	8.6, 1.2 ^d
Nylon 6	PhCH ₂ -OH	PhCH ₂ -OH	KOBu ^t	6.1, 2.0 ^d
	PhCH ₂ -OH-Bu ^t OH	PhCH ₂ -OH	NaO-CH ₂ Ph	<0.2 ^h
			KOBu ^t	<0.2 ^j <0.2 ^k

^a Sulphone : amide group ratio 1 : 1. ^b 0.1—0.2M. ^c Dimethylacetamide. ^d After sublimation at 210°C and 0.1 Torr. ^e At b.p. Dimethyl sulphoxide. ^f 4 h at 140 °C. ^g 6 h at 135 °C. ^h 5 h at 175 °C. ⁱ At b.p. ^j At b.p. ^k At b.p.

The polymer is soluble in dimethylacetamide and the results of reactions with *p*-tolyl vinyl sulphone are shown in Table 2. The extent of reaction is gauged by the degree of incorporation of sulphur into the recovered polymer. The calculated value for complete sulphonylethylolation is about 10%. The extent of sulphur incorporation is reduced only slightly by reprecipitation and by sublimation under severe conditions. In the latter case, some loss of sulphur content may be due to

Typical Alkylation Procedures.—(a) *Alkylation of N-butylacetamide with p-tolyl vinyl sulphone in t-butyl alcohol.* The amide (1.15 g, 10 mmol) was added to solution of potassium (0.39 g, 10 mg atom) in *t*-butyl alcohol (50 ml). *p*-Tolyl vinyl sulphone (10 mmol), in *t*-butyl alcohol (50 ml), was added with stirring. After 6 h, the mixture was neutralised (AcOH) and water (200 ml) was added. The product was

¹⁷ G. D. Buckley, J. L. Charlish, and J. D. Rose, *J. Chem. Soc.*, 1947, 1514.

¹⁸ M. V. Lock and B. F. Sager, *J. Chem. Soc. (B)*, 1966, 690.

¹⁹ W. E. Backmann, W. J. Horton, E. L. Jenner, N. W. MacNaughton, and C. E. Maxwell, *J. Amer. Chem. Soc.*, 1950, **72**, 3132.

²⁰ F. F. Blicke and H. Zinnes, *J. Amer. Chem. Soc.*, 1955, **77**, 4849.

²¹ H. J. Taverne, *Rec. Trav. chim.*, 1897, **16**, 33.

extracted with dichloromethane and distilled to give three fractions: (i) *N*-butylacetamide (59%), $n_D^{18.5}$ 1.4422, b.p. 73° at 0.05 Torr, (ii) 2-*t*-butoxyethyl *p*-tolyl sulphone (28%), n_D^{22} 1.5131, b.p. 133° at 0.01 Torr (Found: C, 60.6; H, 7.9. $C_{13}H_{20}O_3S$ requires C, 60.9; H, 7.8%), ν_{max} 1 320 and 1 145 cm^{-1} (SO_2), τ (CCl_4) 2.15—2.8 (4 H, m), 6.2—6.95 (4 H, m), 7.6 (3 H, s), and 9.0 (9 H, s); (iii) a mixture of 2-*p*-tolylsulphonylethanol and *N*-butyl-*N*-*p*-tolylsulphonylethylacetamide (1.56 g), b.p. 181—184° at 0.05 Torr (1:3 by 1H n.m.r.).

(b) *NN'*-Ethylenediacetamide and acrylonitrile. Acrylonitrile (20 mmol) in *t*-butyl alcohol (10 ml) was added dropwise with stirring to potassium (6.4 mg atom) and the diamide (10 mmol) in *t*-butyl alcohol (100 ml). After 3 days, neutralisation with acetic acid, concentration, and filtration gave the biscyanoethylamide (37%), m.p. and mixed m.p.

and the precipitated polymer was taken up in methanol and reprecipitated with acetone. The analytical figures for the product (1.2 g) were: C, 67.6; H, 9.5; S, 2.9%. The polymer was then kept at 210 °C and 0.1 mmHg for 3 h. After this time the S content had fallen to 1.5%. An attempt to obtain recognisable fragments from the *N*-alkylated polymer by acidic hydrolysis (6*M*-HCl; 8 h; 130 °C) and chromatography of the hydrolysate failed.

(b) *Nylon* 6. Sodium (0.3 g) and Nylon 6 (2.5 g) were dissolved in benzyl alcohol and the mixture was kept at 120 °C to dissolve the nylon. *p*-Tolyl vinyl sulphone (3.6 g) in benzyl alcohol (75 ml) was added, and the mixture was kept at 135 °C for 6 h. Neutralisation was carried out with acetic acid, and after steam distillation of the mixture addition of dichloromethane to the residue gave a solid (2.3 g) (Found: S < 0.2%).

TABLE 3

Properties of amine- and amide-alkene adducts

	n_D^{20}	M.p. (°C) [B.p./Torr]	Yield (%)	Found (%)			Formula	Required (%)			1H n.m.r. (τ)
				C	H	N		C	H	N	
$NC-CH_2-CH_2-NHBu$	1.4379	[115/18]	82	(lit., ^a b.p. 103° at 10 Torr)							
$(NC-CH_2-CH_2-NH-CH_2)_2$ ($ArSO_2-CH_2-CH_2-NH-CH_2$) ₂	1.4784	[152/19] 86	80 88	(lit., ^b b.p. 152° at 20 Torr)							
$ArSO_2-CH_2-CH_2-NHMe$	1.5427	[150/0.15]	99	56.9	6.8		$C_{10}H_{12}NO_2S$	56.4	7.0		2.1—2.7 (4 H, m), 6.6—7.2 (4 H, m), 7.4 (2 H, s), 7.6 (3 H, s), 8.35 (1 H, s)
$NC-CH_2-CH_2-NAcBu$	1.4628	[106/0.05]	83	64.4	9.4	16.8	$C_9H_{16}N_2O$	64.3	9.5	16.7	2.0—2.6 (4 H, m), 6.5—7.15 (4 H, m), 7.55 (3 H, s), 7.6 (3 H, s), 8.0 (1 H, s), 8.6 (4 H, q, J 6 Hz), 7.4 (2 H, t, J 6 Hz), 8.0 (3 H, s), 8.3—9.2 (7 H, m)
$ArSO_2-CH_2-NAcBu$	1.5275	[192/0.1]	62	60.3	7.6		$C_{15}H_{22}O_3NS$	60.6	7.7		2.1—2.7 (4 H, m), 6.4—6.9 (6 H, m), 7.6 (3 H, s), 8.2 (3 H, s), 8.4—9.4 (7 H, m)
$(NC-CH_2-CH_2-NAc-CH_2)_2$ ($ArSO_2-CH_2-CH_2-NAc-CH_2$) ₂		143 191	57 78	57.2 56.5	7.0 6.2	12.9 ^c	$C_{12}H_{18}N_2O_2$ $C_{24}H_{32}NO_6S_2$	57.6 56.7	7.2 6.3	12.6	6.3 (4 H, m), 7.2 (2 H, m), 7.7 (3 H, s), 2.0—2.6 (4 H, m), 6.0—6.9 (6 H, m), 7.5 (3 H, s), 8.0 (3 H, s)
$PhCH_2-CO-NMe-CH_2-CH_2-SO_2Ar$		83	99	65.0	6.1		$C_{18}H_{21}NO_3S$	65.3	6.3		2.0—2.8 (3 H, m), 6.2—6.6 (2 H, m), 6.95 (1 H, s), 7.5 (1 H, s)
$ArSO_2-CH_2-CH_2-CHPh-CO-NMe_2$		121	65 ^d	66.6	6.8		$C_{19}H_{23}NO_3S$	66.1	6.7		2.1—2.7 (9 H, m), 5.9 (1 H, t, J 7 Hz), 6.75—7.2 (8 H, m), 7.55 (3 H, s), 7.8 (2 H, m)

^a A. E. Frost and A. E. Martell, *J. Org. Chem.*, 1950, **15**, 51. ^b A. E. Martell and S. Chaberek, *J. Amer. Chem. Soc.*, 1950, **72**, 5375. ^c S Analysis. ^d From vinyl sulphone and amide.

141—143°. The mother liquors yielded unchanged amide (57%).

Preparation of Authentic Amide-Alkene Adducts.—The general procedure is illustrated for *NN'*-bis-*p*-tolylsulphonylethyl-*NN'*-ethylenediacetamide. *p*-Tolyl vinyl sulphone (20 mmol) in benzene (75 ml) was treated dropwise with 1,2-diaminoethane (10 mmol) in benzene (25 ml). After 24 h, evaporation gave the *amino-sulphone* (87%), m.p. 85—86° (from ethanol) (details in Table 3). The *amino-sulphone* (5.6 mmol) in acetic acid (25 ml) was treated with acetic anhydride (9 mmol). After being kept at 25 °C for 1 h and at 100 °C for 1 h, the mixture was poured into aqueous sodium hydrogen carbonate and extraction with dichloromethane gave the diamide, m.p. 190—192° (details in Table 3).

Examples of Reactions with Polyamides.—(a) (with R. PEAK) *Ultramid* 1C. The polymer (1.6 g) in dimethylacetamide (320 ml) at 70 °C was treated with *p*-tolyl vinyl sulphone (4.6 g), *t*-butyl alcohol (32 ml), and then potassium *t*-butoxide (2.8 g). The mixture was kept at 65—70 °C for 20 h and was then added to aqueous 4% acetic acid (500 ml),

(c) *Nylon* 66. The polymer (4.0 g) was stirred under reflux with *t*-butyl alcohol (100 ml) for 18 h, then potassium *t*-butoxide [from potassium (0.9 g) in *t*-butyl alcohol (100 ml)] was added. After 1 h, *p*-tolyl vinyl sulphone (6.3 g, 1 equiv. per amide group) in *t*-butyl alcohol was added, and after a further 4 h refluxing the mixture was cooled and neutralised with acetic acid. Decantation left a residue which was washed with *t*-butyl alcohol (150 ml) and then with acetone (2 × 150 ml). The remaining solid (4.05 g) (Found: N, 10.3; S, 8.6%) was sublimed at 160 °C and 0.01 Torr; the S content of the residue was 1.2%. The residue from evaporation of the decantate and washings combined (5.8 g), on extraction with dichloromethane, left a residue (2.2 g) (Found: S, 6.9; N, < 0.5%). Evaporation of the extracts gave a mixture (3.6 g) of the alcohol (2) and the ether (1).

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