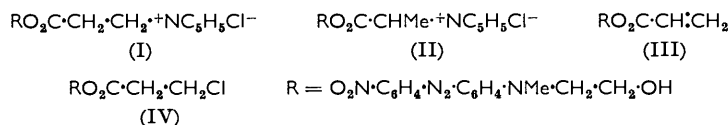


171. *Reaction of $\alpha\beta$ -Unsaturated Acid Chlorides with Alcohols in the Presence of Tertiary Amines.*

By P. W. HICKMOTT.

The reaction of acryloyl chloride with alcohols in the presence of pyridine and other tertiary amines has been shown to give the water-soluble 1-2'-alkoxycarbonylethylpyridinium chloride, etc., as the main product, in addition to the alkyl acrylate. A mechanism for this reaction has been proposed.

DURING an investigation into the effect of various substituents on the affinity of dyes for synthetic fibres, it was found that reaction of acryloyl chloride with 4-(*N*-2-hydroxyethyl-*N*-methylamino)-4'-nitroazobenzene, in the presence of pyridine, gave, in addition to a small amount of the expected acrylate (III), a water-soluble product whose analysis indicated that an adduct of pyridine, acryloyl chloride, and the hydroxyethylated dye had been formed. This, coupled with the fact that the adduct was salt-like, led to assignment of structure [(I) or (II)].



This reaction has been described before,¹ but no evidence for the structure of the water-soluble product or the mechanism of the reaction has been given. For patent purposes² it was necessary to know the correct structure of the adduct and the scope of the reaction. Degradation of the water-soluble adduct with cold sodium hydroxide solution gave a water-insoluble compound which was shown by its analysis and infrared spectrum to be the acrylate (III), formed by elimination of pyridine hydrochloride. This was strong evidence that the adduct had the β -structure (I), since the corresponding dye having the known α -structure (II) gave a water-insoluble compound which corresponded in analysis and infrared absorption to the parent hydroxyethylated dye formed by hydrolysis of the ester linkage. Quaternisation of 4-[*N*-2-(α -chloropropionyloxy)ethyl-*N*-methylamino]-4'-nitroazobenzene with pyridine gave compound (II), but attempted synthesis of the β -structure (I) by quaternisation of the corresponding ester from β -chloropropionyl chloride (IV) failed. Esters from β -bromo- and β -iodo-propionyl chloride were prepared and found to quaternise readily with pyridine (Table 1), giving reference compounds which contained cations identical with that of (I) but different anions (bromide and iodide, respectively), and their infrared spectra showed small differences from those of the compound under investigation. The structure was finally verified by converting the original water-soluble adduct and compounds having the known α - and β -structure into salts with a common anion, namely, the nitrate. The infrared spectra of the adduct and the β -nitrate [as (I)] were then identical and significantly different from that of the α -analogue [as (II)].

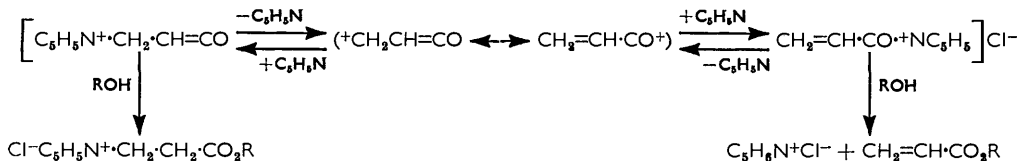
Other tertiary amines, such as quinoline, triethylamine, benzyldimethylamine, and 4-methylmorpholine, but not aromatic amines such as dimethylaniline, give water-soluble adducts. As regards the unsaturated acid chloride, the reaction has been found to be less general. Water-soluble adducts were obtained from α -chloroacryloyl chloride, crotonoyl chloride, and methacryloyl chloride, in the presence of pyridine, but in considerably reduced yield (Table 2); cinnamoyl chloride and $\alpha\beta$ -trichloroacryloyl

¹ G.P. 869,489.

² Imperial Chemical Industries Limited, B.P. 914,075.

chloride gave only the corresponding $\alpha\beta$ -unsaturated ester; and but-3-enoyl chloride gave the $\beta\gamma$ -unsaturated ester.

The mechanism that we postulate for this reaction depends on the fact that acid chlorides form complexes with tertiary amines, of structure $R\cdot CO\cdot NR_3^+Cl^-$ which in many cases have been isolated³ and shown to be powerful acylating agents.⁴ The carbon atom of the carbonyl group may be regarded as being activated to attack by nucleophilic reagents by the close proximity of the charged nitrogen atom. However, it is likely that the acylium ion $R\cdot CO^+$ is formed as a transition state either in the formation of the acid chloride-tertiary amine adduct or in the acylation of the alcohol. In the case of acryloyl chloride the possibility of mesomerism in the acylium ion gives rise to the annexed mechanism for the reaction.



For $\alpha\beta$ -unsaturated acid chlorides in general, the yield of water-soluble adduct (Table 2) can be correlated with the electronic effects (inductive, conjugative, or hyperconjugative) exerted by α - and β -substituents, both in the transition state and in one of the products ($\alpha\beta$ -unsaturated ester) of the reaction. For example, stabilisation of the $\alpha\beta$ -unsaturated form, by conjugative electron displacements of the types shown, result in exclusive formation of the unsaturated ester from $\alpha\beta$ -trichloroacryloyl and cinnamoyl chloride; crotonyl chloride gives some water-soluble product, but in lower yield than acryloyl chloride, owing to hyperconjugative stabilisation of the $\alpha\beta$ -unsaturated form.



In support of this mechanism, it has been shown that quaternisation of the β -chloropropionate (IV) with pyridine does not occur in the conditions of the acryloyl chloride-pyridine-alcohol reaction, which takes place extremely rapidly in the cold. This is in agreement with the conclusions of Dowbenko,⁵ who has shown that the reaction of acrylamide and pyridinium chloride in boiling alcohol, to give 1-2'-carbamoyl ethyl-pyridinium chloride does not take place by way of β -chloropropionamide. Similarly, it has been shown that the reaction does not involve protonation of the acrylate (III) followed by nucleophilic 1,2- or 1,4-addition of pyridine, a mechanism similar to that proposed by Dowbenko for the acrylamide reaction, since treatment of a dioxan solution of the acrylate with hydrogen chloride in the presence of pyridine at 25° gave no water-soluble adduct. Some water-soluble product is formed when a pyridine solution of the acrylate and pyridinium chloride is heated, but the reaction is slow and the yield poor.

EXPERIMENTAL

Preparation of the halogeno-substituted and unsaturated acid chlorides used in this work is adequately described in the literature, except for β -iodopropionyl and α -chloroacryloyl chloride. The former was prepared by the action of phosphorus trichloride on β -iodopropionic acid, the

³ Baumgarten, *J. Amer. Chem. Soc.*, 1953, **75**, 1239; Lowman, Diss., Columbia Univ., 1948 (*Chem. Rev.*, 1955, **55**, 541); Doering and McEwan, *J. Amer. Chem. Soc.*, 1951, **73**, 2104.

⁴ Adkins and Thompson, *J. Amer. Chem. Soc.*, 1949, **71**, 2242; Thompson, *ibid.*, 1951, **73**, 5841; Lur'e, *Zhur. obshchei Khim.*, 1948, **18**, 1517 (*Chem. Abs.*, 1949, **43**, 4240h).

⁵ Dowbenko, *J. Org. Chem.*, 1960, **25**, 1123.

use of thionyl chloride as described by Karrer and Schmid⁶ affording large quantities of iodine on attempted distillation. The ready polymerisation of α -chloroacryloyl chloride rendered the recorded methods^{7,8} for its preparation unsatisfactory, and a modification of the patented method⁸ was used.

A mixture of triethylamine (0.4 c.c.), thiodiphenylamine (0.1 g.), and $\alpha\beta$ -dichloropropionyl chloride (20 g.), in a flask set for distillation and evacuated to 200 mm., was immersed in a bath preheated to 130°. After 15 min. at this temperature the pressure was reduced to 75 mm. for a few minutes and the distillate collected in an ice-cooled receiver. The pressure was readjusted to 200 mm. and heating at 130° continued for a further 15 min., the pressure then being reduced to 75 mm. and more distillate collected. This procedure was repeated twice more. The crude product (12 g.) was redistilled twice, to give α -chloroacryloyl chloride (6 g.), b. p. 41—43°/68 mm. High-boiling residues were obtained from each distillation.

4-(*N*-2-Hydroxyethyl-*N*-methylamino)-4'-nitroazobenzene.—*p*-Nitroaniline was diazotised and coupled with *N*-2-hydroxyethyl-*N*-methylaniline in the presence of sodium acetate, to give the azo-dye, m. p. 175—177° (from ethanol-Cellosolve) (Found: C, 60.1; H, 5.3; N, 18.9. Calc. for C₁₅H₁₆N₄O₃: C, 60.0; H, 5.3; N, 18.7%).

p-(*N*-2-Hydroxyethyl-*N*-methylamino)benzaldehyde.—Phosphorus oxychloride (110 c.c.) was added to dimethylformamide⁹ (400 c.c.) with stirring below 20°. *N*-2-Acetoxyethyl-*N*-methylaniline (208 g.) was then added below 20° and the solution stirred for 2.5 hr. at 95—100°, cooled, poured into ice-water (2 l.), and stirred for 6 hr., with neutralisation with sodium acetate. The acetoxyethyl-aldehyde (210 g.) separated as an oil. This (100 g.) was boiled for 0.5 hr. with concentrated aqueous sodium hydroxide (100 c.c.), water (200 c.c.), and sufficient ethanol to give a homogeneous solution. The ethanol was then evaporated off and the precipitated oil extracted with pentyl alcohol, to give *p*-(*N*-2-hydroxyethyl-*N*-methylamino)-benzaldehyde (75 g.) as an oil, which solidified.

TABLE I.

(A) 4-Nitro-4'-[*N*-methyl-*N*-2-(α -pyridiniopropionyloxy)ethylamino]azobenzene halides and (B) 4-nitro-4'-[*N*-methyl-*N*-2-(β -pyridiniopropionyloxy)ethylamino]azobenzene halides.

Product	Yield (%) [*]	M. p.	Found (%)				Formula	Required (%)			
			C	H	Hal	N		C	H	Hal	N
A, Cl	42	196—197°	—	—	7.4	14.6	C ₂₃ H ₂₄ ClN ₅ O ₄	—	—	7.6	14.9
A, Br	39	202—204	54.0	5.0	—	13.7	C ₂₃ H ₂₄ BrN ₅ O ₄	53.7	4.7	—	13.6
B, Br	46	185—186	—	—	—	13.2	C ₂₃ H ₂₄ BrN ₅ O ₄	—	—	—	13.6
B, I	37	197—198	48.6	4.3	22.0	12.4	C ₂₃ H ₂₄ IN ₅ O ₄	49.15	4.3	22.6	12.5

* After crystallisation from aqueous ethanol.

α -Cyano- β -[*p*-(*N*-2-hydroxyethyl-*N*-methylamino)phenyl]acrylamide.—A solution of *p*-(*N*-2-hydroxyethyl-*N*-methylamino)benzaldehyde (15 g.), cyanoacetamide (8.46 g.), and piperidine (1 c.c.) in ethanol (50 c.c.) was boiled for 1 hr., and then cooled to give the acrylamide (16.1 g.), m. p. 200—201° (from Cellosolve) (Found: C, 63.4; H, 6.0; N, 16.9. Calc. for C₁₃H₁₅N₃O₂: C, 63.7; H, 6.1; N, 17.1%).

Preparation and Reaction of α - and β -Halogeno-esters with Tertiary Amines.—The halogeno-esters were prepared by acylation of 4-(*N*-2-hydroxyethyl-*N*-methylamino)-4'-nitroazobenzene in dioxan with excess of the α - or β -halogenopropionyl chloride at the b. p. (1—2 hr.) or at room temperature in the presence of an excess of pyridine (18 hr.). This gave the following esters: α -, m. p. 123—126°, and β -chloropropionate, m. p. 124—126°; β -bromo-, m. p. 109—111°, and β -iodo-propionate, m. p. 110—112°.

Quaternisation was affected by refluxing the ester (2 g.) with pyridine (10 c.c.) for 5—30 min. The products [as (I) or (II)] separated from the hot solution, or on cooling, or on dilution with benzene. In this way the compounds shown in Table I were prepared. Attempted quaternisation of the β -chloro-ester with triethylamine and the β -bromo-ester with 4-ethylmorpholine failed: a mixture of the amine salt and the acrylate (III) was obtained.

⁶ Karrer and Schmid, *Helv. Chim. Acta*, 1944, **27**, 116.

⁷ Marvel, Dec, Cooke, and Cowan, *J. Amer. Chem. Soc.*, 1940, **62**, 3495.

⁸ U.S.P. 2,388,657.

⁹ Campaigne and Archer, *J. Amer. Chem. Soc.*, 1953, **75**, 989.

4-Nitro-4'-[N-methyl-N-2-(β -pyridiniopropionyloxy)ethylamino]azobenzene Chloride. — Pyridine (0.85 c.c.) was added to a solution of 4-(N-2-hydroxyethyl-N-methylamino)-4'-nitroazobenzene (3 g.) in dioxan (100 c.c.), followed by acryloyl chloride (1.3 c.c.) at 20° with stirring. There was immediate formation of a red precipitate. After 18 hr. the product was collected, washed with dioxan, and dissolved in the minimum amount of boiling aqueous ethanol. The solution was diluted with an equal volume of propan-2-ol; a water-soluble dye (2.1 g., 45%) crystallised, having m. p. 194—197° (i.r.), the analysis of which corresponded with that of the compound (I) (cf. Table 1) (Found: Cl, 7.7; N, 14.8%).

The dioxan solution, from which the water-soluble product had been separated, was diluted with water (100 c.c.), and the precipitated dye was washed with water and crystallised from glacial acetic acid, to give 4-(N-2-acryloyloxyethyl-N-methylamino)-4'-nitroazobenzene (III) (0.54 g., 15%), m. p. 127—128° (Found: C, 60.9; H, 5.0; N, 15.7. $C_{13}H_{15}N_4O_4$ requires C, 61.0; H, 5.1; N, 15.8%).

The same water-soluble product was obtained (in slightly lower yield) when the suspension was stirred for only 10 min. after the addition of acryloyl chloride.

In the same way the reactions summarised in Table 2 were carried out. Any water-soluble adduct formed was precipitated immediately and was collected, after stirring for any convenient time (10 min. to 18 hr.), usually in the form of a tar, which crystallised from the solvent named.

Attempted Quaternisation of 4-[N-2-(β -Chloropropionyloxy)ethyl-N-methylamino]-4'-nitroazobenzene (IV) with Pyridine.—The ester (IV) and a slight excess of pyridine in dioxan gave no

TABLE 2.

Reaction of unsaturated acid chlorides with (A) 4-(N-2-hydroxyethyl-N-methylamino)-4'-nitroazobenzene or (B) α -cyano- β -[p-(N-2-hydroxyethyl-N-methylamino)phenyl]acrylamide in the presence of a tertiary base.

No.	Alcohol	Acid chloride	Base	Unsat. ester (cf. III)		H ₂ O-sol. product (cf. I)			
				% *	M. p.	Solvent	%	M. p.	Solvent †
1	A	CH ₂ :CH·COCl	Pyridine	15	127—128°	AcOH	45	194—197°	X
2	A	"	NEt ₃	—	—	—	47	175—176	Pr ⁿ OH
3	A	"	Quinoline	48	126—127	AcOH	17	158—160	Aq. EtOH
4	A	"	CH ₂ Ph·NMe ₂	—	—	—	40	146—148	X
5	A	"	4-Methyl-morpholine	—	—	—	30	161—163	EtOH
6	B	"	Pyridine	—	—	—	46	217—219	X
7	B	CH ₂ :CMe·COCl	"	63.5	157—159	EtOH	8.2	188—192	X
8	B	Me·CH:CH·COCl	"	32	122—124	"	19.5	201—204	Y
9	B	CH ₂ :CH·COCl	NEt ₃	—	—	—	37	141—144	X
10	B	"	Ph·NMe ₂	17	115—116	EtOH	0	—	—
11	A	CH ₂ :C(Cl)·COCl	Pyridine	51	128—130	AcOH	23 ‡	120—125	Aq. EtOH
12	A	Ph·CH:CH·COCl	"	63	165—167	"	0	—	—
13	A	CCl ₂ :CCl·COCl	"	61	151—153	"	0	—	—
14	A	CH ₂ :CH·CH ₂ ·COCl	"	68	114—116	"	0	—	—
15	B	"	"	64	112—114	"	0	—	—

* A dash in this column denotes that no such product was isolated. † X = Aq. EtOH-PrⁿOH; Y = PrⁿOH-n-C₃H₁₁·OH. ‡ Nitrate.

Products of type, RO₂C-M-Base⁺ Cl⁻.

No.	ROH	M	Base	Found (%)				Formula	Required (%)			
				C	H	Cl	N		C	H	Cl	N
1	A	CH ₂ :CH ₂	Pyridine	—	—	7.7	14.8	C ₂₅ H ₂₄ ClN ₂ O ₄	—	—	7.6	14.9
2	A	"	NEt ₃	58.2	7.1	6.9	—	C ₂₄ H ₃₄ ClN ₂ O ₄	58.6	6.9	7.2	—
3	A	"	Quinoline	—	—	6.2	12.9	C ₂₇ H ₂₆ ClN ₂ O ₄	—	—	6.8	13.5
4	A	"	CH ₂ Ph·NMe ₂	—	—	7.4	12.8	C ₂₇ H ₃₀ ClN ₂ O ₄	—	—	6.8	13.3
5	A	"	4-Methyl-morpholine	—	—	7.8	—	C ₂₃ H ₃₀ ClN ₂ O ₅	—	—	7.2	—
6	B	"	Pyridine	60.5	5.8	8.7	13.4	C ₂₁ H ₂₃ ClN ₂ O ₃	60.8	5.5	8.6	13.5
7	B	CHMe·CH ₂ §	"	—	—	12.6	—	C ₂₂ H ₂₅ ClN ₂ O ₃	—	—	—	13.1
8	B	CH ₂ :CHMe §	"	—	—	8.9	—	—	—	—	8.3	—
9	B	CH ₂ :CH ₂	NEt ₃	—	—	7.5	—	C ₂₂ H ₃₀ ClN ₂ O ₃	—	—	8.1	—
11	A	CHCl·CH ₂ §	Pyridine	52.0	4.7	6.6	15.2	C ₂₃ H ₂₃ ClN ₂ O ₇ ¶	52.0	4.3	6.7	15.8

§ Left-hand C attached to CO₂R. ¶ Nitrate.

water-soluble dye at room temperature or at the b. p. Addition of a few drops of water to a solution in dry pyridine caused a small amount of water-soluble dye to separate after several weeks at 20°. The infrared absorption spectrum of this product was very similar to, but not identical with, that of compound (I).

Addition of Pyridine Hydrochloride to 4-(N-2-Acryloyloxyethyl-N-methylamino)-4'-nitroazobenzene.—(a) The acrylate (III) (2 g.) was dissolved in dioxan (150 c.c.), pyridine (0.92 c.c.) was added, and hydrogen chloride bubbled in until the solution was strongly acid. After 3 hr. at 20°, pyridine was added below 25° until the reaction mixture was no longer acid and the mixture was stirred for 18 hr. No water-soluble dye was formed.

(b) A solution of the acrylate (III) (1 g.) and pyridine hydrochloride (1 g.) in pyridine (10 c.c.) was boiled for 2 hr. After 12 hr. at room temperature. 0.19 g. of water-soluble dye was obtained (m. p. 180—185°). The pyridine solution gave the unchanged acrylate (0.7 g.) on dilution with water.

Partial Degradation of the Water-soluble Adduct (I) with Alkali.—The water-soluble product (2 g.) from the reaction of acryloyl chloride and 4-(N-2-hydroxyethyl-N-methylamino)-4'-nitroazobenzene in the presence of pyridine was dissolved in water (2 l.), and concentrated aqueous sodium hydroxide was added dropwise, with stirring, at 20—25° until the solution became cloudy. After coagulation, the precipitate (0.9 g.; m. p. 112—117°) crystallised from glacial acetic acid to give 4-(N-2-acryloyloxyethyl-N-methylamino)-4'-nitroazobenzene, m. p. 112—114°, undepressed on admixture with (III) (i.r.) (Found: C, 60.55; H, 5.15; N, 15.95. $C_{18}H_{18}N_4O_4$ requires C, 61.0; H, 5.1; N, 15.8%). The infrared absorption spectrum was identical with that of (III).

The same product was obtained by boiling the aqueous solution in the presence of sodium acetate.

Partial Degradation of 4-Nitro-4'-[N-2-(α -pyridiniopropionyloxy)ethyl-N-methylamino]azobenzene Chloride with Alkali.—The salt was decomposed, as described in the preceding paragraph, giving a water-insoluble compound (0.9 g.), m. p. 150—155°, which, after two crystallisations from ethanol, had m. p. 155—160° but corresponded in analysis to 4-nitro-4'-(N- β -hydroxyethyl-N-methylamino) azobenzene, m. p. 175° (Found: C, 59.5; H, 5.3; N, 18.5. Calc. for $C_{15}H_{16}N_4O_3$: C, 60.0; H, 5.3; N, 18.7%). The infrared absorption spectrum showed a strong hydroxyl band at 2.85 μ , and only a weak carboxyl band at 5.8 μ , and no band due to absorption by the vinyl group at 10.05 μ . For identification the m. p.s of both water-soluble and water-insoluble products were of limited value in this work, tending to vary by 10—15° according to the method of preparation, so that identifications were made by analysis and infrared spectra in this and in other cases marked “(i.r.)” after the m. p.

4-[N-Methyl-N-2-(β -pyridiniopropionyloxy)ethylamino]-4'-nitroazobenzene Nitrate.—(a) The water-soluble adduct (2 g.) was dissolved in distilled water (200 c.c.) and sufficient ethanol to maintain a clear solution, and concentrated nitric acid (0.5 c.c.) was added. The nitrate was precipitated and crystallised as flakes (1.5 g.), m. p. 183—185°, from aqueous ethanol (Found: N, 16.8. $C_{23}H_{24}N_6O_7$ requires N, 16.9%).

(b) The bromide (1 g.) was converted into the nitrate (0.85 g.) as above and crystallised as needles (from aqueous ethanol), m. p. 174—176° (i.r.) (Found: N, 16.7%).

4-[N-Methyl-N-2-(α -pyridiniopropionyloxy)ethylamino]-4'-nitroazobenzene Nitrate.—The α -N-pyridiniopropionate chloride (1.5 g.) was converted into the nitrate (1.35 g.) in the same way; crystallised from water this had m. p. 201—203° (Found: C, 55.1; H, 5.2; N, 16.7. $C_{23}H_{24}N_6O_7$ requires C, 55.6; H, 4.8; N, 16.9%).

This work was carried out in the Research Laboratories of Imperial Chemical Industries Ltd., Dyestuffs Division, Manchester.