

Short Communications

Pakistan J. Sci. Ind. Res., Vol. 18, No. 6, December 1975

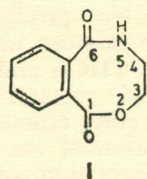
REACTION OF PHTHALIC ANHYDRIDE WITH 2-AMINOETHANOL HYDROCHLORIDE

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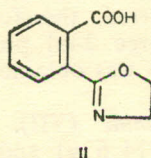
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(Received September 3, 1975)

Derivatives of benzoxazocines show interesting pharmacological activity¹⁻⁴ and we have been interested for some time in the synthesis of 1, 6-diketo-3, 4, 5, 6-tetrahydro-1H-2,5-benzoxazocine (I).



Synthesis of (I) was claimed by Gabriel in 1905 by the hydrolysis of 2-bromoethylphthalimide with aqueous potassium hydroxide solution followed by acidification.⁵ It was later shown in 1962 that the product, obtained by Gabriel, was 2-(*o*-carboxy phenyl)- Δ^2 -oxazoline (II) instead of (I).⁶

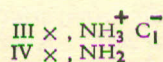
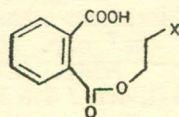


Recently, we have shown that the initial product in the hydrolysis of 2-bromoethylphthalimide is (II) but it converts on recrystallization into (I).⁷

In order to find an alternate route for the synthesis of (I), we have studied the reaction of phthalic anhydride with 2-aminoethanol hydrochloride and report here some interesting results.

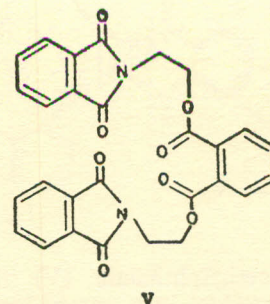
Discussion

Condensation of 2-aminoethanol hydrochloride with phthalic anhydride should afford 2-aminoethylphthalic acid ester hydrochloride (III) which could be treated with a base to yield the free amine (IV). Cyclization of (IV) could afford (I).

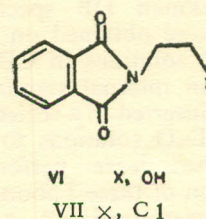


Reaction of phthalic anhydride with 2-aminoethanol hydrochloride was, therefore, carried out at different temperatures. Reaction at 150° gave the desired hydrochloride (III), but free base could not be isolated from the reaction medium on treatment of (III) with aqueous sodium bicarbonate solution or triethylamine.

Heating of phthalic anhydride with 2-aminoethanol hydrochloride at 200° gave diphtalimidoethylphthalate (V).



It appears that (V) is an end-product of a complicated sequence of reactions. Its isolation indicates the intermediate formation of 2-phthalimidoethanol (VI) in the reaction as condensation of (VI) with phthalic anhydride also results in the formation of (V).⁸

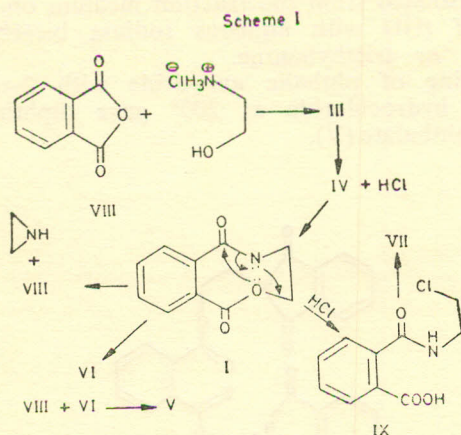


Ester hydrochloride (III) appears to be involved also as an intermediate in the reaction as heating of (III) at 200° also afforded (V) and 2-chloroethylphthalimide (VII) which could not be isolated in the experimental conditions attempted but could be a product as well in the direct reaction of phthalic anhydride with 2-aminoethanol hydrochloride at 200°.

The isolation of compounds (V) and (VII) on heating ester hydrochloride (III) indicated disassociation of (III) into free base (IV) which could cyclize easily to oxazocine (I). Such disassociation of (III) into (IV) is possible as it is known that ammonium chloride also disassociates into ammonia and hydrogen chloride on sublimation.⁹ Disassociation of quaternary ammonium salts is also known.¹⁰⁻¹²

Nucleophilic attack of amide nitrogen in (I) on ester carbonyl carbon could lead to (VI) while nucleophilic attack of ester oxygen in (I) on amide carbonyl carbon could form phthalic anhydride (VIII) and elements of aziridine. Condensation of (VI) and phthalic anhydride, both produced in the reaction, would afford (V). Hydrogen chloride, resulting from disassociation of (III) could attack (I)

leading to the intermediate formation of 2-chloroethylphthalamic acid (IX) which could cyclize to (VII).



Diphthalimidoethylphthalate (V) thus appears to be the final product in a complicated sequence of reactions which perhaps proceed through a common oxazocine intermediate (I).

Experimental

IR spectra were recorded on a Perkin-Elmer IR-137E spectrophotometer and calibrated against 6.238 μ peak of polystyrene. UV spectra were recorded on a Beckman DB spectrophotometer. The NMR spectra were obtained on Varian DP-60 spectrometer as 10% solutions in CDCl_3 or D_2O -TMS was used as an internal standard in CDCl_3 solutions, but it was inserted in a sealed capillary into the sample tube in D_2O solutions to use as a reference. Microanalyses were performed by the microanalytical section of these Laboratories. Melting points were determined on a Gallenkamp melting point apparatus and are uncorrected. All solvents, used in chromatography, were dried by standard procedures and distilled before use. Petroleum ether refers to a hydrocarbon fraction which boils at 60–80°. Na_2SO_4 was used routinely as a drying agent. Heating was done in an oil bath. Solvents were evaporated under reduced pressure at 40°.

2-Aminoethanol Hydrochloride. A solution of 2-aminoethanol (20 g) in ethanol (20 ml) was acidified to pH 1 by fuming hydrochloric acid. Crystals separated on keeping the reaction mixture overnight in cold. Filtration and drying of the crystals afforded 2-aminoethanol hydrochloride (12 g, 38%).

2-Aminoethylphthalic Acid Ester Hydrochloride (III).⁵ 2-(*o*-Carboxyphenyl)- Δ^2 -oxazoline (1.4 g), obtained by reported procedure,⁷ was dissolved in water (5 ml) by heating on a water bath for 10 min. Acidification to pH 1 by fuming hydrochloric acid gave no precipitate, therefore, the solution was evaporated under reduced pressure and crystallization of the residue from methanol gave the hydrochloride (III) (1.0 g, 58%), m.p. 150–160°. Two further recrystallizations from ethanol gave the

product (260 mg), m.p. 173–175° (lit.⁵ m.p. 189°), λ_{max} in 95% EtOH (log ϵ): 217 (3.88), 275 (3.1) nm; ν_{max} (KBr): 2940, 1720, 1600, 1575 cm^{-1} . NMR (D_2O) δ : 3.9 (t, 2H, J 3.5 Hz), 5.0 (t, 2H, J 3.5 Hz) and 8.0 (m, 4H). Calcd. for $\text{C}_{10}\text{H}_{12}\text{NO}_4$: C, 48.8; H, 4.8; N, 5.7%. Found: C, 48.9; H, 4.8; N, 5.8%.

Isolation of (III) from Phthalic Anhydride and 2-Aminoethanol Hydrochloride. A mixture of phthalic anhydride (6.4 g) and 2-aminoethanol hydrochloride (9.76 g) was heated at 150–155° for 1 hr. Residue, on crystallization from chloroform-ethanol, gave the product (3.3 g, 28%) m.p. 161–168°, which on recrystallization from the same solvent yielded the pure material (1.06 g), m.p. 168–170°, whose IR spectrum was the same as that of (III).

Treatment of (III) with NaHCO_3 . To a solution of (III, 200 mg) in water (2 ml), NaHCO_3 (68 mg) was added. It was noticed that pH of the solution was nearly neutral. No precipitation occurred, therefore, the reaction mixture was extracted with three 1-ml portions of CHCl_3 and then with three 1-ml portions of ethyl acetate. Evaporation of dried chloroform and ethyl acetate extracts yielded no product. Acidification of the aqueous solution to pH 2 followed by extraction with three 1-ml portions of ethyl acetate also afforded no product on evaporation of the dried extract.

Treatment of (III) with Triethylamine. To a solution of triethylamine (100 mg) in methylene chloride (10 ml), III (200 mg) was added. Reaction mixture was then evaporated after leaving it overnight. The residue was dissolved in water (2 ml) and the aqueous solution was acidified to pH 2. No precipitation occurred, therefore, the solution was extracted with three 2-ml portions of ethyl acetate, but no product was obtained on evaporation of the dried extract.

2-Chloroethylphthalimide (VII). A mixture of 2-phthalimidoethanol (14.6 g) and PCl_5 (16.5 g) was heated at 200–210° for 3 hr according to a known procedure.¹³ Reaction mixture was then cooled and poured into crushed ice and the light brown precipitate was filtered and dried. Recrystallization from ethanol gave 2-chloroethylphthalimide (14.2 g, 89%), m.p. 79–81° (lit.¹³ 79–81°), ν_{max} (KBr) 1770 and 1710 cm^{-1} .

Diphthalimidoethylphthalate (V). Following reported procedure,⁸ 2-phthalimidoethanol (10.3 g) was dissolved in dry benzene (75 ml) containing conc H_2SO_4 (0.1 ml), and phthalic anhydride (4.0 g) was added during refluxing in portions. Refluxing of the reaction mixture, after addition, was continued for 20 hr and then the reaction mixture was cooled and diluted with equal amount of absolute ethanol. A crystalline product (9.3 g) m.p. 105–120°, was obtained on keeping in refrigerator. Three recrystallizations from chloroform-ethanol gave pure product, m.p. 155–157° (lit.⁸ m.p. 161–162°), ν_{max} (KBr) 1770, 1710 cm^{-1} ; NMR (CDCl_3) δ : 4.33 (t, 4H, J 4.6 Hz), 4.76 (t, 4H, J 4.6 Hz), 7.56–8.01 (m, 12 H).

Reaction of Phthalic Anhydride with 2-Aminoethanol Hydrochloride at 200°. A mixture of phthalic anhydride (4.88 g) and 2-aminoethanol hydrochloride

(3.2 g) was heated at 180–200° for 1 hr. The residue gave a material (0.73 g), m.p. 124–130°, on recrystallization from ethanol. Recrystallization from chloroform–petroleum ether gave (V) (430 mg), m.p. 159–160° (lit.⁸ m.p. 161–162°), identified from its IR spectrum.

Heating of (III) at 200°. 2-Aminoethylphthalic acid ester hydrochloride (1.5 g) was heated for 15 min at 180–200°. The residue was then chromatographed on a column of silica gel (30 g) and the column was eluted progressively with five 25-ml fractions each of petroleum ether, benzene, chloroform and ethyl acetate. No product was isolated on evaporation of petroleum ether fractions, but evaporation of benzene and chloroform fractions gave 273 mg of a product, m.p. 78–80°. Recrystallization of this product from ethanol gave 2-chloroethylphthalimide (78 mg), m.p. 80–81° (lit.¹³ 79–81°), identified from its m.p., mixed m.p. and IR spectrum.

Evaporation of ethyl acetate fractions gave 648 mg of a product whose IR spectrum was similar to (V). This material, after two recrystallizations from ethanol and chloroform–ethanol respectively, afforded diphthalimido-ethylphthalate (46 mg), m.p. 159–160° (lit.⁸ 161–162°), identified from its m.p., mixed m.p. and IR spectrum.

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Pakistan J. Sci. Ind. Res., Vol. 18, No. 6, December 1975

ELECTROLYSIS OF DIETHYLACETIC ACID

NASER-UD-DIN

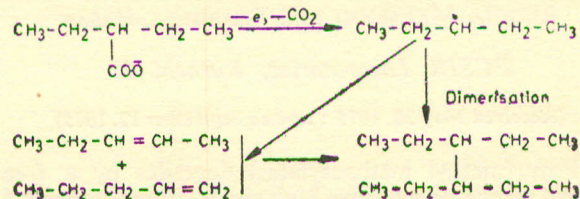
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(Received August 7, 1975)

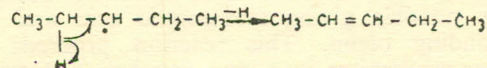
It has been reported that α -alkyl-substituted acids give very low yields of coupled products.^{1,2} The radicals produced in these reactions, $R_1R_2\dot{C}H$, are considered to be more stable than primary radicals, but the low yields may be due to steric effects hindering the union of such two radicals. It is reported that the electrolysis of diethylacetic acid in water gives a 5.5% yield of 3,4-diethylhexane.³

Since it is known that the yields of the coupled products in methanol are usually better than in water,^{4,5} therefore, the electrolysis of diethylacetic acid in methanol was reinvestigated, and an improved yield of 10% of 3,4-diethylhexane was obtained. The present investigation has also revealed that a low-boiling olefinic product (41% theor.) is also formed during the electrolysis of the above acid. This has been shown to contain pent-2-ene (29.1% theor.) and pent-1-ene (8.3% theor.) by GLC analysis (20% Carbowax, M20, 20°).

The low yields of the products can be accounted due to the side reaction taking place in the cell such as the formation of ester of the starting acid and polymerization as well as high volatility of the volatile products formed during the electrolysis.



Pent-2-ene is presumably formed by the hydrogen atom abstraction from the secondary radical.



Information is as yet not available to show whether the formation of pent-1-ene is due to the double bond migration or the rearrangement of the free radical.

Diethylacetic acid was electrolysed in a cell⁴ of simple cylindrical tube (20×4 cm) with a side arm, fitted with a cold trap (coded) by solid carbon dioxide and acetone, for the collection of volatile products, and two bright platinum electrodes (3×2 cm, 0.002 in thickness). The volatile products collected in the trap had strong absorption at 970 cm^{-1} (*trans*-CH=CH) and 1640 cm^{-1} (—CH=CH₂). The absorption at 970 cm^{-1} indicates the presence of *trans*-pent-2-ene. The GLC analysis compared with authentic samples indicated pent-2-ene and pent-1-

ene. The contents of the cell were worked up for the isolation of 3,4-diethylhexane.

Acknowledgement. The above work was carried out at the Department of Chemistry, Queen Mary College, University of London. The facilities extended by Professor B.C.L. Weedon in this respect are gratefully acknowledged.

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THERMAL DEGRADATION OF POLY (TETRAHYDROFURFURAL METHACRYLATE)

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(Received May 30, 1975 ; revised September 17, 1975)

Poly (methyl methacrylates) degrades by a free radical mechanism to give high yields of monomer.¹⁻⁵ The radicals are formed at random or at weak chain terminal structures. With the polymers of higher methacrylate esters, ester decomposition reaction becomes possible giving methacrylic acid and the corresponding olefin. This reaction proceeds by molecular mechanism involving interaction between the carbonyl group and hydrogen atoms on the β -carbon atoms of the ester group.

In the present work a study has been made of the thermal degradation of poly (tetrahydrofurfural methacrylate) in order to study the effect of higher ester, where the hydrogen atoms of the β -carbon atoms of the ester group are part of a tetrahydrofuran ring. Three fractions of poly (tetrahydrofurfural methacrylate) having molecular weights FA-1 (613000), FA-2 (537000) and FA-3 (356000) were degraded at 205, 250 and 288°C under vacuum. Tetrahydrofurfuryl methacrylate was the only product of degradation when analysed by using gas chromatograph and IR spectroscopy at lower temperatures the polymer gels in the beginning but then depolymerises to give monomer. The degradation

of polymer in presence of 1,4-diaminoanthraquinone was inhibited and the rates of degradation were enhanced in the presence of small quantities of benzoyl peroxide. These results clearly suggests that the degradation of poly (tetrahydrofurfuryl methacrylate) follows a free radical mechanism yielding largely free monomer. It appears, therefore, that the hydrogen atoms on the β -carbon atoms of the ester, which are part of tetrahydrofuran ring are not available for interaction with the carbonyl group. Hence the ester breakdown is not preferred here.

Experimental

Preparation of Tetrahydrofurfuryl methacrylate. The monomer was prepared by the ester interchange method.⁶

Polymerisation Procedure. Freshly distilled monomer (40 ml) was changed in a dilatometer containing 0.5 g 2,2'-azoisobutyronitrile. The solutions were sealed under high vacuum after degassing. Polymerisation were carried out up to 5% conversion at 60°C. The polymer were precipitated in cold toluene and dried in vacuum at 50°C. The polymer was then fractionated by controlled precipitation using excess toluene. Three fractions (PFA-1, PFA-2 and PFA-3) of the polymer were thus obtained. Viscosity average molecular weights M_v were obtained by taking their viscosities at 30°C using suspended level dilution viscometer in chloroform. The α - and k 10^5 values⁷ used were 0.72 and 11.63 respectively.

Degradation of Poly (tetrahydrofurfuryl methacrylate.) The degradation was carried out at 205, 250

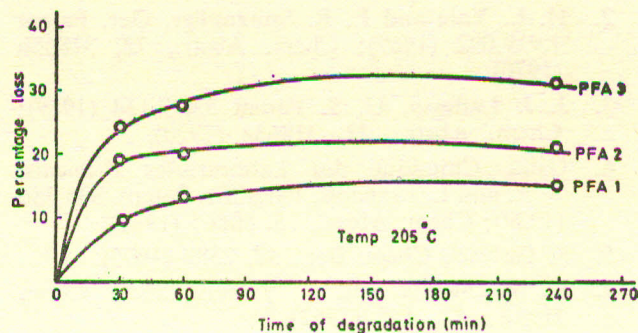


Fig. 1.

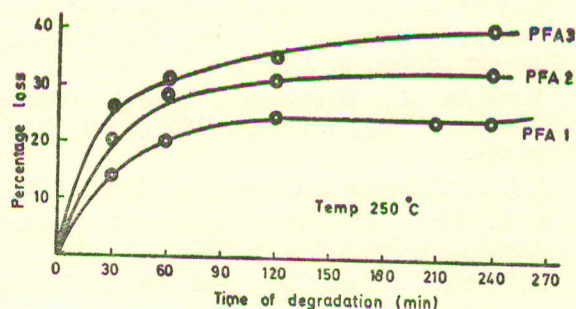


Fig. 2.

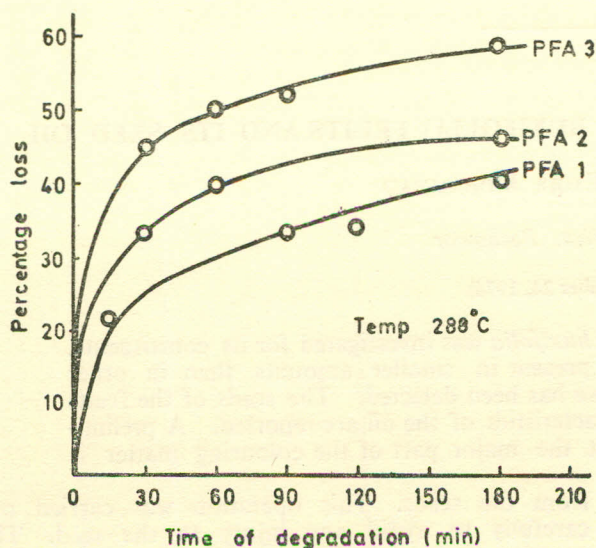


Fig. 3.

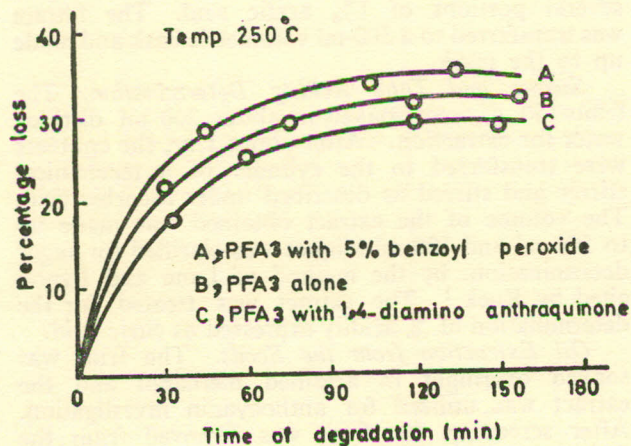


Fig. 4.

and 288°C under vacuum in an apparatus described earlier.⁸ The polymer fractions were weighed in a small fusion tube and introduced into degradation tube which is connected to a high vacuum line. The tube is immersed in a constant vapour both made from benzyl alcohol (b.p. 205°C), benzoic acid (b.p. 250°C) and *K*-naphthol (b.p. 288°C). After a given time the tubes were taken out and reweighed and degradation products were analysed by using IR spectroscopy and gas chromatography (Fig.1-4).

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