99. *The Reaction between Amines and Unsaturated Compounds containing Halogen attached to one of the Ethylenic Carbon Atoms. Part III. The Influence of a* gem-*Dimethyl Group.*

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Reactions similar to those reported in Part II (J., 1938, 963) have been investigated. The presence of a *gem*-dimethyl group on the β-carbon atom leads to simple replacement of the halogen by the amine as the main reaction; apparently some simultaneous addition of the amine to the double bond also occurs.

It has previously been shown by one of us (Parts I and II, J., 1936, 1169; 1938, 963) that compounds of the type $CHR{:}CX{\cdot}CO_2Et$ (X = halogen; R = Me or Ph) react readily with strongly basic secondary amines to yield αβ-diamines. It is now shown that ethyl α-bromoacrylate (X = Br; R = H) reacts similarly. However, ethyl α-bromo-ββ-dimethylacrylate reacted with piperidine to yield mainly ethyl α-piperidino-ββ-dimethylacrylate, isolated and identified as the *platinichloride*; the pure free base was not obtained. The rate of production of ionisable bromine was comparatively slow. Dimethylamine reacted similarly, ethyl α-dimethylamino-ββ-dimethylacrylate being isolated as its *hydrochloride*. In both instances analysis of the basic initial product indicated contamination with some other substance of higher nitrogen content which we believe to be the corresponding diamine. Attempts to separate the free bases by fractional distillation in a vacuum were unsuccessful.

The presence of the *gem*-dimethyl group on the β-carbon atom thus diminishes the reactivity of the ester towards the addition of the amine across the double bond. This is undoubtedly due to the marked electron-release capacity of the *gem*-dimethyl group which will render the double bond less liable to attack by the

nucleophilic reagent. It is significant that ββ-dimethylacrylic acid shows an enhanced reactivity (compared with other αβ-unsaturated acids) towards the addition of bromine—an electrophilic reagent (Sudborough and Thomas, J., 1910, **97**, 2450; Anantakrishnan and Venkataraman, *Chem. Reviews*, 1943, **33**, 44).

Experimental.

Ethyl α-Bromoacrylate.—The pure ester has apparently never been prepared. Of three different methods of preparation investigated, Michael's modification (*Amer. Chem. J.*, 1887, **9**, 121) of Wagner and Tollens's method (*Annalen*, 1874, **171**, 350) yielded the purest product. From silver α-bromoacrylate (5 g.) and ethyl bromide (8 c.c.) were obtained 1·25 g. of crude ester, which was dried (sodium sulphate) and distilled in a vacuum, Pregl's micro-apparatus being used. Ethyl α-bromoacrylate (0·75 g.) was obtained as a colourless oil, b. p. 63·5—65°/15 mm. (Found: Br, 45·8. Calc. for $C_5H_7O_2Br$: Br, 44·7%). Only small quantities were prepared at one time, since on storage for a few days, even in a sealed container and in the dark, the ester turned into a glass.

Reaction between Ethyl α-Bromoacrylate and Dimethylamine.—(i) 0·136 G. of the ester was treated with 0·31 g. of a 33% solution of dimethylamine (3 mols.) in absolute alcohol. Heat was evolved and colourless crystals separated. After ¾ hour, water and an excess of dilute nitric acid were added; titration with 0·1N-silver nitrate indicated that 99·6% of the bromine had been removed from the ester.

(ii) 1·38 G. of dimethylamine (3 mols.) solution were added slowly to 0·61 g. of the ester; the mixture was cooled in ice when necessary and then kept for 1 hour. The basic product (about 0·2 c.c.), isolated in the usual way (similar to that for the isolation of ethyl αβ-dipiperidinobutyrate, Part II), yielded a picrate (from alcohol) identical (crystalline form, m. p. and mixed m. p.) with that of ethyl αβ-bis(dimethylamino)propionate. The free base was more conveniently prepared on a larger scale from ethyl αβ-dibromopropionate (see below).

Reaction between Ethyl α-Bromoacrylate and Piperidine.—0·172 G. of the ester was treated with 0·89 c.c. of a solution of piperidine (0·245 g., 3 mols.) in absolute alcohol. Much heat was evolved and a little white colloidal matter separated. After ½ hour 79·3% of the bromine had been removed from the ester.

Ethyl αβ-Bis(dimethylamino)propionate.—40 G. of αβ-dibromopropionic acid, esterified with alcoholic hydrogen chloride, yielded the ethyl ester (32·5 g.), b. p. 215—218°/757 mm. (Münder and Tollens, *Annalen*, 1873, **167**, 230, give b. p. 211—214°/746 mm.). This ester, on treatment with dimethylamine (4 mols.) solution, yielded 96·2% of the bromine in an ionisable state after ¾ hour. Dimethylamine (4 mols.) solution was added gradually and with cooling to 15·2 g. of ethyl αβ-dibromopropionate. After ¾ hour, the basic product (2·2 g., yield 20%) was isolated in the usual manner, but with a reduction in the volume of water since the product is water-soluble. *Ethyl αβ-bis(dimethylamino)propionate* was obtained as a colourless oil of unpleasant basic odour, b. p. 95—96°/14 mm., very easily soluble in water (Found: C, 57·1; H, 10·8; N, 14·7. $C_9H_{20}O_2N_2$ requires C, 57·4; H, 10·6; N, 14·9%). The *picrate* separated from alcohol in yellow prisms, m. p. 122—123° (decomp.) (Found: N, 17·2. $C_9H_{20}O_2N_2,2C_6H_3O_7N_3$ requires N, 17·3%). The *platinichloride* crystallised in small orange-coloured cubes which started to decompose at 186° and melted (decomp.) at 190° (Found: Pt, 32·3. $C_9H_{20}O_2N_2,H_2PtCl_6$ requires Pt, 32·6%).

Ethyl αβ-Dipiperidinopropionate.—13·7 G. of piperidine (4 mols.), dissolved in absolute alcohol (30 c.c.), were added dropwise and with shaking to ethyl αβ-dibromopropionate (10·5 g.) immersed in crushed ice. During the addition the mixture was kept as near 0° as possible and was afterwards left overnight at room temperature. Addition of water (200 c.c.) and sodium chloride (50 g.)—the latter to increase the density of the aqueous phase—caused a pale yellow oil to float on the surface. The oil was removed and treated with crushed ice and an excess of dilute hydrochloric acid to dissolve the basic ester. The solution was then purified, and the product (3·84 g., 36%) isolated in the usual way. *Ethyl αβ-dipiperidinopropionate* was obtained as a colourless viscous oil of basic unpleasant odour, b. p. 175—176·5°/13 mm., insoluble in water (Found: C, 67·2; H, 10·1; N, 10·7. $C_{15}H_{28}O_2N_2$ requires C, 67·2; H, 10·5, N, 10·5%). A crystalline picrate could not be obtained.

Ethyl α-Bromo-ββ-dimethylacrylate.—Of two different methods of preparation which were investigated, the following proved the more satisfactory:

$$CMe_2{:}CH{\cdot}CO_2H \xrightarrow[HCl]{EtOH} CMe_2{:}CH{\cdot}CO_2Et \xrightarrow{Br_2} CMe_2Br{\cdot}CHBr{\cdot}CO_2Et \xrightarrow{EtONa} CMe_2{:}CBr{\cdot}CO_2Et$$

90 G. of bromine (1·06 mols.), dissolved in carbon tetrachloride (50 c.c.), were slowly added in the cold to 68 g. of ethyl ββ-dimethylacrylate in carbon tetrachloride (250 c.c.); the reaction mixture was protected from light. After standing for a few days, the excess of bromine and the carbon tetrachloride were distilled from a water-bath, and the residue distilled in a vacuum, yielding ethyl αβ-dibromo*iso*valerate (133 g.), b. p. 112—114°/18 mm. (Prentice, *Annalen*, 1896, **292**, 273, gives b. p. 127—128°/30 mm.). The dibromo-ester (133 g.) was treated with a solution of sodium ethoxide prepared from sodium (10·6 g., 1 atom) and absolute alcohol (283 c.c.). The sodium bromide was removed by filtration, and the alcohol distilled off; the residue was dissolved in ether, washed with water, dried (calcium chloride), the solvent evaporated, and the residue distilled in a vacuum, yielding 76·5 g. of *ethyl α-bromo-ββ-dimethylacrylate*, b. p. 88—89°/13 mm. (Found: C, 40·1; H, 5·7; Br, 38·3. $C_7H_{11}O_2Br$ requires C, 40·6; H, 5·4; Br, 38·6%).

Reaction between Ethyl α-Bromo-ββ-dimethylacrylate and Piperidine.—Small-scale experiments, carried out as before, with 1 mol. of ester and 3 mols. of piperidine in absolute alcohol yielded the following results:

Time of reaction, hours	½	2	3	4	48
Bromine replaced, %	11	17	23	30	82

20 G. of ethyl α-bromo-ββ-dimethylacrylate were treated with 28·1 c.c. of piperidine (3 mols.) dissolved in 32·3 c.c. of alcohol (95%), and the mixture kept at room temperature for 3 days. Isolation of the basic product by the usual method gave a pale yellow oil (12·5 g.), b. p. 130—134°/20 mm. Refractionation yielded a colourless oil, b. p. 121—123°/17 mm. (Found: N, 7·1. Calc. for the monopiperidino-ester: N, 6·6. Calc. for the dipiperidino-ester: N, 9·5%). On treatment of ethyl α-bromo-ββ-dimethylacrylate with alcoholic piperidine (2 mols.) a product was obtained of b. p. 122—124°/18 mm. (Found: N, 7·0%). This did not afford a crystalline picrate, but with platinichloric acid, it gave orange-coloured crystals with yellow wart-like incrustations; two recrystallisations from small quantities of alcohol (80%) yielded the pure *platinichloride* of ethyl α-piperidino-ββ-dimethylacrylate as orange-coloured, square platelets, which sintered at 179° and melted at 183° (decomp.) (Found: C, 34·6; H, 5·4; N, 3·2; Pt, 23·5. $2C_{12}H_{21}O_2N,H_2PtCl_6$ requires C, 34·6; H, 5·3; N, 3·4; Pt, 23·4%).

Reaction between Ethyl α-Bromo-ββ-dimethylacrylate and Dimethylamine.—Speed of reaction:

Time of reaction, hours	½	1½	3½	18	24	68
Bromine replaced, %	15	21	30	60	72	93

12·6 G. of ethyl α-bromo-ββ-dimethylacrylate were treated with 31·5 g. of 26% dimethylamine (3 mols.) solution in alcohol and left at room temperature for 3 days. The usual method of isolation yielded an oil (3·2 g.), b. p. 76—78°/

18 mm. [Found : N, 8·8. Calc., for the dimethylamino-ester : N, 8·2. Calc., for the bis(dimethylamino)-ester : N, 13·0%]. No platinichloride or picrate could be obtained, but when 2·3 g. of the crude base were dissolved in absolute alcohol (2 c.c.) and mixed with 4 c.c. of a 10·1% (w/v) solution of hydrogen chloride (1 equiv.) in absolute alcohol, and the mixture was diluted with dry ether (150 c.c.), the viscous oily *hydrochloride* of ethyl α-dimethylamino-ββ-dimethylacrylate separated. This was washed with a little dry ether and dried in a vacuum over phosphoric oxide, and after some weeks a very deliquescent white powder was formed (Found : Cl, 14·7. $C_9H_{17}O_2N,HCl$ requires Cl, 14·4%).

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