118. *The Sydnones. A New Class of Compound containing Two Adjacent Nitrogen Atoms.*

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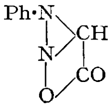
Several analogues of the substance previously obtained by the action of acetic anhydride on *N*-nitrosophenylglycine have been prepared and studied. These substances all yield the corresponding hydrazines on decomposition with hydrochloric acid. Their molecular structure is still in doubt and they are therefore referred to as " sydnones ". They are crystalline, relatively stable compounds and offer some promise as reagents in view of the ease with which the hydrazines can be generated from them.

In an earlier communication (Earl and Mackney, *J.*, 1935, 899) a crystalline product formed by the action of acetic anhydride on *N*-nitrosophenylglycine was described. The structure assigned to the substance after a study of its decomposition with acid and alkaline reagents was that of a lactone of 2-hydroxy-1-phenyldiaziridine-3-carboxylic acid :



There is at present no further evidence for or against this structure. It is, however, of such an unusual type that it cannot be finally accepted without a deeper consideration of the stereochemical and other factors involved. It is proposed in the meantime to refer to substances of this type as " sydnones," the example given above being *N*-phenylsydnone.

Before undertaking a detailed structural study, we have prepared several other sydnones. In general, the *N*-nitrosoarylglycines pass more or less readily into the corresponding sydnones when treated with acetic anhydride. Exposure to sunlight was found to affect the reaction adversely, especially with the *o*- and *p*-nitrophenyl derivatives. All the products were crystalline, white or pale yellow, and soluble in hot benzene and hot alcohol (except *p*-nitrophenylsydnone), but not very soluble in the cold.

Decomposition of the crystalline products by heating with hydrochloric acid gave carbon dioxide and the substituted phenylhydrazines. A large excess of acid sometimes brought about a further decomposition of the hydrazine (*e.g.*, *p*-ethoxyphenylhydrazine) and only 50% excess was used in such cases, the hydrazine being brought into reaction with *p*-nitrobenzaldehyde as soon as possible. The relative stability of the sydnones, compared with the free hydrazines or their salts, suggests that they may be useful reagents for the characterisation of carbonyl compounds, since a solution of the corresponding hydrazine salt can be so quickly prepared from them.

Experimental.

Preparation of the Glycine Ethyl Esters.—General method. The amine (M/2), ethyl chloro- or bromo-acetate (M/2), and sodium acetate crystals (M/2), together with a small amount of alcohol, were heated in an oil-bath at 120—125° for 5 hours under reflux. The reaction mixture was poured into water, made strongly acid with hydrochloric acid, and extracted with ether to remove non-basic substances. The solution was then cooled to 0—5° and neutralised with 20% sodium hydroxide solution. The glycine ethyl ester was extracted with ether and purified either by fractional distillation under reduced pressure, or, if a solid of high m. p., by recrystallisation from a suitable solvent.

o-*Methoxyphenylglycine ethyl ester.* The crude ester was prepared by Diepholder (*Ber.*, 1899, **32**, 3518). The present preparation, using ethyl chloroacetate, gave 52 g. of purified ester (50%), a colourless oil rapidly darkening in air; b. p. 177—178°/15 mm. The p-*nitrobenzoyl* derivative, recrystallised from alcohol, had m. p. 123° (Found : C, 60·20; H, 5·05. $C_{18}H_{18}O_6N_2$ requires C, 60·30; H, 5·06%).

o-*Ethoxyphenylglycine ethyl ester.* This ester was mentioned by Vater (*J. pr. Chem.*, 1884, **29**, 295) who obtained it as a solid but did not give its m. p. or b. p. Using ethyl chloroacetate, 49 g. (44%) of ester were obtained; b. p. 183—184°/18 mm. The p-*nitrobenzoyl* derivative, recrystallised from alcohol, had m. p. 127° (Found : C, 61·22; H, 5·47. $C_{19}H_{20}O_6N_2$ requires C, 61·28; H, 5·43%).

m-*Methoxyphenylglycine ethyl ester.* *m*-Anisidine was prepared by reducing *m*-nitroanisole with hydrogen at atmospheric pressure using Raney nickel as a catalyst. From *m*-anisidine and ethyl bromoacetate, 61 g. of crude *ester*, m. p. 36—37°, were obtained. On redistilling, this gave 51 g. (49%), m. p. 39—40°, b. p. 199°/24 mm. (Found : C, 63·10; H, 7·26. $C_{11}H_{15}O_3N$ requires C, 63·15; H, 7·23%). The p-*nitrobenzoyl* derivative, recrystallised from alcohol, had m. p. 130—131° (Found : C, 60·11; H, 5·09. $C_{18}H_{18}O_6N_2$ requires C, 60·30; H, 5·06%).

m-*Nitrophenylglycine ethyl ester.* Previously prepared by Deutsch (*J. pr. Chem.*, 1907, **76**, 353) from methyl chloroacetate and *m*-nitroaniline. A purer product was prepared using ethyl bromoacetate. The crude ester was precipitated by pouring the reaction mixture with stirring into 1% hydrochloric acid (400 ml.), then ground with more 1% hydrochloric acid (400 ml.), washed with water and dried in a vacuum. 13·5 G. of *m*-nitroaniline were recovered by neutralising the acid filtrates. The crude ester (86 g.; m. p. 81—83°) was recrystallised twice from alcohol, giving 71 g. (63%), m. p. 86—87°. Further repeated recrystallisation raised the m. p. to 87—88°. The highest m. p. previously recorded was 84° (Deutsch, *loc. cit.*) (Found : C, 53·46; H, 5·31. Calc. for $C_{10}H_{12}O_4N_2$: C, 53·57; H, 5·39%).

β-*Naphthylglycine ethyl ester* (cf. Bischoff and Hausdorfer, *Ber.*, 1892, **25**, 2296). The crude product was purified by melting it under water, followed by two crystallisations from alcohol. Yield of purified ester after 20 hours' heating of the reaction mixture was 40 g. (34%), m. p. 87°.

Hydrolysis of the Esters.—The esters were hydrolysed by refluxing with 50% excess of sodium hydroxide solution (10%) containing 10% of alcohol for several minutes after complete solution had been effected. Hydrolysis was usually complete in 5 to 10 minutes and in some cases the reaction was very vigorous. The solution was neutralised to Congo red with hydrochloric acid, and the precipitated glycine was filtered off, washed, and dried in a vacuum. The product was usually pure enough for nitrosation without further purification. In the hydrolysis of *m*-methoxyphenylglycine ethyl ester the alcohol was omitted as the glycine was appreciably soluble in aqueous alcohol.

m-*Methoxyphenylglycine* separated as an oil on neutralising the hydrolysis mixture and crystallised on standing; m. p. 65—66°. Recrystallisation from hot water gave colourless crystals of the same m. p. containing water of crystallisation, removed by drying at 78°/2 mm.; m. p. of the anhydrous substance, 85—86° (Found : C, 59·43; H, 6·23; N, 7·83. $C_9H_{11}O_3N$ requires C, 59·65; H, 6·12; N, 7·77%).

Direct Preparation of Glycines.—The following glycines were prepared directly from chloro- or bromo-acetic acid by published methods : *p*-methoxyphenyl- (Vater, *J. pr. Chem.*, 1884, **29**, 294); *o*-nitrophenyl- (Plöchl, *Ber.*, 1886, **19**, 7); *p*-nitrophenyl- (G.P. 88,433; Friedländer, **4**, 1156); α-naphthyl- (Jolles, *Ber.*, 1889, **22**, 2372).

By increasing the ratio of *o*-nitroaniline to bromoacetic acid, the yield of *o*-nitrophenylglycine was raised from 42 to 80% (based on the amount of bromoacetic acid taken). It was not found possible to raise the m. p. of α-naphthylglycine above 192°, compared with 198—199° recorded by Bischoff and Nastvogel (*Ber.*, 1889, **22**, 1808). A sample prepared from the ethyl ester also had m. p. 192°.

Nitrosation of the Glycines.—Some of the nitroso-compounds, especially those with *o*-substituents, were changed on exposure to light. The nitrosations were therefore carried out in the absence of direct sunlight. The nitroso-compounds were usually recrystallised, but, when too unstable, the crude products were used directly for the next stage. The method of nitrosation varied according to the glycine being treated.

N-*Nitroso*-N-(o-*methoxyphenyl*)*glycine*. The glycine (M/10) was dissolved in a mixture of 10N-HCl (16 ml.) and water (80 ml.). The solution was cooled to 0° and a slight excess of sodium nitrite (7·1 g.) in water (20 ml.) added with stirring during ½ hour. The *nitroso* compound commenced to precipitate in the first few minutes. After another 1½ hours' stirring at 0°, the nitroso-compound was filtered off and washed successively with 5% hydrochloric acid and water. The crude product (a buff powder, changing colour on keeping) was dried in a vacuum over sodium hydroxide. Yield, 95%; m. p. 76—78° (decomp.). After being crystallised several times from aqueous alcohol, the compound had m. p. 82—83° (decomp.) (Found : N, 12·8. $C_9H_{10}O_4N_2$ requires N, 13·3%).

N-*Nitroso*-N-(o-*ethoxyphenyl*)*glycine* was prepared similarly to the *o*-methoxy compound. Yield of crude product, 85%; m. p. 89—90° (decomp.). After recrystallisation from aqueous alcohol the compound had m. p. 94·5—95·5° (decomp.) (Found : N, 12·2. $C_{10}H_{12}O_4N_2$ requires N, 12·5%).

N-*Nitroso*-N-(p-*methoxyphenyl*)*glycine* was also prepared similarly to the *o*-methoxy compound. Yield of crude product, 91%; m. p. 120·5° (decomp.). Recrystallisation from aqueous alcohol raised the m. p. to 121·5° (decomp.) (Found : N, 13·2. $C_9H_{10}O_4N_2$ requires N, 13·3%).

N-*Nitroso*-N-(m-*methoxyphenyl*)*glycine* was prepared by the method used by Earl and Mackney for *N*-nitrosophenylglycine (*loc. cit.*). Yield of crude product, 90%; m. p. 89—91° (decomp.). After purification by dissolving in dilute sodium hydroxide, treating with charcoal and regenerating with acid, it had m. p. 92—93° (decomp.) (Found: C, 51·56; H, 4·82. $C_9H_{10}O_4N_2$ requires C, 51·42; H, 4·79%).

N-*Nitroso*-N-(m-*nitrophenyl*)*glycine* was also prepared by the method of Earl and Mackney, and recrystallised from aqueous alcohol. Yield of purified product, 76%; m. p. 160—161° (decomp.) (Found : C, 42·69; H, 3·20. $C_8H_7O_5N_3$ requires C, 42·65; H, 3·13%).

N-*Nitroso*-N-(o-*nitrophenyl*)*glycine*. The glycine (50 g.) was dissolved in 36N-H_2SO_4 (350 ml.) by gentle warming. The solution was cooled to 0° and finely powdered sodium nitrite (19 g.) added during ½ hour with vigorous stirring After another 1½ hours at 0°, with continued stirring, the solution was poured on crushed ice. The viscous product soon solidified, and was filtered off, washed by grinding with water, and dried in a vacuum. Yield, 49·5 g., m. p. 107—108° (decomp.). The *product* was too unstable to be recrystallised from a solvent, but was purified by treating it with excess of saturated sodium bicarbonate solution, filtering off insoluble material, and acidifying the filtered solution. Yield 48 g.; m. p. 112—113° (decomp.) (Found : N, 18·12. $C_8H_7O_5N_3$ requires N, 18·65%).

N-*Nitroso*-N-(p-*nitrophenyl*)*glycine* was prepared similarly to the *o*-nitrophenyl compound. Crude yield 51 g.; m. p. 143—144° (decomp.). After two recrystallisations from aqueous alcohol 47·2 g. were recovered, m. p. 147·5° (decomp.) (Found : N, 18·9. $C_8H_7O_5N_3$ requires N, 18·65%).

Action of Acetic Anhydride on the Nitroso-compounds. Formation of the Sydnones.—General method. The nitrosoglycine (M/10) was mixed with acetic anhydride (90 ml.), out of direct sunlight. The nitroso compound sometimes dissolved in a few minutes, sometimes after some hours. After 1 to 4 days, the reaction product had sometimes partly separated. The mixture was poured into water (600 ml.) and the excess of acetic anhydride allowed to hydrolyse, after which ammonia or sodium bicarbonate solution was added until the mixture was slightly alkaline. The crude product was filtered off and purified by crystallisation from water or alcohol.

o-*Methoxyphenylsydnone.* Reaction time, 24 hours. Crude yield, 13·8 g.; m. p. 84—86° (decomp.). Recrystallised several times from alcohol, with decolorising charcoal, the purified *product* (6·5 g.), had m. p. 96·5—97·5° (Found : C, 56·17; H, 4·16; N, 14·62. $C_9H_8O_3N_2$ requires C, 56·24; H, 4·19; N, 14·58%).

m-*Methoxyphenylsydnone.* Reaction time, 48 hours. Crude yield, 17·7 g.; m. p. 136·5—137·5°. Recrystallisation did not raise the m. p. of the *compound* (Found : C, 56·42; H, 4·17; N, 14·62%).

p-*Methoxyphenylsydnone.* Reaction time, 24 hours. Crude yield, 17·7 g.; m. p. 124—125° (decomp.). Recrystallisation from alcohol gave 14·7 g. of the *compound*, m. p. 125—126° (decomp.) (Found : C, 56·26; H, 4·18; N, 14·56%).

o-*Ethoxyphenylsydnone.* Reaction time, 48 hours. Crude yield, 17·1 g.; m. p. 96—97° (decomp.). Recrystallisation from aqueous alcohol gave 13·5 g. of the *compound*, m. p. 102° (decomp.) (Found : C, 58·00; H, 4·84; N, 13·63. $C_{10}H_{10}O_3N_2$ requires C, 58·23; H, 4·89; N, 13·59%).

β-Naphthylsydnone. Reaction time 4 days (using *N*-nitroso-*N*-*β*-naphthylglycine prepared according to Jolles, *loc. cit.*). Crude yield, 18·8 g.; m. p. 141—143°. Recrystallisation from alcohol gave 13·0 g. of the *compound*, m. p. 159° (decomp.) (Found : C, 67·90; H, 3·81; N, 13·23. $C_{12}H_8O_2N_2$ requires C, 67·89; H, 3·81; N, 13·21%). On acidifying the alkaline filtrate 0·5 g. of unchanged nitroso-compound was recovered.

o-*Nitrophenylsydnone.* The crude nitrosoglycine (45 g., M/5) was mixed with acetic anhydride (180 ml.) in which it dissolved completely in 1 hour. After standing for 14 days, the mixture was poured into water (1300 ml.). The dilute acetic acid solution was decanted off and the residual viscous mass warmed with dilute acetic acid which was decanted off. The combined acid solutions on the addition of ammonia gave 2·6 g. of a light yellow solid, m. p. 141—142° (decomp.). Two recrystallisations from alcohol gave 1·9 g. of the *compound*, m. p. 147·5° (Found : C, 46·43; H, 2·46; N, 20·30. $C_8H_5O_4N_3$ requires C, 46·39; H, 2·43; N, 20·27%).

m-*Nitrophenylsydnone.* The nitrosoglycine (22·5 g. M/10) was treated with a mixture of acetic anhydride (90 ml.) and acetic acid (45 ml.). After 30 days the nitroso-compound had completely dissolved and after another 30 days the crude product was isolated and washed well with a solution of sodium bicarbonate. Crude yield 18·1 g.; m. p. 112—115°, still giving a Liebermann nitroso test. Four recrystallisations from alcohol yielded 6·4 g. of the *compound*, m. p. 139—140° (decomp.) (Found : C, 46·41; H, 2·40; N, 20·01. $C_8H_5O_4N_3$ requires C, 46·39; H, 2·43; N, 20·27%).

p-*Nitrophenylsydnone.* The nitrosoglycine (22·5 g. M/10) was mixed with acetic anhydride (90 ml.). After 4 days it was completely dissolved and after six days a precipitate began to form. After 14 days the precipitate was filtered off, washed with acetic anhydride, and dried in a vacuum. Crude yield, 7·4 g.; m. p. 178—179° (decomp.). Two recrystallisations from butyl acetate yielded 5·2 g. of the *compound*, m. p. 187—188° (decomp.) (Found: C, 46·42; H, 2·47; N, 20·21. $C_8H_5O_4N_3$ requires C, 46·39; H, 2·43; N, 20·27%). Pouring the acetic anhydride solution into water gave a mixture of substances from which nothing definite was isolated.

Acid Hydrolysis of the Sydnones.—The sydnone (M/200), water (5 ml.), alcohol (5 ml.), and 10N-HCl (5 ml.) were heated in a boiling water-bath. A vigorous evolution of carbon dioxide took place and the reaction was completed in about 10 minutes, the hydrazine hydrochloride often crystallising out. After concentration to 5—10 ml. the solution was cooled and the hydrochloride filtered off.

o-*Nitrophenylhydrazine.* Yield, 0·8 g. (90%); m. p. (rapid heating) 200—201° (decomp.). The hydrochloride was converted into benzaldehyde *o*-nitrophenylhydrazone, m. p. 191·5° (Gastaldi, *Gazzetta*, 1912, **42**, 616, records m. p. 187°).

m-*Nitrophenylhydrazine.* Yield 0·8 g. (90%); m. p. 195—197° (decomp.). Benzaldehyde *m*-nitrophenylhydrazone was prepared, m. p. 130° (Van Ekenstein and Blanksma, *Rec. Trav. chim.*, 1905, **24**, 36, record m. p. 130°).

p-*Nitrophenylhydrazine.* The hydrochloride was not isolated. Benzaldehyde *p*-nitrophenylhydrazone (1·1 g.) was prepared, m. p. 190—191° (Ciusa and Vecchiotti, *Gazzetta*, 1912, **42**, 529, record m. p. 195—196°).

β-Naphthylhydrazine. Yield 0·85 g. (92%); m. p. 240° (decomp.). Benzaldehyde *β*-naphthylhydrazone, m. p. 191° (Fichter and Fröhlich, *Chem. Zentr.*, 1903, II, 427, record m. p. 194°).

Hydrolysis of the Alkoxyphenylsydnones.—Milder conditions were necessary for this group of sydnones. The sydnone (M/200), alcohol (6 ml.), and 10N-HCl (0·75 ml., 50% excess) were refluxed for 25 minutes, the solution darkening considerably. Water was added to precipitate any unchanged sydnone, which was filtered off. To the filtrate an aqueous alcoholic solution of *p*-nitrobenzaldehyde (0·7 g.) and excess of sodium acetate were added. The hydrazone was finally precipitated with water and recrystallised from alcohol. p-*Nitrobenzaldehyde* o-*methoxyphenylhydrazone* had m. p. 160° (Found : N, 15·47. $C_{14}H_{13}O_3N_3$ requires N, 15·49%). p-*Nitrobenzaldehyde* m-*methoxyphenylhydrazone* had m. p. 153·5—154·5° (Found : N, 15·47%). p-*Nitrobenzaldehyde* p-*methoxyphenylhydrazone* had m. p. 176·5—177·5° (Found: C, 61·80; H, 4·87. $C_{14}H_{13}O_3N_3$ requires C, 61·96; H, 4·83%). p-*Nitrobenzaldehyde* o-*ethoxyphenylhydrazone* had m. p. 134—135° (Found : C, 63·20; H, 5·33. $C_{15}H_{15}O_3N_3$ requires C, 63·18; H, 5·30%).

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