

Photolysis of Quinolyl Azides in Aliphatic Thiols. Synthesis of *o*-Alkylthioquinolylamine

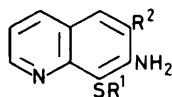
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Photolysis of 5- or 8-quinolyl azide in various thiols gives *o*-alkylthioquinolylamines. The beneficial effect of a 6-methoxy-group in 8-quinolyl azide on the yields is noted.

IN a preliminary account we have described that the photolysis of aryl azides in ethanethiol yields *o*-ethylthioamines.¹ Here we report an extension of that work to the decomposition of quinolyl azides in various alkanethiols and the results are compared with those from the decomposition of these azides in the presence of amines² and methoxide ion.³

5- and 8-Quinolyl azides prepared as described previously² were photolysed in a large excess of alkanethiol, with or without a co-solvent, and gave *o*-alkylthioquinolylamines (1)–(6), typically in 24–29% yield. The alkylthio-group occupies the position originally that of the azide group. The 5- or 8-quinolylamine (30–60%) was a by-product in each case.

We consider the mechanism of this reaction to be essentially as previously described,¹ with the proviso that the first step might involve attack by thiol on a dihydroazepine⁴ intermediate, for example compound (7), rather than the azirine (8), but experimental evidence that would allow distinction is lacking at present.



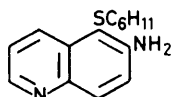
(1) R¹ = Et, R² = H

(2) R¹ = cyclo-C₆H₁₁, R² = H

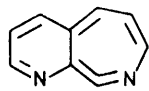
(3) R¹ = (CH₂)₂CO₂Me, R² = H

(5) R¹ = cyclo-C₆H₁₁, R² = OMe

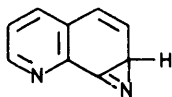
(6) R¹ = (CH₂)₂CO₂Me, R² = OMe



(4)



(7)



(8)

Structures of the products (1)–(6) were assigned on the basis of spectroscopic evidence. For instance, 8-cyclohexylthio-7-quinolylamine (2) has i.r. absorptions at 3 350 and 3 450 cm⁻¹ (NH₂). Signals in the ¹H n.m.r. spectrum at τ 7.0 (alkyl C-H) and 8.0–8.8 (10 H, br m)

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indicate incorporation of cyclohexyl. The aromatic region shows five doublets at τ 1.3, 2.75, 2.05, 2.55, 3.05 which are assigned to protons at the 2-, 3-, 4-, 5-, and 6-positions, respectively. The amino-group appears at τ 4.2 (exchanges with D₂O). The mass spectrum gave the correct molecular ion value at 258.

The 5- and the 8-quinolyl azides react with cyclohexanethiol to give the corresponding *o*-cyclohexylthioquinolylamines (4) and (2), but the 6-isomer does not undergo this reaction with any of the thiols used. This was surprising as the 6-azido-isomer gives higher yields of the analogous *o*-diamines on photolysis in amine than do either the 5- or the 8-isomers.²

Recently, we found that bicyclic azides bearing a *meta*-methoxy-substituent give much higher yields of azepines and diamines than the parent azide on photolysis in amine. Therefore, we photolysed 6-methoxy-8-quinolyl azide in cyclohexanethiol and methyl 3-mercaptopropionate and were able to confirm a similar yield increase, *i.e.* twice as much of the methoxy-derivatives (5) and (6) being obtained as of compounds (2) and (3). The aminothioesters (3) and (6) do not cyclise to thiazepines *in situ* as is the case in a related situation.⁵

None of the above reactions led to ring-expansion products which is not surprising since phenyl azide does not give an azepine under similar conditions.¹ The above reactions constitute a one-step synthesis of certain rather inaccessible *o*-alkylthioamines in quinolines and other fused bicyclic compounds. The yields are, however, lower than those from the azepine and *o*-diamine forming reactions of azides with amines and methoxide ion.⁶

EXPERIMENTAL

I.r. spectra were recorded on a Perkin-Elmer 257 instrument and ¹H n.m.r. spectra on a Varian EM360 or Perkin-Elmer R32 using tetramethylsilane as internal standard. Mass spectra were recorded on an AEI MS12 or MS9 instrument.

Light petroleum refers to the fraction with b.p. 60–80 °C. Yields quoted are based on starting material consumed. Accurate mass measurements only were taken for products (2)–(5) because of their instability.

Azides.—These were prepared by diazotisation of the corresponding amine followed by treatment with sodium azide. All are known compounds and their physical properties are in agreement with those reported in the literature.

General Procedure of Photolysis.—A solution of the azide

(5 mmol) in the appropriate alkanethiol (40 ml) and dioxan [or tetramethylethylenediamine (TMEDA)] (40 ml) was irradiated (125 W medium-pressure mercury lamp) in a quartz (or Pyrex) apparatus for at least 3 h. The solvent was removed from the photolysed solution and the residue chromatographed on alumina (type H, supplied by B.D.H. Ltd.). Photolysis and chromatographic conditions are indicated thus: (alkanethiol, co-solvent, time, apparatus, and eluant).

Photolysis of 8-Quinolyl Azide.—(a) [Ethanethiol (80 ml), 3 h, quartz, benzene]. 8-Ethylthio-7-quinolylamine (1) (0.26 g, 27%) was obtained as a yellow oil, b.p. 148 °C/0.01 mmHg (Found: C, 64.7; H, 5.9; N, 13.7. $C_{11}H_{12}N_2S$ requires C, 64.7; H, 5.9; N, 13.7%); ν_{\max} (Nujol) 3 480 and 3 360 cm^{-1} (NH_2); τ ($CDCl_3$) 1.3 (1 H, dd, $J_{2,3}$ 6 Hz, 2-H), 3.3 dd, $J_{3,4}$ 8 Hz, 3-H), 2.16 (1 H, dd, $J_{2,4}$ 2 Hz, 4-H), 2.5 (1 H, d, J 8 Hz, 5-H), 3.1 (1 H, d, 6-H), 4.8 (2 H, s, NH_2 , exchangeable with D_2O), 7.3 (2 H, q, J 7 Hz, CH_2), and 9.0 (3 H, t, CH_3); m/e 204 (M^+). Further elution with benzene-ethyl acetate (4 : 1 v/v) gave 8-quinolylamine (0.27 g, 40%), m.p. 65 °C, identical with an authentic sample.

(b) (Ethanethiol, TMEDA, 5 h, Pyrex, benzene). 8-Ethylthio-7-quinolylamine was obtained (0.28 g, 29%), b.p. 148 °C/0.01 mmHg, identical with compound (1).

(c) [Cyclohexanethiol, dioxan, quartz, 5 h, light petroleum-toluene (1 : 1)]. 8-Cyclohexylthio-7-quinolylamine (2) (0.31 g, 26%) was obtained as a yellow oil, b.p. 159 °C/0.02 mmHg (Found: M^+ , 258.1190. $C_{15}H_{18}N_2S$ requires M , 258.1190); ν_{\max} (Nujol) 3 460 and 3 360 cm^{-1} (NH_2); τ ($CDCl_3$) 1.3 (1 H, dd, $J_{2,3}$ 5 Hz, 2-H), 2.75 (1 H, dd, $J_{3,4}$ 8 Hz, 3-H), 2.05 (1 H, dd, $J_{2,4}$ 2 Hz, 4-H), 2.54 (1 H, d, J 8 Hz, 5-H), 3.05 (1 H, d, J 8 Hz, 6-H), 4.22 (2 H, s, NH_2 , exchangeable with D_2O), 7.0 (1 H, m, CH), and 8.1–8.8 [10 H, m, $(CH_2)_6$]. Further elution with ethyl acetate gave 8-quinolylamine (0.3 g, 44%), m.p. 64 °C, identical with an authentic sample.

(d) (Methyl 3-mercaptopropionate, dioxan, 6 h, quartz, toluene). 8-Quinolylamine was obtained (0.4 g, 59%), m.p. 64 °C, identical with an authentic sample. Further elution with toluene-ethyl acetate (9 : 1) gave 8-methoxycarbonyl ethylthio-7-quinolylamine (3) (0.3 g, 24%), b.p. 193 °C/0.2 mmHg (Found: M^+ , 262.0074. $C_{13}H_{14}N_2O_2S$ requires M , 262.0074); ν_{\max} (Nujol) 3 460, 3 360 (NH_2), and 1 730 cm^{-1} (C=O); τ ($CDCl_3$) 1.25 (1 H, dd, $J_{4,3}$ 5 Hz, 2-H), 2.7 (1 H, dd, $J_{3,4}$ 6 Hz, 3-H), 1.25 (1 H, dd, $J_{2,4}$ 2 Hz, 4-H), 2.4 (1 H, d, J 8 Hz, 5-H), 3.2 (1 H, d, J 8 Hz, 6-H), 4.2 (2 H, s, NH_2 , exchangeable with D_2O), 6.4 (3 H, s, OCH_3), 7.0 (2 H, t, J 7 Hz, SCH_2), and 7.43 (CH_2 , t, J 7 Hz, $CH_2C=O$).

Photolysis of 6-Quinolyl Azide.—(a) [Butanethiol (80 ml), quartz, 6 h, toluene-ethyl acetate (6 : 1)]. 6-Quinolylamine (0.41 g, 40%) was obtained, m.p. 113 °C, identical with an authentic sample.

(b) (Cyclohexanethiol, dioxan, quartz, 7 h, toluene). 6-Quinolylamine (0.43 g, 64%) was obtained, m.p. 113 °C, identical with an authentic sample.

(c) (Methyl 3-mercaptopropionate, dioxan, quartz, 6 h, toluene). 6-Quinolylamine (0.41 g, 61%) was obtained, m.p. 113 °C, identical with an authentic sample.

Photolysis of 5-Quinolyl Azide.—(a) [Cyclohexanethiol, dioxan, quartz, 6.5 h, light petroleum-toluene (1 : 1)]. 5-Quinolyl azide (0.24 g, 30%) was obtained, m.p. 63 °C, identical with an authentic sample. Further elution with

toluene gave 5-cyclohexylthio-6-quinolylamine (4) (0.23 g, 27%) as a yellow powder, m.p. 120 °C (light petroleum) (Found: M^+ 258.1190. $C_{15}H_{18}N_2S$ requires M^+ , 258.1190); ν_{\max} (Nujol) 3 300 and 3 200 cm^{-1} (NH_2); τ ($CDCl_3$) 1.12 (1 H, dd, $J_{2,3}$ 5 Hz, 2-H), 2.67 (1 H, dd, $J_{3,4}$ 8 Hz, 3-H), 1.84 (1 H, dd, $J_{2,4}$ 2 Hz, 4-H), 2.3 (1 H, dd, $J_{7,8}$ 8 Hz, 8-H), 2.45 (1 H, d, 7-H), 4.9 (2 H, s, NH_2 , exchangeable with D_2O), 7.0 (1 H, m, CH), and 8.1–8.8 [10 H, m, $(CH_2)_6$]. Further elution with ethyl acetate gave 5-quinolylamine (0.23 g, 34%), m.p. 109 °C, identical with an authentic sample.

(b) (Methyl 3-mercaptopropionate, dioxan, quartz, 6 h, toluene). 5-Quinolyl azide (0.27 g, 34%) was obtained, identical with an authentic sample. Further elution with toluene-ethyl acetate (4 : 1) gave 5-quinolylamine (0.3 g, 44%), m.p. 109 °C, identical with an authentic sample.

Photolysis of 6-Methoxy-8-quinolyl Azide.—(a) (Cyclohexanethiol, dioxan, quartz, 3 h, toluene). 8-Cyclohexylthio-6-methoxy-7-quinolylamine (5) (0.54 g, 47%) was obtained, m.p. 94 °C, yellow crystals (light petroleum) (Found: M^+ , 288.1295. $C_{16}H_{20}N_2OS$ requires M^+ , 288.1295); ν_{\max} (Nujol) 3 460 and 3 360 cm^{-1} (NH_2); τ ($CDCl_3$) 1.42 (1 H, dd, $J_{2,3}$ 5 Hz, 2-H), 2.75 (1 H, dd, $J_{3,4}$ 8 Hz, 3-H), 1.14 (1 H, dd, $J_{3,4}$ 2 Hz, 4-H), 3.32 (1 H, s, 5-H), 4.8 (2 H, s, NH_2 , exchangeable with D_2O), 6.1 (3 H, s, 6- OCH_3), 7.1 (1 H, s, CH), and 8.2–8.8 (10 H, m, $(CH_2)_6$). Further elution with ethyl acetate gave 6-methoxy-8-quinolylamine (0.14 g, 20%), m.p. 48 °C, identical with an authentic sample.

(b) (Methyl 3-mercaptopropionate, dioxan, quartz, 3 h, toluene). 6-Methoxy-8-methoxycarbonyl ethylthio-7-quinolylamine (6) (0.58 g, 49%) was obtained, m.p. 89 °C, yellow crystals (light petroleum) (Found: C, 57.4; H, 5.6; N, 9.95. $C_{14}H_{16}N_2O_3S$ requires C, 57.5; H, 5.5; N, 9.6%); ν_{\max} (Nujol) 3 460, 3 360 (NH_2), and 1 720 cm^{-1} (C=O); τ ($CDCl_3$) 1.4 (1 H, dd, $J_{2,3}$ 5 Hz, 2-H), 2.6 (1 H, dd, $J_{3,4}$ 8 Hz, 3-H), 1.2 (1 H, 4-H), 3.3 (1 H, s, 5-H), 4.7 (2 H, s, NH_2 , exchangeable with D_2O), 6.05 (3 H, s, 6- OCH_3), 6.45 (3 H, s, $COOCH_3$), 7.05 (2 H, t, s- CH_2), and 7.55 (2 H, t, CH_2CO). Further elution gave the amine (29%) as in (a).

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