Some 4-Alkyl *s*-Triazolo[4,3-*a*]quinoxalines (1)

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A number of higher homologs of 4-alkyl 2-triazolo[4,3-*a*]quinoxalines, some of which have a methyl or dichloromethyl group at position 1, have been prepared and characterized.

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In an earlier communication (2), we reported the synthesis of some quinoxaline derivatives having oil-solubleizing side-chains. Among the compounds reported were some 2-chloro-3-alkylquinoxalines **1**. These intermediates react readily with hydrazine hydrate in refluxing ethanol to yield the corresponding 2-hydrazinoquinoxalines **2** (3). The 2-hydrazinoquinoxalines are readily converted to fused *s*-triazolo[4,3-*a*]quinoxalines, **3**, on heating with an acid, acid anhydride or orthoester (4). Of the *s*-triazolo[4,3-*a*]-quinoxalines (**3**) reported in the literature (4,5,6), only those cases where R = hydrogen, methyl or phenyl have been prepared.

SCHEME I

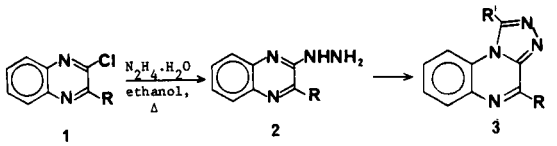
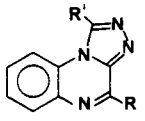


Table I

Substituted *s*-Triazolo[4,3-*a*]quinoxalines (a)



Compound #	R	R'	Method	Yield (%) (b)
3a	$-C_2H_5$	-H	(c)	44
3b	$-C_2H_5$	$-CH_3$	(d)	40
3c	$-C_2H_5$	$-CHCl_2$	(e)	69
3d	$-CH_2CH_2CH_3$	-H	(c/e)	65/65
3e	$-CH_2CH_2CH_3$	$-CH_3$	(d)	79
3f	$-CH_2CH_2CH_3$	$-CHCl_2$	(e)	88
3g	$-(CH_2)_4CH_3$	$-CH_3$	(d)	82
3h	$-(CH_2)CH_3$	$-CH_3$	(d)	59

(a) Physical constants and analyses are reported in experimental section. (b) No attempts were made to maximize yields. (c) From ortho ester. (d) From anhydride. (e) From carboxylic acid.

Having available several examples of compound **1**, where R = ethyl, *n*-propyl, *n*-pentyl or *n*-nonyl, we prepared the 2-hydrazino derivatives **2**, previously reported by Reinheckel (3), and converted these to 4-alkyl-2-triazolo[4,3-*a*]quinoxalines **3**, having a hydrogen, methyl or dichloromethyl group at position 1. The compounds reported here are shown in Table I, and properties are reported in the experimental. The infrared spectra of all of these compounds **3** are essentially indentical to those previously reported for related systems (4,5).

EXPERIMENTAL

Melting points were taken on a Thomas-Hoover melting point apparatus and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer Model 137-B spectrophotometer using potassium bromide pellets unless stated otherwise. Nuclear magnetic resonance spectra were determined on a Varian Model T60 spectrophotometer using tetramethylsilane (TMS) as an internal standard. Mass spectra were obtained on a Hewlett-Packard Model 5992A GC/MS mass spectrometer. Elemental analyses were preformed at Midwest Micro Labs Inc., Indianapolis, Indiana and at Canadian Microlab, Vancouver, British Columbia.

General Procedure for the Preparation of 2-Hydrazino-3-alkylquinoxalines (**2**).

One equivalent of 2-chloro-3-alkylquinoxaline (2) was dissolved in absolute ethanol (sometimes heating was necessary for all the chloroquinoxaline to dissolve). An excess of hydrazine hydrate (usually between 0.15-0.2 ml of 85% hydrazine hydrate per millimole of chloride) was added and the solution heated to reflux for 3 hours. On cooling to room temperature, a crystalline solid precipitated. The reaction mixture was further cooled in a refrigerator, the solid collected by filtration, washed with ethanol and dried under vacuum. Sometimes the volume of filtrate was reduced on a rotary evaporator and a second crop of crystals obtained after refrigeration.

2-Hydrazine-3-ethylquinoxaline.

This compound was prepared in 92% yield from 4.35 g (22.6 mmoles) of 2-chloro-3-ethylquinoxaline, 2.85 ml of hydrazine hydrate and 10 ml of absolute ethanol, mp 190-192° (lit (3) mp 192-193°).

2-Hydrazino-3-propylquinoxaline.

This compound was prepared in 100% yield from 20 g (96.87 mmoles) of 2-chloro-3-propylquinoxaline, 20 ml of hydrazine hydrate and 100 ml of absolute ethanol, mp (ethanol) 144-144.5° (lit (3) mp 145-146°).

2-Hydrazino-3-pentylquinoxaline.

This compound was prepared in 79% yield from 1.5 g (6.39 mmoles) of 2-chloro-3-pentylquinoxaline, 1 ml of hydrazine hydrate and 10 ml of absolute ethanol, mp (ethanol) 132-134° (lit. (3) mp 132-133°).

2-Hydrazino-3-nonylquinoxaline.

This compound was prepared in 83% yield from 980 mg (3.37 mmoles)

of 2-chloro-3-nonylquinoxaline, 1 ml of hydrazine hydrate and 10 ml of absolute ethanol, mp 98-100° (lit. (3) mp 101-102°).

4-Ethyl-*s*-triazolo[4,3-*a*]quinoxaline (**3a**).

Seven milliliters of trimethyl orthoformate was added to 500 mg (2.659 mmoles) of 2-hydrazino-3-ethylquinoxaline and the mixture heated to reflux overnight. The contents were allowed to cool to room temperature, then diluted with methylene chloride/ethyl acetate. The solution was wased with water (2x), dried (magnesium sulfate), treated with activated charcoal and filtered through celite. The solvent was removed on a rotary evaporator and trace solvent removed on a vacuum pump to yield 230 mg (44%) of a white solid, mp (ethanol) 230°; nmr (deuteriochloroform): δ 1.55 (t, 3H, J = 7 Hz), 3.22-3.63 (q, 2H, J = 7 Hz), 7.48-8.17 (m, 4H), 9.25 (s, 1H).

Anal. Calcd. for $C_{11}H_{10}N_4$: C, 66.65; H, 5.09; N, 28.27. Found: C, 66.90; H, 5.10; N, 28.47.

1-Methyl-4-ethyl-*s*-triazolo[4,3-*a*]quinoxaline (**3b**).

A mixture of 1 g (5.319 mmoles) of 2-hydrazino-3-ethylquinoxaline and 1.09 ml (11 mmoles) of acetic anhydride was heated to reflux for 1 hour, then cooled to room temperature and dissolved in ethyl acetate. The solution was washed with 5% sodium bicarbonate (3x), dried (magnesium sulfate), treated with activated charcoal and filtered through celite. The solvent was removed on a rotary evaporator and trace solvent removed on a vacuum pump to yield 450 mg (40%) of white silklike crystals, mp (methanol/water) 196°; nmr (deuteriochloroform): δ 1.52 (t, 3H, J = 7 Hz), 3.10-3.60 (m, 5H, overlapping $-CH_3$ singlet at 3.13 and $-CH_3-$ quartet, J = 7 Hz), 7.43-8.18 (m, 4H).

Anal. Calcd for $C_{12}H_{12}N_4$: C, 67.90; H, 5.70; N, 26.40. Found: C, 67.76; H, 5.96; N, 26.38.

1-Dichloromethyl-4-ethyl-*s*-triazolo[4,3-*a*]quinoxaline (**3c**).

A mixture of 1 g (5.32 mmoles) of 2-hydrazino-3-ethylquinoxaline and 4 ml of dichloroacetic acid was heated to reflux for 3 hours. The mixture was allowed to cool to room temperature and diluted with methylene chloride/ethyl acetate. The solution was washed with 5% sodium bicarbonate (2x), dried (magnesium sulfate), treated with activated charcoal and filtered through celite. The solvent was removed on a rotary evaporator and trace solvent removed on a vacuum pump to yield 1.03 g (69%) of an off-white fluffy solid, mp (ethanol) 176-177°; nmr (deuteriochloroform): δ 1.53 (t, 3H, J = 7 Hz), 3.22-3.67 (q, 2H, J = 7 Hz), 7.53-8.83 (m, 5H, including $-CHCl_2$ singlet at 7.65).

Anal. Calcd. for $C_{12}H_{10}Cl_2N_4$: C, 51.26; H, 3.59; N, 19.94. Found: C, 51.46; H, 3.67; N, 19.73.

4-Propyl-*s*-triazolo[4,3-*a*]quinoxaline (**3d**).

Method A. Using Trimethyl Orthoformate.

A mixture of 1 g (4.95 mmoles) of 2-hydrazino-3-propylquinoxaline and 7 ml of trimethyl orthoformate was treated as described under **3a**, above, to yield 680 mg (65%) of fine white needles, mp (ethanol) 182.5-184°; nmr (deuteriochloroform): δ 1.12 (t, 3H, J = 7 Hz). 1.73-2.40 (sextet, 2H), 3.38 (t, 2H, J = 7 Hz), 7.48-8.18 (m, 4H), 9.27 (s, 1H).

Anal. Calcd. for $C_{12}H_{12}N_4$: C, 67.90; H. 5.70; N, 26.40. Found: C, 67.57; H, 5.60; N, 26.03.

Method B. Using Formic Acid.

A mixture of 1 g (4.95 mmoles) of 2-hydrazine-3-propylquinoxaline and 4 ml of 97% formic acid was heated to reflux for 3 hours. The mixture worked up as described for **3c**, to yield 680 mg (65%) of white solid, mp (crude) 183-185°; nmr was identical to compound prepared by method A.

1-Methyl-4-propyl-*s*-triazolo[4,3-*a*]quinoxaline (**3e**).

A mixture of 1 g (4.95 mmoles) of 2-hydrazino-3-propylquinoxaline and 2 ml of acetic anhydride was treated as described for **3b**, to yield 880 mg (79%) of fine white needles, mp (methanol) 169°; nmr (deuteriochloroform): δ 1.12 (t, 3H, J = 7 Hz), 1.70-2.33 (sextet, 2H), 3.06-3.47 (m, 5H, overlapping $-CH_3$ singlet at 3.13 and $-CH_2-$ triplet, J = 7 Hz), 7.42-8.18 (m, 4H).

Anal. Calcd. for $C_{13}H_{14}N_4$: C, 69.00; H, 6.24; N, 24.76. Found: C, 68.74; H, 6.16; N, 24.53.

1-Dichloromethyl-4-propyl-*s*-triazolo[4,3-*a*]quinoxaline (**3f**).

A mixture of 1 g (4.95 mmoles) of 2-hydrazino-3-propylquinoxaline and 2 ml of dichloroacetic acid was treated as described for **3c**, to yield 1.28 g (88%) of an off-white fluffy solid, mp (ethanol) 162°; nmr (deuteriochloroform): δ 1.15 (t, 3H, J = 7 Hz), 1.73-2.40 (sextet, 2H), 3.40 (t, 2H, J = 7 Hz), 7.57-8.87 (m, 5H, including $-CHCl_2$ singlet at 7.70).

Anal. Calcd. for $C_{13}H_{12}Cl_2N_4$: C, 52.89; H, 4.10; N, 18.98. Found: C, 52.62; H, 3.99; N, 18.72.

1-Methyl-4-pentyl-*s*-triazolo[4,3-*a*]quinoxaline (**3g**).

A mixture of 300 mg (1.30 mmoles) of 2-hydrazino-3-pentylquinoxaline and 1 ml of acetic anhydride was treated as described for **3b**, to yield 270 mg (82%) of a white solid, mp (ethanol) 117-118°; nmr (deuteriochloroform): δ 0.77-2.13 (m, 9H), 3.07-3.47 (m, including $-CH_3$ singlet at 312), 7.40-8.17 (m, 4H).

Anal. Calcd. for $C_{15}H_{18}N_4$: C, 70.84; H, 7.13; N, 22.03. Found: C, 70.95; H, 7.09; N, 22.11.

1-Methyl-4-nonyl-*s*-triazolo[4,3-*a*]quinoxaline (**3h**).

A mixture of 500 mg (1.74 mmoles) of 2-hydrazino-3-nonylquinoxaline and 1 ml of acetic anhydride was treated as described for **3b**, to yield 320 mg (59%) of a white solid, mp (ethanol) 91-92.5°; nmr (deuteriochloroform): δ 0.73-2.27 (m, 17H), 3.07-3.50 (m, 5H, including $-CH_3$ singlet at 3.13), 7.43-8.20 (m, 4H).

Anal. Calcd. for $C_{19}H_{26}N_4$: C, 73.51; H, 8.44; N, 18.05. Found: C, 73.76; H, 8.37; N, 18.11.

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REFERENCES AND NOTES

(1) Taken from a thesis submitted by A. R. M. to Indiana University in partial fulfillment of the requirements for the degree Doctor of Philosophy, August, 1981.

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