A Convenient Synthesis of Furoxano[3,4-b]quinoxalines and Furazano[3,4-b]quinoxalines

D. N. NICOLAIDES*, J. K. GALLOS

Laboratory of Organic Chemistry, University of Thessaloniki, Thessaloniki, Greece

Few compounds are known in which a furoxan ring is condensed with other heterocyclic rings and no furoxano[3,4-b]quinoxaline rings have been described in the literature. Boulton and Ghosh\textsuperscript{1} considered as furoxano[3,4-b]quinoxalines, some 6,7-dinitrosquinoxalines prepared by Boyer and Burik in 1960\textsuperscript{2}. It is well known that 1,2-dioximes are oxidized to 1,2,5-oxadiazole N-oxides (furoxans) by several suitable oxidizing agents\textsuperscript{3,4} and recently Spyroudis and Varvoglis\textsuperscript{5} prepared 3,4-diphenylfuroxan in 91% yield by oxidation of

\[ \text{1a} \quad R^1 \cdot R^2 = H \]
\[ \text{b} \quad R^1 = H, R^2 = \text{CH}_3 \]
\[ \text{c} \quad R^1 \cdot R^2 = -(\text{CH} = \text{CH})_2 - \]

\[ \text{3a-c} \quad \text{PI(O)ClHj3} \]

\[ \text{4a-c} \]
benzildioxide with phenylidone difluoroacetate (2). We now report a convenient preparation of the furoxano[3,4-]
3b quinoloxines 3a-c by the oxidation of the readily accessible
2,3-bis(hydroxymethyl)-1,2,3,4-tetrahydroquinoloxines 1a-c through
with two equivalents of 2 in dichloromethane at 20°C.

Compounds 3a-c were prepared in good yields (66–94%) and
were easily separated from the reaction mixture. They were
further deoxygenated by triethyl phosphate in boiling ethanol
to give the new furazano[3,4-b]quinoloxines 4a-c. Although
some similar furazanopryrazines and furazanquinoloxines
have also been recently prepared in good yields by the con-
densation of 3,4-diaminofuran with 1,2-dicarbonyl com-
ounds4,7,8,9,10; it has been stated11 that no furazan can be ob-
tained by direct oxidation of a furan. From this point of
view our method seems interesting for the preparation of
the title compounds.

The proposed structures of compounds 3a-c and 4a-c were
confirmed by their spectral data and microanalyses. The mass
spectra of compounds 3a-c showed, besides the expected mo-
cular ion (M+), a weak (M + 2) ion, as do mass spectra of
benzofuroxan and other quinoid compounds11,12. The extra
hydrogen atoms probably originate from adsorbed water12
and do not belong to the studied compounds, since the proposed
compositions are in good agreement with the microanalyses and
the other spectral data of compounds in question. The ion
m/z = 30 (NO2)13, was found as the base peak in the mass spec-
tra of compounds 3a-c and their fragmentation pathways
were very similar to each other and also to the general frag-
mentation mechanisms reported for other furoxans13,14. Com-
ounds 3a-c are coloured and their electronic spectra show
absorptions in the U.V. and visible region, while their I.R.
spectra show the typical bands of furoxans in the 1625–
1590 cm⁻¹ region. It is important to note that no absorptions
for the NH group were detected in the I.R. and ¹H-N.M.R. (in
CDCl3, or DMSO-d₆) spectra of compounds in question. Com-
ounds 4a-c are also coloured and gave the expected molecular
ion (M⁺) in the mass spectra and generally all their spectral
data are in good agreement with the proposed structure.

Although benzofuroxan reacts with enolate anions giving quin-
oloxine di-N-oxides14, some attempts of ours for such reac-
tions with compounds 3a-c were unsuccessful but are under
further consideration.

Furoxano[3,4-b]quinoloxines 3a-c; General Procedure:
To a magnetically stirred suspension of a 2,3-bis(hydroxymethyl-
1,2,3,4-tetrahydroquinoloxine15 1a (0.5 mmol) in dichloromethane
(15 ml), a solution of phenylidone difluoroacetate (2; 1 mmol) in
dichloromethane (30 ml) is added at 20°C. After 10–20 min, all diox-
ine is dissolved and consumed, as monitored by T.L.C. (silica gel
plates, chloroform as solvent, U.V. lamp) to give a deep orangish-
coloured solution. The solvent and trifluoroacetic acid produced are
vaporated under reduced pressure and the residue is separated by col-
umn chromatography using silica gel as adsorbent and chloroform/
petroleum ether (60:40) as eluent. The title compounds are obtained
after iodobenzene in 66–95% yield and recrystallized from chloroform.
The furazano[3,4-b]quinoloxines are also separated in sufficient purity,
without chromatography, by the removal of the iodobenzene from the
concentrated reaction mixture with petroleum ether and recrystall-
ization of the precipitate.

Furazano[3,4-b]quinoloxines 4a-c; General Procedure:
A solution of a furazano[3,4-b]quinoloxine 3a-c (0.5 mmol) and tri-
ethyl phosphate (2 mmol) in absolute ethanol (10 ml) is heated under
reflux for 4 h. The solvent is removed under reduced pressure and
the residue separated by preparative T.L.C. on silica gel, using chloroform
as eluent. The prepared furazano[3,4-b]quinoloxine 4a-c is collected

Table. Furoxano[3,4-b]quinoloxines 3a-c and Furazano[3,4-b]quinoloxines 4a-c

<table>
<thead>
<tr>
<th>Product No.</th>
<th>Yield [%]</th>
<th>m.p. [°C]</th>
<th>Molecular formulaa</th>
<th>U.V.-Vis (C₆H₅OH) λₘₐₓ [nm] (log ε)</th>
<th>I.R. (KBr) ν [cm⁻¹]</th>
<th>H-N.M.R. (CDCl₃) δ [ppm]</th>
<th>M.S. m/z (rel. intensity %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3a</td>
<td>94</td>
<td>161–162°</td>
<td>C₄H₆N₂O₃</td>
<td>243 (4.49); 329 (3.62); 414 (3.54); 505 (3.39)</td>
<td>1625, 1614, 7.53–7.97 (m)</td>
<td>190 (7); 189 (3); 188 (M⁺, 22); 172 (21); 159 (11); 158 (75); 144 (16); 143 (19); 142 (30); 128 (16); 101 (23); 90 (33); 30 (100)</td>
<td></td>
</tr>
<tr>
<td>3b</td>
<td>66</td>
<td>128–129°</td>
<td>C₄H₆N₂O₃</td>
<td>245 (4.53); 333 (3.71); 413 (3.57); 513 (3.58)</td>
<td>1624, 1596, 6.26 (s); 1575, 1555, 7.42–7.75 (m)</td>
<td>204 (4); 203 (3); 202 (M⁺, 21); 186 (13); 173 (53); 172 (85); 158 (8); 157 (45); 156 (15); 142 (29); 129 (18); 115 (67); 114 (30); 30 (100)</td>
<td></td>
</tr>
<tr>
<td>3c</td>
<td>66</td>
<td>195–196°</td>
<td>C₄H₆N₂O₃</td>
<td>218 (4.53); 286 (4.52); 415 (3.87); 513 (3.69)</td>
<td>1612, 1585, 7.35–7.92 (m)</td>
<td>240 (4); 239 (1); 238 (M⁺, 6); 222 (25); 209 (58); 208 (21); 194 (25); 193 (12); 192 (29); 179 (37); 178 (92); 165 (31); 154 (58); 151 (52); 140 (98); 30 (100)</td>
<td></td>
</tr>
<tr>
<td>4a</td>
<td>35</td>
<td>181–182°</td>
<td>C₄H₆N₂O</td>
<td>225 (4.36); 314 h; 328 (3.71); 344 (3.75); 421 (3.02)</td>
<td>1620, 1605, 7.53–7.97 (m)</td>
<td>172 (M⁺, 65); 142 (94); 115 (6); 90 (100); 88 (6); 30 (23)</td>
<td></td>
</tr>
<tr>
<td>4b</td>
<td>45</td>
<td>138–139°</td>
<td>C₄H₆N₂O</td>
<td>230 (4.56); 318 h; 330 (3.87); 345 (3.92); 450 (3.27)</td>
<td>1620, 1605, 2.77 (s); 1555, 1507, 7.43–7.80 (m)</td>
<td>186 (M⁺, 57); 156 (100); 130 (11); 129 (72); 114 (8); 105 (17); 104 (18); 103 (22); 102 (97); 30 (33)</td>
<td></td>
</tr>
<tr>
<td>4c</td>
<td>54</td>
<td>199–200°</td>
<td>C₄H₆N₂O</td>
<td>217 (4.54); 274 (4.51); 282 (4.58); 388 (3.95); 438 h</td>
<td>1596, 1538, 7.47–7.97 (m)</td>
<td>222 (M⁺, 3); 192 (6); 167 (5); 166 (4); 165 (19); 140 (34); 105 (81); 77 (100); 30 (7)</td>
<td></td>
</tr>
</tbody>
</table>

a The microanalyses showed the following maximum deviations from the calculated values: C ± 0.34%, H ± 0.14%, N ± 0.28%. 
from the faster moving coloured band in 35–54% yield and recrystallized from chloroform. No starting furoxan 3a–e is recovered from the other bands.

Received: April 9, 1981

* Address for correspondence.
8 A. Gasco et al., J. Heterocycl. Chem. 6, 769 (1969).