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## Cyclization of *N*-Acylanthranilic Acids with Vilsmeier Reagents. Chemical and Structural Studies

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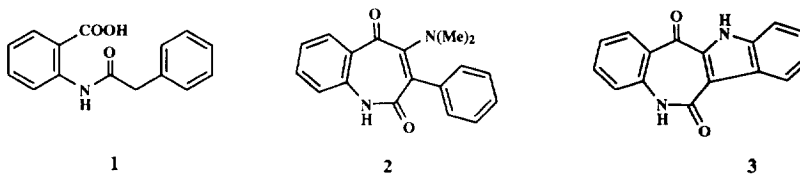
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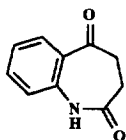
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*Dedicated to Professor Hans Suschitzky on the occasion of his 80th birthday*

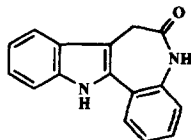
**Abstract:** Vilsmeier reagents, generated from e.g. *N,N*-dimethylformamide and oxalyl chloride, react with *N*-acetylanthranilic acid to produce the 2-(2'-dimethylamino)ethenyl-4*H*-3,1-benzoxazin-4-one **13a**. *N*-phenylacetylanthranilic acid similarly gave 2-(2'-dimethylamino-1'-phenyl)ethenyl-4*H*-3,1-benzoxazin-4-one **6a**, whose structure has been determined by X-ray crystallography. The benzoxazinone **6a** could readily be converted to fused heterocyclic systems, thus e.g. **13a** and hydrazine hydrate gave pyrazolo[5,1-*b*]-4*H*-quinazoline **20a**. Reaction of *N*-acetylated anthranilic acids and oxalyl chloride alone gave the fused oxazolidine-4,5-diones **24**. The structure of one representative, **24a**, was established by X-ray crystallography. Thermolysis of **24a** gave, after elimination of CO+CO<sub>2</sub>, 2-benzyl-4*H*-3,1-benzoxazin-4-one **7** in quantitative yield.

Cyclization of the phenylacetylated anthranilic acid **1** induced by oxalyl chloride in dimethyl formamide (DMF) has been claimed<sup>1</sup> to yield the yellow benz-1-azepine-2,5-dione **2**. We were attracted by this readily available (reported yield: 86%) multifunctional benzazepine because we considered it as a potential precursor to indolobenzazepines, such as **3**. Interestingly, Kunick<sup>2-4</sup> as well as Kozikowski<sup>5, 6</sup> reasoned along similar lines, have recently converted **4**, *via* Fischer indolization, to **5**.

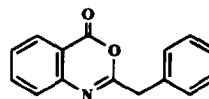




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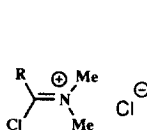


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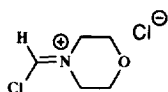


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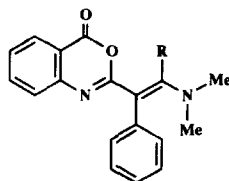
Cyclization of **1** could be performed as described<sup>1</sup>, (i.e. a solution of **1** and oxalyl chloride in toluene was treated with DMF and the mixture heated at 50°C for 20h). Inspection of the IR and NMR data of the yellow product obtained immediately revealed, however, that its purported structure **2** cannot possibly be correct, because the carbonyl absorptions (1737 and 1618 cm<sup>-1</sup>) in the IR spectrum are incompatible<sup>7-9</sup> with its conjugated system. Furthermore the IR spectrum did not exhibit any NH peak. The information obtained from the <sup>13</sup>C NMR and PMR spectra were even more pertinent because 8 CH signals, rather than 7 required for **2**, were clearly visible. Hence the previously assigned structure **2** was abandoned in favour of the 4*H*-3,1-benzoxazin-4-one derivative (**6a**)<sup>#</sup>, whose formation can be rationalized in terms of initial cyclization of **1** to **7**, which is subsequently attacked at the active methylene site by the electrophilic reagent (**8a**), (formed from oxalyl chloride and DMF). This view could be substantiated by the fact that 2-benzyl-4*H*-3,1-benzoxazin-4-one **7** (a known compound<sup>10, 11</sup> prepared from **1** and Ac<sub>2</sub>O through reflux) could be converted to **6a** by reaction with ClCOCOCI/DMF.



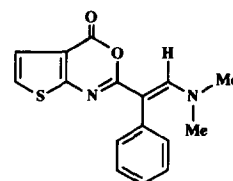
**8a** R=H  
**b** R=Cl



9



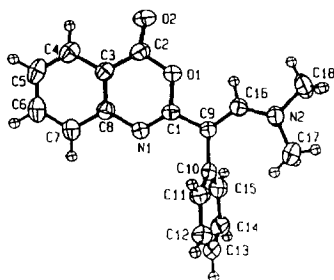
**6a** R=H  
**b** R=Cl



10

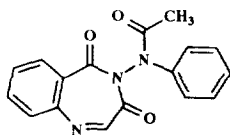
To fully confirm this reassignment the yellow product was subjected to an X-ray analysis. A perspective view of molecule **6a** is shown in Fig. 1 and selected distances and angles in Table 1. The benzoxazin part of the molecule is planar within 0.05 Å and form an angle of 74.3° with the best plane through the phenyl ring. Some thiophene analogues of **6a** previously likewise incorrectly assigned<sup>1</sup> could also, by NMR technique, be shown to be fused 4*H*-3,1-oxazin-4-ones (e.g. **10**). All these oxazinones had *E*-configuration at the enamine double bond as evidenced by the coupling constants ( $J = 5\text{Hz}$ )<sup>12</sup> observed between the enamine proton and C-2-carbon atom in the oxazinone ring. *Z*-isomers of **6** and **10** were never observed as co-products.

# After the completion of this work Auberson and Winkler have based on analysis of NMR data<sup>51</sup> arrived at the same conclusion.

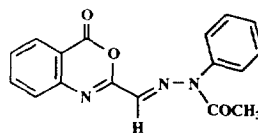


**Figure 1.** ORTEP view of molecule **6a** with numbering of the atoms. Thermal ellipsoids are drawn at the 40% probability level, hydrogen atoms on arbitrary scale.

A related reassignment, supported by X-ray crystallography, was reported<sup>13</sup> in 1975 by Gilman and Fryer, who found that a compound, (obtained from anthranilic acid, by subsequent treatment with chloral, phenylhydrazine and acetic anhydride) originally<sup>14</sup> described as the 1,4-benzodiazepine **11** is in fact the benzoxazinone **12**.

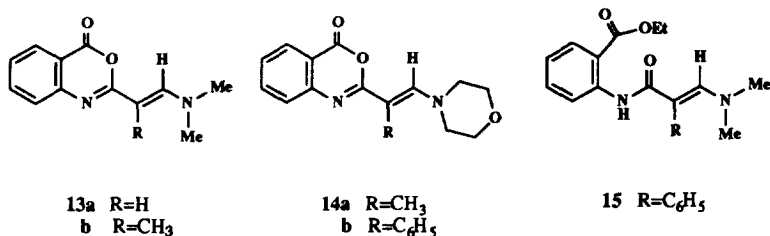


**11**



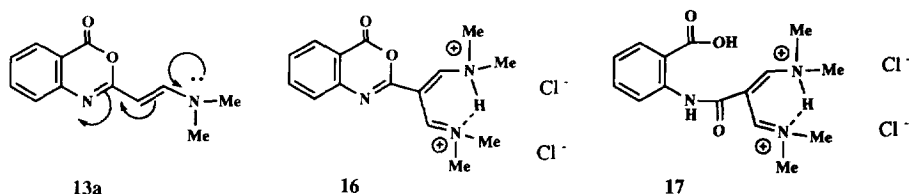
**12**

Subsequent studies revealed that addition of solid Vilsmeier salts<sup>15, 16</sup>, *viz.* **8a** and **9**, to solutions or suspensions of the appropriate oxazinones or amides in acetonitrile quickly (< 3 min at reflux) gave e.g. **6a** and **13a** as hydrochlorides (with C=O, absorption at 1770 cm<sup>-1</sup>) in almost quantitative yields. The free bases could easily be liberated by careful treatment with sodium carbonate or sodium hydroxide in aqueous solution at 5-10°C. Treatment with sodium hydroxide in a mixed water-ethanol solution at 30°C, however, resulted in ring opening of the oxazinone ring with the formation of the ethyl ester **15**. During these studies it was noted that the morpholine-based Vilsmeier reagent **9** was more reactive and easier to handle than the more common reagent **8a**. Higher reactivity of this reagent **9**<sup>17, 18</sup>, as compared with **8a**, has previously been observed, e.g. versus activated alkenes<sup>18</sup>.



Whereas the PMR signals from the *N*-methyl groups in **6a** and **13b** appeared as sharp singlets (around 2.8 ppm) at 30°C those of the analogue **13a**, with a less substituted olefinic bond, appeared as a broadened singlet around 2.9 ppm which at +15°C become a doublet indicating that distribution of electrons from the lone pair on the -N(CH<sub>3</sub>)<sub>2</sub> group to heterocyclic ring, which requires planarity, is disturbed by twisting the -N(CH<sub>3</sub>)<sub>2</sub> out of the plane in the phenyl and methyl substituted derivatives **6a** and **13b**. Similar effects, *i.e.* the barrier to rotation of the amino group is lowered with increasing size of the substituents, have previously been observed<sup>19, 20</sup> on simple 2-acylenamines.

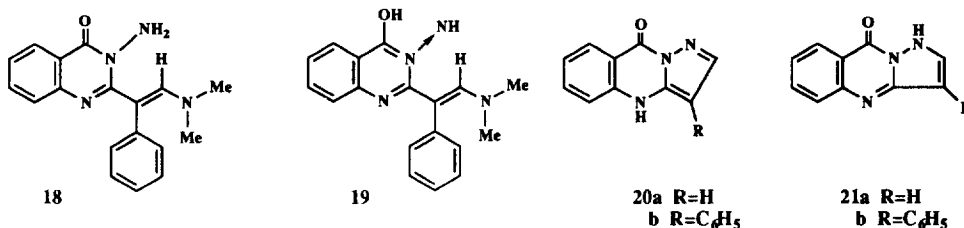
Reaction of *e.g.* 2-methyl-4*H*-3,1-benzoxazin-4-one (or less suitable *N*-acetylanthranilic acid) with Vilsmeier salts under more forcing conditions (addition of solid reactant to a melt of **8a**) quickly resulted in the formation of the salt **16** (*i.e.* two C<sub>1</sub>-units had now been introduced), which easily reacted with water yielding the ring-opened salt **17**. Similar disubstitutions, using DMF-POCl<sub>3</sub> reagents, have previously been observed by Seshadri<sup>21</sup>, who inferred the formation of such salts from secondary reactions, such as interaction with hydrazine.



The IR spectrum of the protonated vinamidinium salt **17** featured a C=O vibration at 1791 cm<sup>-1</sup>, and the proton NMR spectrum showed that the molecule is identical after the bifurcation point indicating a fast tautomeric equilibrium involving the proton on the nitrogen atom. This proton also exchange quickly with the proton in the carboxy function. The signals from the four methyl groups appeared as two sharp singlets indicating restricted rotation around the bonds joining the dimethylamino groups with the rest of the molecule. Unprotonated vinamidinium salts possess similar NMR characteristics<sup>22</sup>.

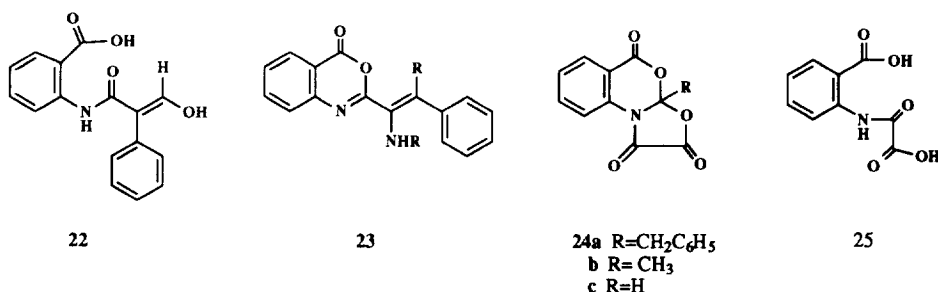
The compounds **6**, **13** and **14** are all representatives of 4*H*-3,1-oxazine-4-ones bearing a secondary amino group in conjugation with the hetero ring and consequently are interesting candidates as inhibitors of leucocyte elastase<sup>23</sup>. In this context it should be noted that some 2-amino-4*H*-3,1-benzoxazin-4-ones are of particular interest because an amino group seems to confer just the right stability against unwanted nucleophilic ring opening during the transport to the enzyme<sup>24</sup>. The benzoxazin-4-one **6a** is quite stable to *N*-nucleophiles as evidenced by the fact that this molecule is intact even after a long reflux period (6h) in

ethanol/ammonia. Heating of **6a** with hydrazine-hydrate in EtOH, however, resulted in a nucleophilic attack on the benzoxazinone ring leading to the quinazoline **18** (rather than its tautomer **19**). Heating of **18** to its melting point (~180°C) resulted in cyclization to 3-phenylpyrazolo[5,1-*b*]4*H*-quinazolin-9-one (**20b**), which in DMSO solution completely existed in the tautomeric form **20b** (rather than **21**) as evidenced by a strong NOE effect between the NH and 5-CH. Similar NOE effects have recently been observed<sup>25</sup> in ethyl pyrazolo[5,1-*b*]4*H*-quinazolin-9-one-2-acetate and related compounds.



The parent compound of **20b** (i.e. **20a**) was formed within a few minutes when **13a** was heated with N<sub>2</sub>H<sub>4</sub>•H<sub>2</sub>O in ethanol. On refluxing in neat N<sub>2</sub>H<sub>4</sub>•H<sub>2</sub>O both pyrazolo[5,1-*b*]4*H*-quinazolin-9-ones were cleaved and e.g. **20** yielded 2-aminobenzhydride and 3-phenylpyrazol-2-one. Both **20a** and **20b** could be independently prepared by heating 2-aminobenzhydrazide with ethyl hydroxymethyleneacetate and ethyl hydroxymethylenephanylacetate, respectively in acetic acid. Heating of 2-aminobenzhydrazide with hydroxymethylene phenylacetaldehyde, however gave *via* a cleavage reaction 4-phenylpyrazole rather than the expected pyrazolo[5,1-*b*]4*H*-quinazolin-9-one derivative.

It might be added that some benzoxazinones of the general structure **23** have recently been reported<sup>26</sup> and ring-opened with amines by El-Faragy. Dissolution of **6a** in dilute (2 %) aqueous hydrochloric acid gave the ring-opened and hydrolyzed anthranilic acid derivative **22**. The enolic tautomer predominated totally and the corresponding formyl tautomer could not be detected by NMR spectroscopy. Finally, it is suggested that apart from the obvious preparative interest for nucleophilic ring-openings and recyclizations compounds of type **13** and **14** also should be of considerable interest in cycloaddition reactions<sup>27</sup>.



In the original procedure<sup>1</sup> the time of reaction of **1** and oxalyl chloride in the solvent (toluene) was not specified. We now deliberately have used long reaction times and had expected to observe a simple cyclization of **1** to the benzoxazinone **7**. However the product isolated had the composition C<sub>17</sub>H<sub>11</sub>NO<sub>5</sub> and

absorbed (C=O) at 1841 and 1741  $\text{cm}^{-1}$  in the IR spectrum, whereas the 4*H*-3,1-oxazinone (**7**) absorbs at 1778 and 1762  $\text{cm}^{-1}$ . These data together with information from the NMR spectra suggested structure **24a** which also was confirmed by an X-ray investigation. A perspective view of molecule **24a** is shown in Fig. 2. Selected distances and angles are given in Table 2 and angles between best planes through parts of the molecule in Table 3. Other members (viz. **24b**) of this ring system could be analogously prepared. In the transformation (**7**  $\rightarrow$  **24a**) it appears as if the 5-membered heterocyclic ring is formed before the 6-membered, because in a separate experiment it could be shown that the benzoxazinone **7** could not serve as precursor to **24a**. Attempts to prepare the parent compound **24c** from *N*-formylanthranilic acid and oxalyl chloride failed, although IR studies of the reaction solution indicated formation of **24c**. The product isolated in excellent yield from this experiment was 2-carboxyoxanilic acid (**25**), perhaps an indication of extreme water sensitivity of **24c**.

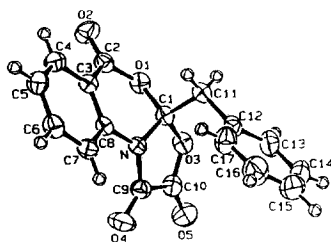
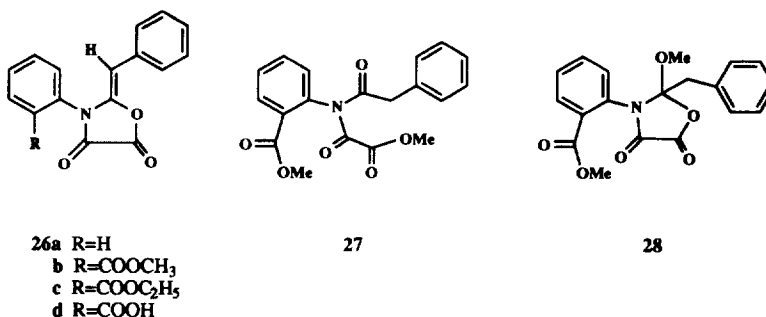


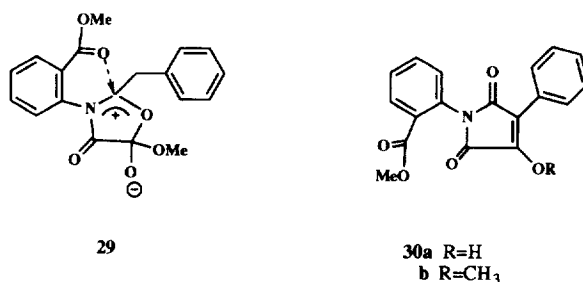
Figure 2. ORTEP view of molecule **24a** with numbering of the atoms. Thermal ellipsoids are drawn at the 40% probability level, hydrogen atoms on arbitrary scale.

Similar cyclizations of amides, induced by oxalyl chloride, have been discussed in the literature.<sup>28-31</sup> Thus Speziale and Smith<sup>30</sup> reported the formation of **26a** when phenylacetamide was treated with oxalyl chloride. It has now been found that the derivatives **25b** and **26c** can be similarly formed when the methyl and ethyl esters of **1**, respectively are subjected to the same conditions as **1** itself. Attempts to generate the acid **26d** from **24a** or from its esters failed<sup>32</sup>.

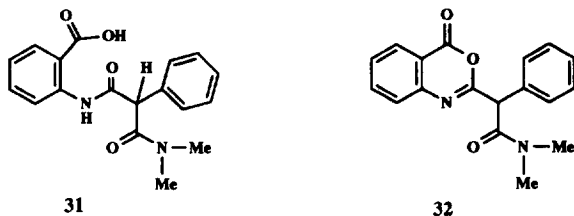
When heated up to its melting point ( $\sim 175^\circ\text{C}$ ) **24a** quantitatively eliminated  $\text{CO}_2$  and  $\text{CO}$  to yield **7**. Similar eliminations, thermal<sup>32-35</sup> as well as base-induced<sup>36</sup> are known in the literature. However, under the conditions previously used ( $50^\circ\text{C}$  in toluene no such conversion did take place) indicating that **24a** does not appear on the reaction pathway leading from **1** to **6a**.



The methyl ester **26b** readily reacted with methanol, yielding an isolable adduct which in the PMR spectrum featured a CH<sub>2</sub> group as an AB quartet ( $J=22$  Hz). The IR spectrum of the adduct showed C=O frequencies at 1749, 1724 and 1697 cm<sup>-1</sup>. Reaction of **26b** and methanol conceivably could involve attack at a carbonyl group in the heterocyclic ring (leading eventually to ring cleavage) or addition to the double bond. The two alternative structures of the adduct should then be **27** and **28**, respectively. However the spectroscopic data led us to suggest a third alternative, namely a zwitterionic adduct **29**, of Adickes-type<sup>37</sup>. In the presence of methoxid in methanol the adduct underwent cyclization to the maleinimide derivative **30a**. The parent compound of **25b**, 2-benzylidene-*N*-phenyloxazolidine-4,5-dione **25a**, undergoes a similar base-induced rearrangement giving 1,4-diphenyl-3-hydroxymaleinimide<sup>38</sup>. Reaction between the methyl ester of **1** with dimethyl oxalate in the presence of sodium methoxide gave the same maleinimide<sup>39</sup> thus proving the structure of **30a**, which was also further characterized by conversion to the methyl ether **30b**, by reaction with diazomethane.



*N,N*-Dimethyldichloromethyleneiminium chloride **8b** (Viehe's salt)<sup>40, 41</sup> often effects transformations similar to those of **8a** and for comparative purposes **8b** was allowed to react with **1**. Work-up gave the phenyl-malonoamide derivative **31** in a good yield thus indicating that the expected compound **6b** indeed had been formed. Heating of the amine **31** in acetic anhydride readily gave the benzoxazinone **32** which could be independently prepared by heating anthranilic acid with  $\alpha$ -(*N,N*-dimethylcarbamoyl)-phenylacetic acid in dioxane in the presence of dicyclohexylcarbodiimide (DCC).



Finally, it should be observed that the benzazepinediones **2** and **3** still are unknown compounds. However work is in progress towards these systems.

### Experimental

Melting points were determined on a Reichert WME Kofler hot stage or on a Leitz 1008 melting point microscope and are uncorrected. IR (KBr) spectra were recorded on a Perkin-Elmer 1600 FT-IR instrument. NMR spectra were obtained on a Varian UNITYplus (400 MHz) or on a Bruker VP-200 (200 MHz) instrument. Unless stated otherwise DMSO-d<sub>6</sub> was used as solvent. Mass spectra were obtained on a Finnigan MAT SSQ710 instrument with direct inlet at 70 eV.

Starting materials: The chemicals used were purchased from Aldrich or Lancaster unless stated otherwise.

*N*-formylmorpholine and 2-aminothiophene-3-carboxylic acid were kind gifts from BASF and Synthetic Chemicals respectively. The following starting materials were synthesized using the indicated methods.

*N,N*-dimethylchloromethyleneiminium chloride (**8a**)<sup>16</sup>, *N,N*-dimethyldichloromethyleneiminium chloride (**8b**)<sup>42</sup>, *N*-phenylacetylanthranilic acid **1**<sup>43</sup>, *N*-acetylanthranilic acid<sup>44</sup>, 2-benzylbenz-4*H*-(3,1)-oxazin-4-one (**7**)<sup>10</sup>, 2-methylbenz-4*H*-(3,1)-oxazin-4-one<sup>45,46</sup>, anthranil hydrazide<sup>25</sup>.

#### Chloromethylenemorpholinium chloride (**9**)

Oxalyl chloride (5.3 ml, 60 mmol) in dry CH<sub>2</sub>Cl<sub>2</sub> (15 ml) was added to a stirred solution of *N*-formylmorpholine (6.35 g, 55 mmol) in dry CH<sub>2</sub>Cl<sub>2</sub> (50 ml) at 10°C. After a stirring period of 30 min the white moisture-sensitive precipitate was collected, washed with CH<sub>2</sub>Cl<sub>2</sub>, dried and stored in an desiccator, yield 8.8 g, (95%). IR: 2875, 2274, 1659, 1374, 1302, 1113, 1020, 858, 659, 594 cm<sup>-1</sup>.

#### *N*-Phenylacetylanthranilic acid methyl ester

Phenylacetyl chloride (7.3 g, 50 mmol) was added to a stirred solution of methyl anthranilate (15.2 g, 100 mmol) in dichloromethane (200 ml) at 15°C, whereupon potassium carbonate (aq., 5%, 200 ml) was added followed by an additional portion of phenylacetyl chloride (7.3 g). The organic phase was separated, washed with water, dried and evaporated, yielding an oil which soon crystallized, yield 23.5 g (87%), m.p. 57-58°C (lit.<sup>47</sup> 58-59°C). IR: 3318, 1707, 1682, 1586, 1531, 1451, 1261, 1083, 757 cm<sup>-1</sup>.



***N*-Phenylacetylanthranilic acid ethyl ester**

The procedure above was used. Yield: 88%, m.p. 60-61°C (lit.<sup>43</sup> m.p. 62°C). IR: 3340 (NH), 2979, 1694, 1676, 1588, 1522, 1445, 1299, 1268, 1248, 1141, 1088, 762, 721 cm<sup>-1</sup>.

**2-(2'-Dimethylamino-1'-phenyl)ethenyl-4*H*-3,1-benzoxazin-4-one (6a)**

**Method A.** *N,N*-dimethylchloromethyleneiminium chloride (7.0 g, 55 mmol) was added to a stirred mixture of acetonitrile (60 ml) and *N*-phenylacetylanthranilic acid **1** (4.60 g, 20 mmol) at 60°C. The mixture was heated to reflux for 3 min. During this short period a clear solution was obtained and the product started to separate as a hydrochloride (6.2 g), which after an additional stirring period of 10 min was collected and then stirred for 3 minutes in a 0.1 mol NaHCO<sub>3</sub>/Na<sub>2</sub>CO<sub>3</sub> buffer at 10 °C. The free base formed was collected, washed with water and dried, yield 5.5 g, (95%) of **6a** as a yellow solid, m.p. 160-161°C. IR: 2916 (w), 1742 (s), 1619 (m), 1537 (s), 1466 (m), 1390 (m), 1254 (m) and 772 (m) cm<sup>-1</sup>. A recrystallization (EtOH) of this material changed neither the m.p. nor the IR spectrum. <sup>1</sup>H NMR: (CDCl<sub>3</sub>): 2.75 (s, 6H, -N(CH<sub>3</sub>)<sub>2</sub>), 7.3-7.6 (m, 8H, arom CH), 7.75 (s, 1H, 2'-H), 8.04 (dd, 1H, arom CH). <sup>13</sup>C NMR (CDCl<sub>3</sub>): 43.4 (q), 99.9 (s, C-1'), 115.1 (s), 124.7 (d), 125.8 (d), 126.6 (d), 127.5 (d), 128.0 (d), 132.3 (d), 135.5 (s), 135.8 (d), 147.6 (d, C-2'), 149.1 (s), 160.6 (s, C-4), 161.4 (s, C-2).

The hydrochloride of **6a** gave the following IR data: 2926 (w), 2580 (m), 1770 (s), 1635 (s), 1569 (s), 1488 (s), 1372 (s), 1270 (s), 1121, 1019 cm<sup>-1</sup>.

**Method B.** A stirred solution of **1** (0.79 g, 3 mmol) in toluene (50 ml) and oxalyl chloride (0.70 g) was treated with DMF (0.4 g) and the mixture heated at 50°C for 20h. The cooled mixture was treated with sodium hydroxide (aq, 10%, 50 ml) and EtOH (75 ml). The organic layer was (after vigorous shaking) separated, washed with water, dried (MgSO<sub>4</sub>) and evaporated. Recrystallization from EtOH gave **6a**, yield 0.43 g, (50%), m.p. 160-161 °C.

This material was identical in every respect with that obtained according to procedure A.

**2-(2'-Dimethylamino-1'-phenyl)ethenyl-4(3*H*)-thieno[5,6-*b*]-oxazin-4-one (10)**

Method A above gave the title compound in 90% yield whereas method B, gave 30% yield, m.p. 169-170°C. (lit.<sup>1</sup> m.p. 169-170°C). IR: 1740, 1617, 1528, 1492, 1437, 1385, 1321, 1227, 1091, 988, 770, 708, 651 cm<sup>-1</sup>.

<sup>1</sup>H NMR: 2.62 (s, 6H, N(CH<sub>3</sub>)<sub>2</sub>), 6.86 (d, 1H, *J*=16.2 Hz), 7.1-7.3 (m, 5H, arom CH), 7.59 (d, 1H, *J*=16.2 Hz), 7.68 (s, 1H, olef. CH). <sup>13</sup>C NMR: 43.2 (s), 99.3 (s), 124.4 (d), 126.5 (d), 127.4 (d), 132.0 (d), 135.2 (s), 135.9 (d), 147.9 (d), 156.3 (s), 169.2 (s), 165.1 (s).

**2-(2'-Dimethylamino)ethenyl-4*H*-3,1-benzoxazin-4-one (13a)**

Method A was used. Yield: 77%, m.p. 145-146°C. IR: 1753, 1631, 1569, 1557, 1466, 1392, 1254, 1112, 1055, 1022, 764 cm<sup>-1</sup>. <sup>1</sup>H NMR(CDCl<sub>3</sub>): 2.9(broad s, 6H, N(CH<sub>3</sub>)<sub>2</sub>), 4.82 (d, *J*=13.2 Hz), 7.21 (dd, 1H, arom CH), 7.28 (d, 1H, arom CH), 7.62 (d, 1H, *J*=13.2 HZ), 7.62 (dd, 1H, arom CH), 8.04 (d, 1H, arom CH).

<sup>13</sup>C NMR: 43.5 (broad, N(CH<sub>3</sub>)<sub>2</sub>), 85.5 (d, C-1'), 114.7 (s), 124.3 (d), 124.5 (d), 127.8 (d), 135.7 (d), 148.7 (s), 150.2 (d, C-2'), 160.1 (s), 160.4 (s).

**2-(2'-Dimethylamino-1'-methyl)ethenyl-4*H*-3,1-benzoxazin-4-one (13b)**

Method A was used. Yield: 85%, m.p. 154-156°C. IR: 1736, 1627, 1574 (s), 1548, 1466, 1389, 1262, 1113, 764 cm<sup>-1</sup>. <sup>1</sup>H NMR (CDCl<sub>3</sub>): 2.1 (s, 3H, CH<sub>3</sub>), 3.0 (s, 6H, N(CH<sub>3</sub>)<sub>2</sub>), 7.15 (t, 1H, arom CH), 7.33 (t, 1H, arom CH), 7.42 (s, 1H, olef CH), 7.57 (t, 1H, arom CH), 8.00 (d, 1H, arom CH). <sup>13</sup>C NMR (CDCl<sub>3</sub>): 11.6(q), 43.2(q), 92.7 (s), 115.0 (s), 124.6 (d), 125.5 (d), 128.0 (d), 135.8 (d), 148.0 (d), 149.1 (s), 160.6 (s), 161.8 (s).

**2-(2'-Morpholino-1'-methyl)ethenyl-4*H*-3,1-benzoxazin-4-one (14a)**

Method A was used. Yield 83%, m.p. 193-193°C. IR: 1741, 1625, 1570, 1555, 1445, 1250, 1114, 1060, 765 cm<sup>-1</sup>. <sup>1</sup>H NMR (CDCl<sub>3</sub>): 2.08 (s, 3H, CH<sub>3</sub>), 3.47 (t, 2H, CH<sub>2</sub>N), 3.73 (t, 2H, CH<sub>2</sub>O), 7.22 (t, 1H, arom CH), 7.89 (t, 1H, arom CH), 7.41 (s, 1H, olef. CH), 7.62 (t, 1H, arom CH), 8.02 (d, 1H, arom CH). <sup>13</sup>C NMR (CDCl<sub>3</sub>): 12.5 (q), 50.9 (t), 66.7 (t), 95.2 (s), 115.3 (s), 125.3 (d), 125.7 (d), 128.1 (d), 136.1 (d), 146.5 (d), 148.6 (s), 160.4 (s), 161.1 (s).

**2-(2'-Morpholino-1'-phenyl)ethenyl-4*H*-3,1-benzoxazin-4-one (14b)**

Method A was used. Yield: 93%, m.p. 163-164°C. IR: 1751, 1579, 1555, 1469, 1422, 1243, 1112, 1014, 780 cm<sup>-1</sup>. <sup>1</sup>H NMR (CDCl<sub>3</sub>): 3.05 (t, 2H, CH<sub>2</sub>N), 3.53 (t, 2H, CH<sub>2</sub>O), 7.2-7.4 (m, 7H, arom CH), 7.56 (t, 1H, arom CH), 7.66 (s, 1H, olef. CH), 8.04 (t, 1H, arom CH). <sup>13</sup>C NMR (CDCl<sub>3</sub>): 50.9 (t), 66.3 (t), 100.8 (s), 115.3 (s), 125.2 (d), 125.9 (d), 127.1 (d), 128.1 (d), 131.7 (d), 135.6 (s), 135.9 (d), 146.0 (d), 148.7 (s), 160.5 (s), 160.9 (s).

**Synthesis of the Dichloride 16**

The Vilsmeier salt **8a** (5.2 g, 40 mmol) was (under nitrogen) heated (ca 135°C) until a clear melt was formed, whereupon 2-methyl-4*H*-3,1-benzoxazin-4-one (1.61 g, 10 mmol) was added. After 10 min at 135-140°C the melt was allowed to cool to ca 80°C and dried acetonitrile was added. Crystals of **16** were quickly formed and they were collected after standing for 1h. Yield: 2.15 g (61%), m.p. 200°C dec. IR: 3367, 1795, 1628, 1560, 1471, 1385, 1302, 1265, 1215, 1110, 970, 931 cm<sup>-1</sup>.

Attempts to obtain NMR data of **16** failed due to low solubility and sensitivity to water.

**Acid hydrolysis of the Benzoxazinone (6a)**

The benzoxazinone **6a** (580 mg, 2 mmol) was dissolved and stirred for 2h in hydrochloric acid (10 ml, aq, 2%) whereupon the pH was adjusted to ca pH 5. The white precipitate of **22** formed and was collected, washed with water and dried. Yield: 380 mg (67%), m.p. 200°C dec. IR: 3271, 3100-2700 (br), 1677, 1636, 1583, 1529, 1404, 1234, 1165, 888, 753 cm<sup>-1</sup>. <sup>13</sup>C NMR: 110.9 (s), 116.6 (s), 120.6 (d), 122.8 (d), 127.6 (d), 128.6 (d), 130.8 (d), 131.4 (d), 133.6 (s), 133.8 (d), 140.6 (s), 162.4 (d), 169.8 (s), 170.7 (s).

<sup>1</sup>H NMR: 6.95 (t, 1H, arom CH), 7.09 (d, 1H, olef. CH, *J* = 11.4Hz), 7.2-7.5 (m, 6H, arom CH), 7.88 (d, 1H, arom CH), 8.63 (d, 1H, arom CH), 11.1 (s, 1H, NH), 13.5 (d, 1H, OH, *J* = 11.4 Hz).

**Synthesis of the ring-opened Dichloride (17)**

Crystals of the dichloride **16** (10 mmol) were added to a stirred solution of water (10 mmol) in acetonitrile (50 ml) at 50°C. After 1h at this temperature the crystals of **17** were collected. Yield: 8.5 mmol,

m.p. 200°C dec. IR: 3320, 3100-2500(br), 1695, 1610, 1514, 1230, 785 cm<sup>-1</sup>. <sup>1</sup>H NMR: 3.07 (s, 3H, N(CH<sub>3</sub>)<sub>2</sub>), 3.35 (s, 3H, N(CH<sub>3</sub>)<sub>2</sub>), 7.22 (dd, 1H, arom CH), 7.58 (dd, 1H, arom CH), 7.95 (d, 1H, arom CH), 8.07 (s, 2H, olef. CH), 8.16 (d, 1H, arom CH), 9.15 (broad s, 2H, NH + COOH), 11.20 (s, 1H, HNCO).

### 2-(2'-Dimethylamino-1'-phenyl)ethenyl-3-amino-4(3H)quinazolinone (18)

A solution of the benzoxazin-4-one **6a** (2.9 g, 10 mmol) and hydrazine-hydrate (0.6 g, 12 mmol) in EtOH (6 ml) was refluxed for 1h, whereupon water was added to the cooled reaction mixture. The white solid formed was collected and dried, 2.7 g (90%), m.p. 180°C dec. IR: 3321, 3200-2700 (br), 1724, 1660 (sh), 1648, 1489, 1449, 926, 755 cm<sup>-1</sup>. <sup>1</sup>H NMR: 2.65 (s, 6H, N(CH<sub>3</sub>)<sub>2</sub>), 6.95 (t, 1H, arom CH), 7.2-7.4 (m, 7H, arom CH), 7.46 (s, 1H, olef. CH), 8.47 (d, 1H arom CH), 9.95 (s, 2H, NH). <sup>13</sup>C NMR: 42.4 (q), 102.0 (s), 119.9 (s), 120.4 (d), 120.9 (d), 127.0 (d), 127.1 (d), 127.9 (d), 130.9 (d), 132.4 (d), 135.4 (s), 139.7 (s), 147.2 (d), 167.0 (s), 167.3 (s).

### Pyrazolo[5,1-b]4H-quinazolin-9-one (20a)

**Method A** The hydrochloride of **13a** (1.26 g, 5mmol) was added to a hot solution of N<sub>2</sub>H<sub>4</sub> • H<sub>2</sub>O (1 ml) in water (12 ml). The solution was refluxed for 90 sec and then allowed to cool and the crystals of **20a** were collected. Yield: 0.65 g (70%), m.p. >260°C. IR 3200-2600 (NH), 1700, 1636, 1575, 1473, 1333, 1198, 953, 749 cm<sup>-1</sup>.

**Method B** A mixture of anthranil hydrazide (1.65 g, 10mmol) and the sodium salt of ethyl hydroxymethylene acetate (1.38, 10mmol) in acetic acid (15 ml) was heated at reflux for 6h, whereupon the mixture was cooled and diluted with water. The solid formed was collected and recrystallized from ethanol. Yield: 1.05 g (55%).

This material was identical with that obtained by method A.

### 3-Phenylpyrazole

Anthranil hydrazide (1.65 g, 10 mmol) and hydroxymethylenephanylacetaldehyde (1.48 g, 10 mmol)<sup>48</sup> in acetic acid (15 ml) was heated at reflux for 6h. The cooled reaction mixture was diluted with 2-propanol (20 ml) and the crystals of 3-phenylpyrazole collected. Yield: 1.3 g (90%), m.p. 230-231°C (lit.<sup>49</sup> m.p. 230-231°C). IR: 3110 (br), 2941 (br), 1606, 1377, 1153, 957, 879, 927, 761 cm<sup>-1</sup>. <sup>1</sup>H NMR: 7.16 (dd, 1H), 7.32 (dd, 2H), 7.59 (d, 2H), 8.05 (s, 2H, CH in the pyrazole ring), 12.93 (s, 1H, NH). <sup>13</sup>C NMR (CDCl<sub>3</sub>): 121.1 (s), 125.0 (d), 125.7 (d), 128.6 (d), 132.8 (s).

### 3-Phenylpyrazolo[5,1-b]4H-quinazolin-9-one (20b)

**Method A.** The quinazolinone **18** (0.608 g, 2mmol) was heated above the m.p. (180°C) which resulted in elimination of dimethylamine. The cooled melt was recrystallized from acetonitrile which gave the pyrazoloquinazolinone **20b**. Yield: 0.38 g (67%), m.p. >260°C. IR: 3292 (br), 1697 (s), 1580, 1523, 1476, 1194, 927, 750 cm<sup>-1</sup>. PMR: 7.28 (m, 2H), 7.34 (dd, 2H), 7.6-7.8 (m, 4H), 8.20 (d, 1H), 8.20 (d, 1H). 8.26 (s, 1H), 11.9 (s, 1H, NH).

**Method B.** Method B given for the parent compound was used. Yield: 72%, m.p. >260°C.

**Synthesis of compound 24a**

Oxalyl chloride (4.4 ml, 50 mmol) was added to a stirred solution of *N*-(phenylacetyl)anthranilic acid (5.10 g, 20 mmol) in acetonitrile (60 ml) at 50°C. After completed addition the solution was stirred for 1h and concentrated, whereupon the syrup formed was diluted with diisopropyl ether. This operation induced crystallization within 2 min. The crystals formed were collected washed with diisopropyl ether and dried. Yield 4.71 g (81%), mp. 180 °C dec. IR: 1824(s), 1753(s), 1605, 1494, 1467, 1396(s), 1314, 1037, 758 cm<sup>-1</sup>. <sup>1</sup>H NMR (CDCl<sub>3</sub>): 3.43 (d, 1H, CH<sub>2</sub>, *J* = 4.5 Hz), 3.62 (d, 1H, CH<sub>2</sub>, *J* = 4.5 Hz), 6.97 (m, 2H, arom CH), 7.88 (t, 1H, arom CH), 7.92 (d, 1H, arom CH), 8.11 (d, 1H, arom CH). <sup>13</sup>C NMR (CDCl<sub>3</sub>): 42.8 (t), 107.7 (s), 115.8 (s), 120.3 (d), 128.9 (d), 129.1 (d), 129.4 (s), 130.3 (d), 131.4 (d), 132.7 (s), 136.9 (d), 148.2 (s), 153.7 (s), 157.4 (s).

**Thermolysis of the compound (24a)**

Compound 24a (10 mmol) was heated above its melting point which resulted in vigorous formation of CO and CO<sub>2</sub>. When the evolution had ceased the remainder was distilled which gave 2-benzyl-4*H*-3,1-benzoxazinone (7) in almost quantitative yield. This sample was identical with authentic 7 prepared according to a literature procedure.<sup>10</sup>

**Synthesis of compound 24b**

The same procedure, using *N*-acetylanthranilic acid, as for 24a was used. Yield: 75%, m.p. ~180°C dec. IR: 1834, 1750, 1604, 1493, 1469, 1400, 1313, 1267, 1955, 964, 759 cm<sup>-1</sup>. <sup>1</sup>H NMR: 2.02 (q, 3H, CH<sub>3</sub>), 7.57 (dd, 1H, arom CH), 7.82 (d 1H, arom CH), 7.93 (dd, 1H, arom CH), 8.07 (d 1H, arom CH). <sup>13</sup>C NMR: 23.9 (q), 107.6 (s), 120.6 (d), 127.7 (d), 130.4 (d), 133.0 (s), 136.4 (d), 149.7 (s), 155.9 (s), 158.1 (s).

**2-Carboxoxyanilic acid 25**

Oxalyl chloride (4.4 ml, 50 mmol) was added to a stirred mixture of *N*-formylantranilic acid (3.10 g, 20 mmol) in acetonitrile (35 ml) at 40°C. A clear solution was quickly obtained. The expected product 24c could not be isolated. The solution was stored for 24h and the precipitate of 25 was collected. Yield 3.70 g (86%), m.p. 229-230°C (lit.<sup>50</sup> m.p. 229-230°C). IR: 3350-2700 (br), 1712, 1698, 1690, 1589, 1531, 1235, 1187, 755 cm<sup>-1</sup>.

**2-Carboxoxyanilic acid methyl ester**

**Method A.** The acid 25 (418 mg, 2 mmol) was treated with diazomethane as described by Späth<sup>50</sup>. Yield: 300 mg (64%), m.p. 151-151°C (lit.<sup>50</sup> m.p. 151.5°C).

**Method B.** Methyl oxalylchloride (6.1 g, 50 mmol) was added to a stirred solution of anthranilic acid (13.7 g, 0.1 mol) in dioxan (60 ml) at 30°C. After 1h water was added to the mixture and the quickly solidifying oil was collected and recrystallized from methanol. Yield: 8.5 g (67%), m.p. 150-151°C. IR: 3260, 1715, 1708, 1702, 1592, 1534, 1438, 1319, 1275, 1227, 1171, 1094, 984, 749 cm<sup>-1</sup>.

The materials prepared according to the two methods were identical.

**Synthesis of compound 26b**

The procedure given for 24a was used starting with methyl *N*-phenylacetylanthranilate. Yield: 88% of 26b as yellow crystals, m.p. 160-162°C. IR: 1824, 1746, 1714, 1681, 1491, 1433, 1406, 1274, 1192, 1169, 1120, 1086, 990, 746 cm<sup>-1</sup>. <sup>1</sup>H NMR (CDCl<sub>3</sub>): 3.82 (s, 3H, OCH<sub>3</sub>), 5.01 (s, 1H, olef. CH), 7.2-7.5 (m, 6H, arom. CH), 7.71 (t, 1H, arom. CH), 7.80 (t, 1H, arom. CH), 8.26 (d, 1H, arom. CH). <sup>13</sup>C NMR (CDCl<sub>3</sub>): 52.7 (q), 92.0 (d), 127.4 (s), 127.6 (d), 128.7 (d), 128.8 (d), 129.8 (d), 130.7 (s), 131.0 (d), 131.4 (s), 132.7 (d), 134.2 (d), 142.0 (s), 149.8 (s), 153.7 (s), 163.9 (s).

**Synthesis of compound 26c.**

This yellow crystalline ester was analogously prepared. Yield 79%, m.p. 155-157°C. IR: 1821, 1745, 1725, 1679, 1492, 1453, 1406, 1279, 1253, 1005, 754, 691 cm<sup>-1</sup>. <sup>1</sup>H NMR (CDCl<sub>3</sub>): 1.35 (t, 3H, CH<sub>3</sub>), 4.31 (q, 2H, OCH<sub>2</sub>), 5.02 (s, 1H, olef. CH), 7.2-7.5 (m, 6H, arom. CH), 7.68 (t, 1H, arom. CH), 7.78 (t, 1H, arom. CH), 8.26 (d, 1H, arom. CH). <sup>13</sup>C NMR (CDCl<sub>3</sub>): 13.8 (q), 61.8 (t), 91.9 (d), 127.5 (d), 127.9 (s), 128.6 (d), 128.7 (d), 129.6 (d), 130.4 (s), 130.9 (d), 131.4 (s), 132.7 (d), 134.0 (d), 141.9 (s), 149.7 (s), 153.7 (s), 163.5 (s).

**Synthesis of compound 29**

The oxazolidine-4,5-dione 26b (323 mg, 1mmol) was refluxed in methanol (4 ml) for ca 3 min (or until the originally yellow solution just had faded. Prolonged reflux results in deacylation reactions). The solution was allowed to cool and diluted with diisopropyl ether and the crystals formed were collected. Yield: 280 mg (79%); m.p. 156-157°C. IR: 2959 (w), 1749, 1724, 1697, 1432, 1337, 1273, 1221, 1186, 1130, 738, 718 cm<sup>-1</sup>. <sup>1</sup>H NMR: 3.55 (q, 2H, CH<sub>2</sub>, *J* = 22Hz), 3.77 (s, 3H, OCH<sub>3</sub>), 7.10 (m, 2H), 7.23 (m, 3H), 7.6-7.8 (m, 3H), 8.10 (m, 1H). <sup>13</sup>C NMR: 41.84 (t, CH<sub>2</sub>), 52.38 (q, OCH<sub>3</sub>), 52.60 (q, OCH<sub>3</sub>), 126.80 (d), 128.09 (d), 128.15 (s), 129.56 (d), 130.41 (d), 131.05 (d), 131.68 (d), 132.64 (s), 134.39 (d), 134.58 (s), 161.26 (s), 162.38 (s), 164.45 (s), 172.79 (s).

**Synthesis of the ethyl analogue of 29**

The experiment just described was repeated but with the oxazolidine-4,5-dione 26c and ethanol as reactants. Yield: 63%, m.p. 89-90°C. IR: 2985 (w), 1738, 1717, 1687, 1340, 1261, 1218, 1183, 1135, 1083, 723 cm<sup>-1</sup>. <sup>1</sup>H NMR(CDCl<sub>3</sub>): 1.32 (2q, 6H, CH<sub>3</sub>), 3.54 (q, 2H, CH<sub>2</sub>), 4.28 (q, 2H, OCH<sub>2</sub>), 4.36 (q, 2H, OCH<sub>2</sub>), 7.00 (m, 2H), 7.17 (d, 1H), 7.25 (m, 3H), 7.59 (m, 2H), 8.18 (d, 1H). <sup>13</sup>C NMR(CDCl<sub>3</sub>): 13.49 (q), 13.55 (q), 41.87 (t), 61.48 (t), 61.85 (t), 126.87 (d), 128.08 (d), 128.76 (s), 129.4 (d), 130.38 (d), 138.98 (d), 131.71 (d), 132.66 (s), 134.12 (d), 134.23 (s), 160.72 (s), 162.45 (s), 164.14 (s), 172.62 (s),

***N*-(2-Carbomethoxyphenyl)-3-hydroxy-4-phenylmaleinimide (30)**

**Method A** Sodium (0.69 g, 30 mmol) was dissolved in methanol (40 ml), whereupon methyl *N*-(phenylacetyl) anthranilate (8.07 g, 30 mmol) followed by dimethyl oxalate (3.24 g, 30 mmol) were added. The stirred mixture was then refluxed for 4h. The clear yellow solution obtained was evaporated and the residue dissolved in hot water (80 ml, and filtered if necessary). Acidification of the filtrate with hydrochloric acid gave the title compound. Yield: 7.0 g (76%), m.p. 220-222°C. IR: 3280, 1774 (w), 1720, 1704, 1669, 1495, 1382, 1327, 1272, 1084, 761, 756, 694 cm<sup>-1</sup>. <sup>1</sup>H NMR: 3.72 (s, 3H, OCH<sub>3</sub>), 7.32 (dd, 1H), 7.44 (m, 2H), 7.5-7.7 (m, 2H), 7.98 (m, 1H), 8.00 (dd, 3H). <sup>13</sup>C NMR: 52.39 (q), 106.26 (s), 127.50 (d), 127.83 (s), 128.30 (d), 128.82 (d),

129.41 (s), 130.58 (d), 130.64 (d), 130.86 (s), 133.24 (d), 153.71 (d), 165.13 (s), 165.48 (s), 169.93 (s).

**Method B.** The oxazolidine-4,5-dione **26b** (323 mg, 1mmol) was dissolved in methanol (10 ml) wherein a trace of sodium had been dissolved. The mixture was evaporated, dissolved in water and acidified. The yellow precipitate was collected. Yield: 305 mg (94%), m.p. 220-222°C.

This material was identical with that obtained by method A.

#### ***N*-(2-Carbomethoxyphenyl)-3-methoxy-4-phenylmaleinimide**

Compound **30** (323 mg, 1mmol) was added in portions to a stirred ether (30 ml) solution containing diazomethane (ca 1.2 mmol) at 20°C. When the acidic starting material had been consumed (ca 2h), the solution was evaporated and the residue crystallized from 2-propanol. Yield: 214 mg (63%), m.p. 80-81°C.

IR: 2947 (w), 1781 (w), 1719, 1711, 1632, 1495, 1455, 1397, 1356, 1270, 1133, 973, 756, 693 cm<sup>-1</sup>.

<sup>1</sup>H NMR: 3.75 (s, 3H, OCH<sub>3</sub>), 4.20 (s, 3H, OCH<sub>3</sub>), 7.4-7.6 (m, 4H), 7.62 (dd, 1H), 7.8 (m, 3H), 8.02 (d, 1H).

#### **Synthesis of the Phenylmalonamide **31****

2-Benzyl-4*H*-3,1-benzoxazin-4-one (2.37 g, 10 mmol) and *N,N*-dimethyldichloromethyleneiminium chloride (1.94 g, 12 mmol) was heated (60°, 1 min) in acetonitrile (15 ml). The cooled solution was poured into water, yielding an oil which soon solidified. Recrystallization from 2-propanol gave **31**, 2.60 g (79%) m.p. 219-22°C.

IR: 3436 (br), 3248, 2935 (br), 1687, 1600, 1518, 1446, 1226, 751 cm<sup>-1</sup>. <sup>1</sup>H NMR: 2.86 (s, 3H, NCH<sub>3</sub>), 2.95 (s, 3H, NCH<sub>3</sub>), 5.29 (s, 1H, CH), 7.10 (t, 1H, arom CH), 7.91 (d, 1H, arom CH), 8.51 (d 1H, arom CH),

11.2 (s, 1H, NH), 13.3 (bs, 1H, COOH). <sup>13</sup>C NMR: 35.2 (q, NCH<sub>3</sub>), 37.1 (q, NCH<sub>3</sub>), 57.4 (d), 116.4 (s), 119.8 (d), 122.7 (d), 127.7 (d), 128.6 (d), 129.1 (d), 130.9 (d), 133.9 (d), 134.0 (s), 140.5 (s), 167.5 (s), 168.2 (s), 168.9 (s).

#### ***α*-(*N,N*-Dimethylcarboxamido)-2-benzyl-4*H*-3,1-benzoxazine-4-one (**32**)**

The phenylmalonoamide **31** (0.652 g, 2 mmol) was refluxed in acetic anhydride (5 ml) for 5 min. The clear solution obtained was concentrated and diluted with diisopropyl ether. The crystals of **32** obtained were collected, 0.455 g, (67%), m.p. 175-176°C. IR: 1749 (s), 1655 (s), 1606, 1474, 1398, 1138, 1015, 779 cm<sup>-1</sup>.

Collection and refinement of X-ray diffraction data.

An Enraf-Nonius CAD4 diffractometer equipped with MoK $\alpha$  radiation was used for the data collections. For both compounds two standard reflections measured every hour did not show any significant variations. The structures were solved by direct methods and refined by full-matrix least-squares without absorption correction. Atomic coordinates, thermal parameters, molecular geometries and structure factors have been deposited with the Cambridge Crystallographic Data Centre. Some data of the specimens and refinements are given below.

**Compound 6a.** A yellow crystal of dimensions 0.10x0.20x0.40 mm obtained by recrystallization from acetonitrile was used for the data collection. Of the measured 2938 independent reflections, 1281 with  $I > 3\sigma(I)$  were used in the refinements and gave  $R=0.035$  and  $R_w=0.044$  with 230 parameters.

A perspective view of molecule **6a** is shown in Fig.1 and selected distances and angles in Table 1. The benzoxazine part of the molecule is planar within 0.05 Å and form an angle of 74.3° with the best plane through the phenyl ring.

**Table 1.** Selected bond lengths(Å) and angles(°) for **6a**.

O(1)-C(1)	1.393(3)	C(1)-O(1)-C(2)	122.2(2)
O(1)-C(2)	1.378(3)	C(1)-N(1)-C(8)	118.4(2)
O(2)-C(2)	1.202(4)	O(1)-C(1)-N(1)	122.8(2)
N(1)-C(1)	1.288(3)	O(1)-C(1)-C(9)	113.3(2)
N(1)-C(8)	1.389(3)	N(1)-C(1)-C(9)	123.9(2)
N(2)-C(16)	1.335(4)	O(1)-C(2)-O(2)	116.9(3)
N(2)-C(17)	1.448(5)	O(1)-C(2)-C(3)	115.3(2)
N(2)-C(18)	1.456(5)	O(2)-C(2)-C(3)	127.9(3)
C(1)-C(9)	1.432(4)	C(2)-C(3)-C(8)	118.9(2)
C(2)-C(3)	1.442(4)	C(3)-C(8)-N(1)	122.1(2)
C(3)-C(8)	1.392(4)	C(1)-C(9)-C(10)	115.6(2)
C(9)-C(10)	1.498(4)	C(1)-C(9)-C(16)	119.3(2)
C(9)-C(16)	1.365(4)	C(10)-C(9)-C(16)	125.1(2)

C<sub>18</sub>H<sub>16</sub>O<sub>2</sub>N<sub>2</sub>, M= 292.34 , space group P2<sub>1</sub>/c, a= 11.315(5), b= 16.602(4), c= 8.291(3) Å,  $\beta= 104.19(3)^\circ$ , V= 1509.9(6) Å<sup>3</sup>, Z=4, D<sub>c</sub>= 1.286 gcm<sup>-3</sup>,  $2\theta_{\max}=52^\circ$ , T= 295 K.

**Compound 24a.** Crystal dimensions 0.20x0.25x0.55 mm. Of the 2701 independent reflections, 1851 with  $I > 3\sigma(I)$  were used in the refinements, which gave  $R=0.032$  and  $R_w=0.045$  with 253 parameters.

$C_{17}H_{11}O_5N$ ,  $M=309.28$ , space group  $P2_1/a$ ,  $a=13.720(2)$ ,  $b=7.693(1)$ ,  $c=14.474(4)$  Å,  $\beta=111.12(2)^\circ$ ,  $V=1425.2(6)$  Å<sup>3</sup>,  $Z=4$ ,  $D_c=1.441$  gcm<sup>-3</sup>,  $2\theta_{max}=50^\circ$ ,  $T=295$  K.

A perspective view of molecule **24a** is shown in Fig.2. Selected distances and angles are given in Table 2 and angles between best planes through parts of the molecule in Table 3.

**Table 2.** Selected bond lengths(Å) and angles( $^\circ$ ) for **24a**.

O(1)-C(1)	1.414(2)	C(1)-O(1)-C(2)	119.9(1)
O(1)-C(2)	1.372(2)	C(1)-O(2)-C(10)	110.5(1)
O(3)-C(1)	1.424(2)	C(1)-N-C(8)	117.5(1)
O(3)-C(10)	1.355(2)	C(1)-N-C(9)	112.5(1)
O(2)-C(2)	1.197(2)	C(8)-N-C(9)	128.7(1)
O(4)-C(9)	1.201(2)	O(1)-C(1)-O(3)	106.5(1)
O(5)-C(10)	1.191(2)	O(1)-C(1)-N	111.1(1)
N-C(1)	1.442(2)	O(1)-C(1)-C(11)	109.6(1)
N-C(8)	1.411(2)	O(2)-C(1)-N	104.6(1)
N-C(9)	1.359(2)	O(2)-C(1)-C(11)	109.7(1)
C(1)-C(11)	1.518(2)	N-C(1)-C(11)	114.9(1)
C(2)-C(3)	1.476(2)	O(1)-C(2)-O(3)	116.7(1)
C(3)-C(8)	1.388(2)	O(1)-C(2)-C(3)	117.3(1)
C(9)-C(10)	1.514(3)	O(3)-C(2)-C(3)	126.0(2)
C(11)-C(12)	1.502(2)	C(2)-C(3)-C(8)	120.2(1)
		N-C(8)-C(3)	116.3(1)
		O(4)-C(9)-N	128.9(2)
		O(4)-C(9)-C(10)	127.0(2)
		N-C(9)-C(10)	104.1(1)
		O(3)-C(10)-O(5)	123.3(2)
		O(3)-C(10)-C(9)	108.1(1)
		O(5)-C(10)-C(9)	128.6(2)
		C(1)-C(11)-C(12)	113.3(1)

**Table 3.** Least-squares planes in **24a**.

Plane	Atoms defining the plane	Largest deviation(Å)	Dihedral angle( $^\circ$ )
A	C(3)-C(8)	0.005	
B	C(2),C(3),C(8),N	0.011	B-A 2.8
C	C(1),N,C(9),C(10),O(3)	0.032	C-A 35.5
D	C(12)-C(17)	0.010	D-A 24.9
			D-C 60.4

The atoms O(1) and C(1) deviate 0.21 and 0.65 Å from plane B.



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7. Thus the IR of e.g. 2,5-*H*-7,8-dimethyl-3-hydroxybenz[*f*]azepine-2,5-dione features<sup>8</sup> carbonyl absorption at 1660 cm<sup>-1</sup> and 2,5-*H*-3-amino-4-methylbenz[*f*]azepine-2,5-dione at 1680 cm<sup>-1</sup>.
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