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Highly substituted, novel, 1,3-dihydro-5-phenyl-2*H*-1,4-benzodiazepin-2-ones were obtained by direct nitration of the corresponding mono- or di-substituted 5-phenyl-1,4-benzodiazepines. Substituent effects and the orientation of aromatic substituents in the nitration products are discussed. The single-crystal X-ray structural data for one of these products, **18**, is given.

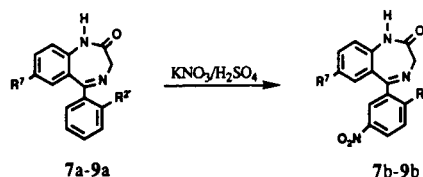
J. Heterocyclic Chem., **28**, 1203 (1991).

The use of variously substituted 2-aminobenzophenones as starting materials in the synthesis of a large variety of heterocyclic ring systems, has been extensively reported by us, in this and in other research journals. For example, the synthesis of 1,4-benzodiazepines and their related rearrangement products, carbostyrils, quinazolines, triazolo-benzodiazepines, triazoloquinolines, triazoloindoles, quinolines, benzopyranoquinolines, indazoles *etc.*, have all utilized these aminoketones as common intermediates [1]. Aromatic ring substituents were generally incorporated prior to the synthesis of the desired heterocycle, and when this was not feasible, direct halogenation [2] or nitration [3] could be carried out on a 1,4-benzodiazepin-2-one. Subsequent hydrolysis of both lactam and imine bonds would then afford highly substituted *o*-aminobenzophenones.

In connection with the synthesis of imidazobenzodiazepine haptens, we required as intermediates, the novel nitro substituted compounds derived from the *para* substituted-5-phenyl-1,4-benzodiazepines shown in Schemes 3 and 4. It has previously been reported that the nitration of

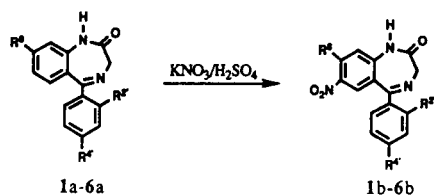
5-phenyl-substituted-1,3-dihydro-2*H*-1,4-benzodiazepin-2-ones with potassium nitrate in cold concentrated sulfuric acid led to 7-nitro-derivatives [4] (Table 1) and that, under the same conditions, 7-substituted-1,3-dihydro-5-phenyl-2*H*-1,4-benzodiazepin-2-one compounds were nitrated in the *meta* position of the 5-phenyl ring [5] (Table 2). It was also reported that reduction of the imine double bond

Table 2. Nitration Products at 5'-Position.



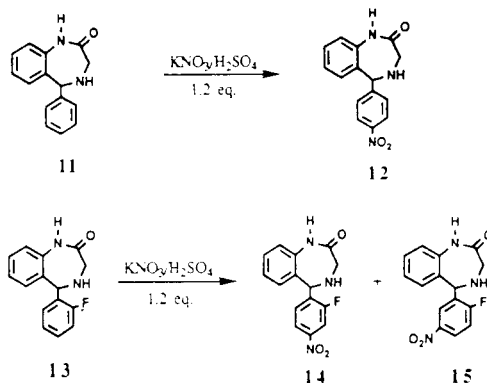
| Compound | R ⁷ | R ^{2'} |
|----------|-----------------|-----------------|
| 7 | NO ₂ | H |
| 8 | NO ₂ | F |
| 9 | Cl | H |

Table 1. Nitration Products at 7-Position.



| Compound | R ⁸ | R ^{2'} | R ^{4'} |
|----------|-----------------|-----------------|-----------------|
| 1 | H | NO ₂ | H |
| 2 | H | H | H |
| 3 | H | F | H |
| 4 | H | H | Cl |
| 5 | CH ₃ | H | H |
| 6 | H | Cl | H |

Scheme 1



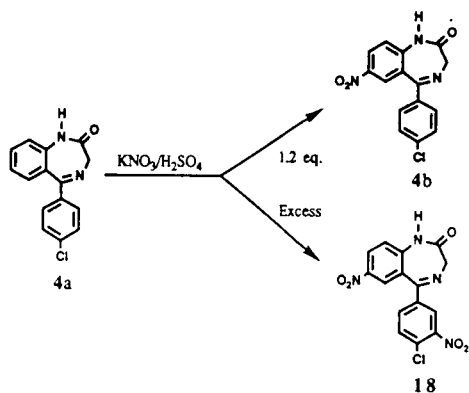
gave the corresponding tetrahydro compounds, in which the 5-phenyl ring had become more activated than the fused benzene ring. Therefore, nitration of 5-phenyl-1,3,4,5-tetrahydro-2*H*-1,4-benzodiazepin-2-ones gave 5-(*para*-nitrophenyl), **12** and **14**, and/or 5-(*meta*-nitrophenyl) **15** derivatives as products, depending upon the *ortho* substituent on the 5-phenyl ring [6] (Scheme 1). It was also noted that further nitration of compound **16** containing the deactivated 5-(3-nitrophenyl) substituent afforded the 9-nitro substituted derivative **17** [5] (Scheme 2).

Scheme 2



We have now shown that either mono- or dinitro-compounds can be obtained from the corresponding 5-(4-chlorophenyl)-1,3-dihydro-2*H*-1,4-benzodiazepin-2-one by controlling the ratio of molar equivalents of potassium nitrate used in the reaction (Scheme 3). Nitration occurred at the

Scheme 3



7-position since the acylamino aromatic substituent is moderately ring activating, whereas the chlorine substituent is weakly deactivating. By using an excess of nitrating agent, the dinitro derivative compound **18** was obtained. The X-ray structure of **18** is shown in Figure 1. In the crystal, the nitro group *ortho* to the halogen is disordered. The major rotamer (75%) is shown in Figure 1, the minor rotamer (25%) is not shown.

Under the same conditions, using 1.2 equivalents of nitrating agent, the 5-(4-methoxyphenyl) analog **19** (Scheme 4), gave a product which seemed to be a single component by thin layer chromatography (tlc) in three different solvent systems and by gas chromatography-mass spectroscopy (gc-ms), with a retention time 9.54 minutes (883 scans) and molecular mass of 311 (no starting mater-

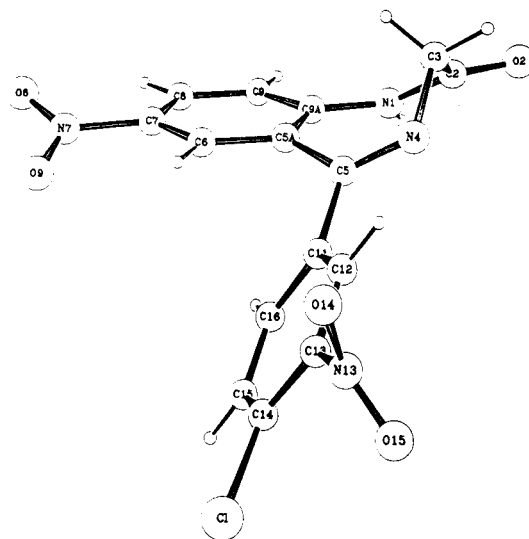
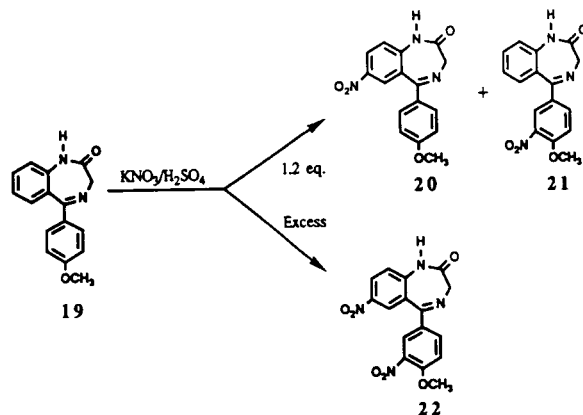


Figure 1. A perspective drawing of compound **18** (major rotamer).

ial **19**, retention time 8.08 minutes at 761 scans, was identified in gc-ms). This indicated that the single component could be either of the mononitro substituted derivatives **20** or **21**. However, after several recrystallizations from ethanol, the melting point range of about 14° could not be

Scheme 4



improved (mp 206-220°), suggesting that the nicely crystalline, pale yellow product, was probably not a single component. Since attempts at running gc-ms of the dinitro derivative **22** (see below) were not successful (**22** was not eluted from the gc column), we examined its mp and mixture mp properties. The mp of **22** was 262-264° and its mixture melting point with mono nitrated material was 186-198°, indicating that the dinitrated product was probably not a contaminant of the mono nitrated product.

An examination of the nmr spectrum for the mono-nitration product, showed a mixture of two compounds, present in a ratio of about 1 to 1.8 (based on integration). Chemical shifts of aromatic protons from the mixture are be-

Table 3
Melting Points and ¹H-NMR Data of Substituted 1,3-Dihydro-5-phenyl-2H-1,4-benzodiazepin-2-ones

| Compound | Mp (°C) | Amide NH (δ) | Aromatic H (δ) | Other H (δ) |
|-----------|---------|-----------------------------|--|--|
| 4a | 259-260 | 10.55 (s, 1H, exchangeable) | 7.1-7.3 (m 1H), 7.45-7.65 (m, 5H) | 4.1 (br s, 2H, CH ₂) |
| 4b | 250-251 | 11.18 (s, 1H, exchangeable) | 7.45 (d, J = 9.0 Hz, 1H), 7.5-7.6 (m, 4H), 8.02 (d, J = 2.6 Hz, 1H), 8.5 (dd, J = 2.6, 9.0 Hz, 1H) | 4.25 (br s, 2H, CH ₂) |
| 18 | 227-228 | 11.22 (s, 1H, exchangeable) | 7.45 (d, J = 9.0 Hz, 1H), 7.75-7.9 (m, 2H), 8.15 (d, J = 1.5 Hz, 1H), 8.2 (d, J = 1.5 Hz, 1H), 8.45 (dd, J = 2.7, 9.0 Hz, 1H) | 4.3 (br s, 2H, CH ₂) |
| 19 | 254-256 | 10.48 (s, 1H, exchangeable) | 6.95 (d, J = 8.8 Hz, 2H), 7.1-7.3 (m, 3H), 7.45 (d, J = 8.87 Hz, 2H), 7.5-7.6 (m, 1H) | 3.8 (s, 3H, OCH ₃), 4.05 (br s, 2H, CH ₂) |
| 22 | 262-264 | 11.15 (s, 1H, exchangeable) | 7.4 (d, J = 9.9 Hz, 1H), 7.45 (d, J = 9.3 Hz, 1H), 7.78 (dd, J = 2.2, 9.0 Hz, 1H), 8.05 (d, J = 2.2 Hz, 1H), 8.1 (d, J = 2.6 Hz, 1H), 8.45 (dd, J = 2.6, 9.0 Hz, 1H) | 3.95 (s, 3H, OCH ₃), 4.25 (br s, 2H, CH ₂) |
| 23 | 210-212 | 10.61 (s, 1H, exchangeable) | 6.97 (dd, J = 2.6, 8.8 Hz, 2H), 7.21 (d, J = 2.2 Hz, 1H), 7.25 (d, J = 8.6 Hz, 1H), 7.4 (dd, J = 2.6, 8.8 Hz, 2H), 7.65 (dd, J = 2.5, 8.8 Hz, 1H) | 3.8 (s, 3H, OCH ₃), 4.1 (br s, 2H, CH ₂) |
| 24 | 226-228 | 10.68 (s, 1H, exchangeable) | 7.3 (d, J = 8.8 Hz, 1H), 7.35 (d, J = 2.4 Hz, 1H), 7.45 (d, J = 8.9 Hz, 1H), 7.65 (dd, J = 2.4, 8.6 Hz, 1H), 7.75 (dd, J = 2.2, 8.8 Hz, 1H) | 4.0 (s, 3H, OCH ₃), 4.15 (br s, 2H, CH ₂) |

tween 7.15-8.48 ppm which are about 0.2 ppm downfield from those of starting material **19**. The chemical shift of one of the amide protons is at 10.58 ppm (relative 1.8 protons) and the other at 11.18 ppm (relative 1 proton), and both being different (0.1 ppm and 0.7 ppm downfield) from the starting material. These downfield shifts could be caused by the electron withdrawing nitro group, since a similar effect was also observed in the other nitration products, such as **4b**, **18** and **22** (see Table 3). The amide proton at 11.18 ppm can probably be assigned to the 7-nitro compound **20**, since the nitro group is on the same ring as the amide group and therefore, would have a more direct conjugative effect, whereas the other amide proton at 10.58 ppm can probably be assigned to the 3'-nitrated compound **21**, because the nitro group is on the ring different from that of the amide group, so that only a very weak downfield shift is observed. The dinitro substituted compound **22** was obtained exclusively by using an excess of nitrating agent in the reactions (Scheme 4). The Distortionless Enhancement by Polarisation Transfer (DEPT) experiment carried out on the fully proton-decoupled ¹³C nmr spectrum of **22** showed eight different types of peaks for the quaternary carbons, indicating that two hydrogen atoms attached to the ring carbons have been substituted. The spectrum only displayed 7 peaks representing the remaining 8 carbons (6 methine, 1 methylene and 1 methyl carbons) since the methyl and methylene carbons overlapped at 57 ppm. This was demonstrated by the proton-coupled ¹³C nmr spectrum which showed a triplet (methylene carbon, J = 143.14 Hz) and a quartet (methyl carbon, J = 147.41 Hz) with the same center. By blocking the 7-position of the benzodiazepine with a chlorine substituent, **23**, we were able to prepare the mono-nitro derivative **24**, required for our other work. This was done by treating **23**

with a controlled amount of nitrating agent. With this compound in hand, and since we were unable to effect a separation of the two components **20** and **21**, we did not pursue the characterization of these compounds any further.

The orientation of the entering 7-nitro group in the nitration of **4a** appears to follow the usual substituent effects for electrophilic aromatic substitution. The *ortho/para* directing activating effect (*para* > *ortho*) of the acylamino group is well known and the formation of 7-nitro derivatives is readily rationalized on this basis [4]. In addition, by introducing a chlorine group at the 7-position (*para*), the 9-position (*ortho*) nitrated compound **17** was obtained [6]. The formation of the dinitro compound **18** under the condition of excess nitrating agent is not unexpected since chlorine is a stronger *ortho/para* directing group than a benzylimine, although it is a weakly deactivating group as discussed above. When the 4'-chloro substituent on the 5-phenyl ring is replaced by a methoxy group (substituent effect comparable to that of acylamino), nitration, using a controlled amount of potassium nitrate, affords a mixture, believed to consist of the 7-nitro and 3'-nitro derivatives. Under conditions in which an excess of nitrating agent was used, only the dinitro compound **22** was obtained. In the case of compound **23** (7-position blocked), electrophilic substitution only occurred, as expected, at the 3'-position, to afford compound **24**. No 9-nitrated compound was observed (*c.f.* **17**, Scheme 2) under controlled condition of nitrating agent, since the electron releasing methoxy group is more strongly activating than chlorine.

The novel nitration products of substituted 5-phenyl-1,3-dihydro-2H-1,4-benzodiazepin-2-ones were obtained by direct electrophilic substitution of the aromatic rings. The orientation of the entering nitro groups is strongly in-

Table 4
Final Atomic Parameters for Compound 18

| Atom | x | y | z | B(A ²) |
|------|------------|------------|------------|--------------------|
| C1 | 0.5839(2) | 0.24145(9) | 0.35606(5) | 8.23(3) |
| O2 | -0.0854(4) | 0.3654(2) | 0.0314(1) | 7.36(9) |
| O8 | 0.8176(4) | 0.5823(2) | 0.0720(1) | 7.22(8) |
| O9 | 0.8292(3) | 0.4852(2) | 0.1366(1) | 6.33(8) |
| O14 | 0.5558(6) | 0.0648(3) | 0.2355(3) | 9.6(2) |
| O15 | 0.3957(8) | 0.0843(2) | 0.3074(2) | 10.2(2) |
| N1 | 0.1197(4) | 0.4455(2) | 0.0617(1) | 4.89(8) |
| N4 | 0.2135(4) | 0.2746(2) | 0.1056(1) | 4.46(7) |
| N7 | 0.7587(4) | 0.5248(2) | 0.0999(1) | 4.89(8) |
| N13 | 0.4706(5) | 0.1103(2) | 0.2687(2) | 7.2(1) |
| C2 | 0.0531(5) | 0.3692(3) | 0.0460(2) | 5.2(1) |
| C3 | 0.1629(5) | 0.2929(3) | 0.0480(2) | 4.9(1) |
| C5 | 0.3154(4) | 0.3249(2) | 0.1276(2) | 3.75(8) |
| C5A | 0.3771(4) | 0.4040(2) | 0.1009(1) | 3.48(8) |
| C6 | 0.5366(4) | 0.4264(2) | 0.1090(2) | 3.59(8) |
| C7 | 0.5913(5) | 0.5033(2) | 0.0895(1) | 3.80(8) |
| C8 | 0.4957(5) | 0.5621(2) | 0.0620(2) | 4.33(9) |
| C9 | 0.3395(5) | 0.5414(2) | 0.038(2) | 4.48(9) |
| C9A | 0.2801(5) | 0.4618(2) | 0.0718(1) | 3.70(8) |
| C11 | 0.3761(5) | 0.3045(2) | 0.1851(2) | 3.68(8) |
| C12 | 0.3949(5) | 0.2197(2) | 0.2009(2) | 4.32(9) |
| C13 | 0.4545(5) | 0.2013(2) | 0.2535(2) | 4.77(9) |
| C14 | 0.4993(6) | 0.2641(3) | 0.2916(2) | 5.1(1) |
| C15 | 0.4776(6) | 0.3488(2) | 0.2764(2) | 5.1(1) |
| C16 | 0.4162(5) | 0.3678(2) | 0.2236(2) | 4.46(9) |
| O14B | 0.582(2) | 0.0858(7) | 0.2909(5) | 6.4(3)* |
| O15B | 0.342(2) | 0.0776(9) | 0.2772(6) | 8.3(4)* |
| HN1 | 0.049 | 0.492 | 0.066 | 5.6 |
| H3A | 0.106 | 0.242 | 0.032 | 5.7 |
| H3B | 0.259 | 0.305 | 0.024 | 5.7 |
| H6 | 0.610 | 0.386 | 0.129 | 4.2 |
| H8 | 0.540 | 0.618 | 0.048 | 5.0 |
| H9 | 0.267 | 0.583 | 0.035 | 5.2 |
| H12 | 0.366 | 0.172 | 0.174 | 5.1 |
| H15 | 0.504 | 0.395 | 0.304 | 6.0 |
| H16 | 0.401 | 0.429 | 0.213 | 5.2 |

The starred atoms were refined isotropically. The parameters of the hydrogen atoms were not refined. Standard deviations are in parentheses. Anisotropically refined atoms are given in the form of the isotropic equivalent displacement parameter defined as: $(4/3) * [a^2*B(1,1) + b^2*B(2,2) + c^2*B(3,3) + ab(\cos \gamma)*B(1,2) + ac(\cos \beta)*B(1,3) + bc(\cos \alpha)*B(2,3)]$

fluenced by substituent effects. The yields of products, while not optimized, ranged from acceptable to very high and therefore, these compounds can serve as synthons, either for developing novel benzodiazepines, or after hydrolysis under acidic conditions [6], to provide nitro substituted 2-aminobenzophenones, difficult to make by other reported methods [7,8].

EXPERIMENTAL

Intensity data used for the structure determination of **18**, were measured on an Enraf-Nonius CAD4 diffractometer (graphite-monochromated Cu K α radiation, ω - 2θ scans). The data were corrected for absorption. Of the 2813 independent reflections for $\theta < 75^\circ$, 1606 were considered observed [$I > 3.0\sigma(I)$].

Table 5
Final Anisotropic Thermal Parameters (U's) for Compound 18

| Atom | U(1,1) | U(2,2) | U(3,3) | U(1,2) | U(1,3) | U(2,3) |
|------|----------|-----------|-----------|------------|------------|-----------|
| C1 | 0.141(1) | 0.0910(8) | 0.0803(6) | -0.0178(9) | -0.0448(7) | 0.0287(6) |
| O2 | 0.045(2) | 0.122(2) | 0.113(2) | -0.009(2) | -0.026(2) | 0.008(2) |
| O8 | 0.079(2) | 0.094(2) | 0.101(2) | -0.034(2) | 0.018(2) | 0.009(2) |
| O9 | 0.054(2) | 0.092(2) | 0.094(2) | -0.011(2) | -0.013(2) | -0.005(2) |
| O14 | 0.103(4) | 0.047(2) | 0.217(6) | 0.017(3) | 0.010(4) | 0.005(3) |
| O15 | 0.264(6) | 0.057(2) | 0.068(2) | -0.022(4) | -0.004(4) | 0.025(2) |
| N1 | 0.041(2) | 0.070(2) | 0.075(2) | 0.013(2) | -0.008(2) | -0.001(2) |
| N4 | 0.056(2) | 0.055(2) | 0.059(2) | -0.006(2) | -0.006(2) | 0.003(1) |
| N7 | 0.056(2) | 0.062(2) | 0.068(2) | -0.016(2) | 0.013(2) | -0.012(2) |
| N13 | 0.104(3) | 0.052(2) | 0.118(3) | -0.012(2) | -0.039(2) | 0.029(2) |
| C2 | 0.048(3) | 0.086(3) | 0.062(2) | 0.004(2) | -0.005(2) | 0.006(2) |
| C3 | 0.057(3) | 0.052(2) | 0.067(2) | -0.011(2) | -0.009(2) | -0.003(2) |
| C5 | 0.042(2) | 0.043(2) | 0.057(2) | 0.000(2) | -0.002(2) | 0.005(2) |
| C5A | 0.039(2) | 0.046(2) | 0.048(2) | 0.003(2) | -0.002(2) | 0.001(2) |
| C6 | 0.042(2) | 0.043(2) | 0.052(2) | 0.002(2) | 0.002(2) | -0.001(2) |
| C7 | 0.048(2) | 0.048(2) | 0.048(2) | -0.006(2) | 0.007(2) | -0.005(2) |
| C8 | 0.069(3) | 0.049(2) | 0.047(2) | -0.005(2) | 0.005(2) | 0.003(2) |
| C9 | 0.076(3) | 0.047(2) | 0.048(2) | 0.013(2) | -0.001(2) | 0.006(2) |
| C9A | 0.044(2) | 0.050(2) | 0.046(2) | 0.006(2) | -0.002(2) | 0.002(2) |
| C11 | 0.047(2) | 0.040(2) | 0.053(2) | -0.001(2) | -0.002(2) | 0.005(2) |
| C12 | 0.056(3) | 0.040(2) | 0.068(2) | -0.003(2) | -0.009(2) | 0.004(2) |
| C13 | 0.066(3) | 0.039(2) | 0.077(2) | -0.044(2) | -0.012(2) | 0.014(2) |
| C14 | 0.074(3) | 0.062(2) | 0.059(2) | -0.002(2) | -0.007(2) | 0.015(2) |
| C15 | 0.087(3) | 0.050(2) | 0.058(2) | -0.006(2) | -0.007(2) | 0.001(2) |
| C16 | 0.070(3) | 0.042(2) | 0.057(2) | 0.004(2) | 0.002(2) | 0.006(2) |

The form of the anisotropic displacement parameter is: $\exp[-2P\{h^2a^2U(1,1) + k^2b^2U(2,2) + l^2c^2U(3,3) + 2hkabU(1,2) + 2hlacU(1,3) + 2klbcU(2,3)\}]$ where a, b, and c are reciprocal lattice constants.

Table 6
Bond Distances (Å) for compound 18

| Atom 1 | Atom 2 | Distance | Atom 1 | Atom 2 | Distance |
|--------|--------|----------|--------|--------|----------|
| C1 | C14 | 1.716(4) | C5A | C6 | 1.399(5) |
| O2 | C2 | 1.216(5) | C5A | C9A | 1.399(5) |
| O8 | N7 | 1.220(4) | C6 | C7 | 1.369(5) |
| O9 | N7 | 1.220(4) | C7 | C8 | 1.383(5) |
| O14 | N13 | 1.278(6) | C8 | C9 | 1.366(6) |
| O15 | N13 | 1.183(6) | C9 | C9A | 1.408(5) |
| N1 | C2 | 1.369(5) | C11 | C12 | 1.388(5) |
| N1 | C9A | 1.393(5) | C11 | C16 | 1.387(5) |
| N4 | C3 | 1.455(5) | C12 | C13 | 1.371(6) |
| N4 | C5 | 1.275(5) | C13 | C14 | 1.385(6) |
| N7 | C7 | 1.469(5) | C14 | C15 | 1.386(5) |
| N13 | C13 | 1.474(5) | C15 | C16 | 1.380(5) |
| C2 | C3 | 1.510(6) | | | |
| C5 | C5A | 1.483(5) | O14B | N13 | 1.14(1) |
| C5 | C11 | 1.485(5) | O15B | N13 | 1.21(1) |

The structure was solved by a multiple-solution procedure [10] and was refined by full-matrix least squares. Eleven reflections, which were strongly affected by extinction, were excluded from the final refinement and difference map. In the final refinement, the nonhydrogen atoms were refined anisotropically, except for the oxygens of the minor rotamer (O14B and O15B), which were refined isotropically as quarter atoms. The hydrogen atoms were

Table 7
Bond Angles (°) for compound **18**

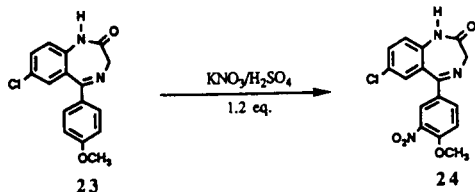
| Atom 1 | Atom 2 | Atom 3 | Angle | Atom 1 | Atom 2 | Atom 3 | Angle |
|--------|--------|--------|----------|--------|--------|--------|----------|
| C2 | N1 | C9A | 127.1(3) | C7 | C8 | C9 | 117.9(3) |
| C3 | N4 | C5 | 117.1(3) | C8 | C9 | C9A | 120.5(3) |
| O8 | N7 | O9 | 124.2(3) | N1 | C9A | C5A | 122.0(3) |
| O8 | N7 | C7 | 117.9(3) | N1 | C9A | C9 | 117.0(3) |
| O9 | N7 | C7 | 117.9(3) | C5A | C9A | C9 | 120.9(3) |
| O14 | N13 | O15 | 125.4(4) | C5 | C11 | C12 | 119.4(3) |
| O14 | N13 | C13 | 116.2(4) | C5 | C11 | C16 | 122.0(3) |
| O15 | N13 | C13 | 118.1(4) | C11 | C11 | C16 | 118.6(3) |
| O2 | C2 | N1 | 120.8(4) | C11 | C12 | C13 | 119.1(3) |
| O2 | C2 | C3 | 123.7(4) | N13 | C13 | C12 | 117.2(3) |
| N1 | C2 | C3 | 115.5(3) | N13 | C13 | C14 | 120.2(4) |
| N4 | C3 | C2 | 111.3(3) | C12 | C13 | C14 | 122.6(3) |
| N4 | C5 | C5A | 125.3(3) | C1 | C14 | C13 | 122.8(3) |
| N4 | C5 | C11 | 118.1(3) | C1 | C14 | C15 | 118.9(3) |
| C5A | C5 | C11 | 116.6(3) | C13 | C14 | C15 | 118.3(4) |
| C5 | C5A | C6 | 119.1(3) | C14 | C15 | C16 | 119.3(3) |
| C5 | C5A | C9 | 123.0(3) | C11 | C16 | C15 | 122.0(3) |
| C6 | C5A | C9A | 117.7(3) | | | | |
| C5A | C6 | C7 | 119.7(3) | O14B | N13 | O15B | 121.0(9) |
| N7 | C7 | C6 | 117.9(3) | O14B | N13 | C13 | 120.8(7) |
| N7 | C7 | C8 | 118.9(3) | O15B | N13 | C13 | 111.5(7) |
| C6 | C7 | C8 | 123.2(4) | | | | |

Standard deviations are in parentheses.

included in the structure-factor calculations but their parameters were not refined. The final discrepancy indices are $R = 0.053$ and $wR = 0.061$ for the 1595 observed reflections. The major peaks ($<0.2 \text{ e } \text{Å}^{-3}$) of the final difference map are near the chlorine atom.

Melting points were determined with a Mel-Temp apparatus and are uncorrected. Infrared spectra were obtained using a Nicolet 2DX FT-IR Spectrometer. Mass spectra were recorded on a Hewlett Packard HP5890 gas chromatography-Finnigan Mat INCOS 50 mass spectrometer (70 eV). ^1H nmr and ^{13}C nmr spectra were taken on a Bruker WP-200SY and Varian 400 Fourier transform spectrometers respectively. Dimethyl- d_6 sulfoxide was used as solvent and spectra were recorded in parts per million (ppm) on the δ scale from tetramethylsilane (TMS) or DMSO- d_6 . Commercially available solvents and reagents were used as received, unless specified otherwise. Compounds **4b**, **19** and **23** were synthesized according to the published procedures [4,8,9]. ^1H nmr data for these compounds, previously unreported, are given in Table 3.

Scheme 5



Nitration of 5-Phenyl-1,4-benzodiazepin-2-ones. General Procedure.

Method A. For Compounds **4b**, **20**, **21** and **24**.

A solution of potassium nitrate (0.48 g, 4.8 mmoles) in 3 ml of concentrated sulfuric acid was added dropwise to a solution of the 5-phenyl-2H-1,4-benzodiazepin-2-one (4 mmoles) in 5 ml of concentrated sulfuric acid. The mixture was stirred for approximately 4 hours at room temperature and poured over ice. After neutralizing with ammonium hydroxide the precipitate was filtered, washed thoroughly with water and then dissolved in methylene chloride. Any insoluble material was removed by filtration, and the filtrates were combined, dried over magnesium sulfate, filtered and concentrated on rotary evaporator to afford an oil-like residue, which was dissolved in the appropriate solvent and allowed to crystallize.

Method B. For Compounds **18** and **22**.

Same as for method A, except that an excess of nitrating agent was used (more than two equivalents).

7-Nitro-1,3-dihydro-5-(3-nitro-4-chlorophenyl)-2H-1,4-benzodiazepin-2-one (**18**).

Compound **18** was purified by silica gel (230-400 mesh, grade 60, From Aldrich) chromatography, and was eluted with a mixture of methylene chloride, ethyl acetate and methanol (4:4:0.5, v:v:v) and was crystallized from ethyl acetate and methanol in 42% yield, mp 227-228°; X-ray crystal data: $a = 8.409(5)$, $b = 15.651(3)$, $c = 23.611(7) \text{ Å}$, $Z = 8$, $d_{\text{calc}} = 1.542 \text{ g cm}^{-3}$, μ (Cu $K\alpha$) = 25.3 cm^{-1} , space group Pcab. Crystal size was approximately $0.08 \times 0.11 \times 0.54 \text{ mm}$. The final parameters, the thermal factors, bond distances and bond angles are given in Tables 4-7 respectively; ir (potassium bromide): $\nu = 3323, 3097, 2964, 1700, 1603, 1532, 1485, 1337 \text{ cm}^{-1}$; ms: (70 eV) 362 (12), 361 (21), 360 (M^+ , 38), 359 (45), 343 (19), 335 (23), 334 (41), 333 (78), 332 (100), 331 (44), 330 (17), 315 (25), 314 (22), 313 (60), 287 (24), 286 (29),

285 (62), 283 (18), 269 (19), 268 (19), 267 (25), 255 (15), 242 (19), 241 (25), 240 (28), 239 (45), 220 (12), 205 (20), 204 (30), 203 (23), 192 (20), 178 (23), 177 (44), 176 (24), 164 (20), 151 (25), 150 (30), 149 (20), 102 (18), 89 (20), 77 (30), 76 (21), 75 (40), 63 (26), 51 (22).

Anal. Calcd. for $C_{15}H_9N_4O_5Cl$: C, 49.95; H, 2.52; N, 15.53. Found: C, 49.67; H, 2.42; N, 15.40.

5-(4-Methoxyphenyl)-1,3-dihydro-2*H*-1,4-benzodiazepin-2-one (**19**).

Compound **19** was synthesized according to the procedures previously referenced, in 80% yield, mp 254-256°; ir (potassium bromide): $\nu = 3323, 3108, 2974, 2916, 1677, 1601, 1401, 1252, 1020 \text{ cm}^{-1}$; ms: (70 eV) 266 (M^+ , 10), 265 (60), 264 (40), 238 (15), 237 (100), 236 (37), 221 (8), 209 (8), 193 (12), 192 (10), 166 (18), 139 (8), 138 (9), 118 (7), 104 (8), 103 (9), 78 (7), 77 (10), 63 (5).

Anal. Calcd. for $C_{16}H_{14}N_2O_2$: C, 72.17; H, 5.30; N, 10.52. Found: C, 71.86; H, 5.31; N, 10.52.

7-Nitro-1,3-dihydro-5-(4-methoxyphenyl)-2*H*-1,4-benzodiazepin-2-one (**20**) and 1,3-Dihydro-5-(3-nitro-4-methoxyphenyl)-2*H*-1,4-benzodiazepin-2-one (**21**).

Compounds **20** and **21** were obtained as a 1:1.8 mixture (nmr), mp 206-220°. No separation was observed in any of the following tlc systems; tlc, Aluminium oxide 60 F_{254} plate: Solvent system (v:v:v); CH_3CN , Rf 0.33; $CH_3CN:CH_2Cl_2$ (1:1), Rf 0.40; $CH_2Cl_2:EtOAc:MeOH$ (4:4:0.5), Rf 0.52; tlc:Silica Gel F_{254} plate: Solvent system (v:v:v); $CH_2Cl_2:EtOAc:MeOH$ (4:4:0.5), Rf 0.36; ms: (70 eV) 311 (M^+ , 50), 310 (20), 283 (100), 282 (25), 263 (19), 235 (41), 207 (32), 180 (12), 152 (9), 104 (15), 90 (12), 77 (18), 63 (11); 1H nmr ($DMSO-d_6$): 4.0 (OCH_3), 4.1 (CH_2), 4.2 (CH_2), 7.15-8.4 (arom), 10.58 (NH), 11.18 (NH).

7-Nitro-1,3-dihydro-5-(3-nitro-4-methoxyphenyl)-2*H*-1,4-benzodiazepin-2-one (**22**).

Compound **22** was isolated by crystallization from ethanol and tetrahydrofuran in 90% yield, mp 262-264° dec; ^{13}C nmr ($DMSO-d_6$): $\delta = 57.22$ (CH_3), 57.22 (CH_2), 114.33 (CH), 122.58 (CH), 125.32 (C), 125.84 (CH), 126.65 (CH), 126.77 (CH), 131.30 (C), 135.09 (CH), 139.93 (C), 141.74 (C), 145.18 (C), 153.59 (C), 166.25 (C), 169.95 (C); ir (potassium bromide): $\nu = 3355, 3070, 2970, 1690, 1615, 1528, 1526, 1342, 1330, 1202 \text{ cm}^{-1}$; ms: (70 eV): 356 (M^+ , 40), 355 (19), 339 (12), 329 (22), 328 (100), 327 (22), 309 (11), 308 (10), 281 (13), 280 (16), 252 (19), 192 (5), 177 (6), 164 (7), 150 (6), 76 (9), 75 (6), 63 (6), 42 (5), 28 (12).

Anal. Calcd. for $C_{16}H_{12}N_4O_6$: C, 53.94; H, 3.40; N, 15.73. Found: C, 53.78; H, 3.50; N, 15.46.

7-Chloro-1,3-dihydro-5-(4-methoxyphenyl)-2*H*-1,4-benzodiazepin-2-one (**23**).

Compound **23** was synthesized by using previously referenced procedures in 87% yield, mp 210-212°; ir (potassium bromide): $\nu = 3342, 3116, 2957, 1692, 1602, 1575, 1491, 1386, 1175 \text{ cm}^{-1}$; ms: (70 eV) 302 (17), 301 (19), 300 (M^+ , 54), 299 (32), 274 (33), 273 (30), 272 (100), 271 (40), 265 (13), 228 (10), 201 (9), 193 (8), 192 (7),

166 (11), 140 (8), 139 (10), 138 (10), 112 (5), 102 (6), 89 (8), 77 (12), 63 (10), 51 (7).

Anal. Calcd. for $C_{16}H_{13}N_2O_2Cl$: C, 63.90; H, 4.36; N, 9.31. Found: C, 63.9; H, 4.32; N, 9.14.

7-Chloro-1,3-dihydro-5-(3-nitro-4-methoxyphenyl)-2*H*-1,4-benzodiazepin-2-one (**24**).

Compound **24** was crystallized from methanol and ethyl acetate in 39% yield, mp 226-228° dec; ir (potassium bromide): $\nu = 3342, 3123, 2966, 1680, 1606, 1531, 1481, 1387, 1352, 1201, 1015 \text{ cm}^{-1}$; ms: (70 eV) 327 (17), 346 (14), 345 (M^+ , 54), 344 (14), 319 (36), 318 (27), 317 (100), 316 (30), 297 (15), 271 (15), 270 (10), 269 (40), 243 (15), 242 (16), 241 (31), 240 (15), 214 (12), 205 (11), 180 (11), 179 (12), 178 (14), 166 (12), 165 (10), 164 (15), 151 (13), 150 (12), 140 (11), 139 (12), 138 (16), 113 (12), 96 (14), 89 (16), 82 (16), 76 (13), 75 (13), 63 (10).

Anal. Calcd. for $C_{16}H_{12}N_3O_4Cl \cdot 0.25H_2O$: C, 54.87; H, 3.60; N, 12.00. Found: C, 54.75; H, 3.40; N, 12.12. * Dried, 95%, high vacuum, 5 hours.

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