Synthesis and Alkylation of 3,4-Dihydro-1*H*-1,3-4-benzotriazepine-2,5-diones and Related Systems

Gary M. Karp

Chemical Discovery, Agricultural Products Research Division, American Cyanamid Company, Princeton, New Jersey 08543-0400

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A synthesis of the 1,3,4-benzotriazepine-2,5-dione **2a** and its 2-thio analog **11** is described. The key step was the mild and efficient cyclization of the *o*-(aminobenzoyl)hydrazine **10**, obtained from the reaction of a protected hydrazine derivative with the *o*-nitrobenzoyl chloride **3**. Alkylation of **2a** takes place exclusively at N-3 while alkylation of **11** takes place on sulfur. Cyclization of the *o*-(aminobenzoyl)hydrazine **14** gave the 2,4(1*H*,3*H*)-quinazolinedione **15** as the sole product.

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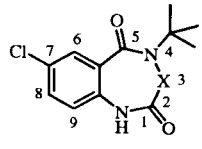
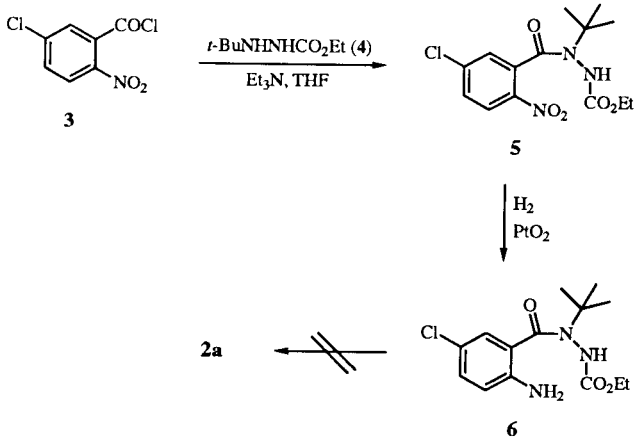
Recently, we described the herbicidal properties of a series of 1,4-benzodiazepine-2,5-diones [1]. Interest in this area led to a brief study of the structurally related 1,3,4-benzotriazepine-2,5-diones. A survey of the literature revealed a number of reported syntheses of the 1,3,4-benzotriazepine-2,5-dione ring system by the reaction of hydrazines with isatoic anhydrides [2,3] and related systems [4-8].



1, X = CH_2
2a, X = NH
2b, X = NCH_3

In a previous report [9], we described the preparation of benzodiazepinedione **1** from methyl *tert*-butyl glycinate and 5-chloro-2-nitrobenzoyl chloride. It was reasoned that the aza analog **2a** might be constructed in a manner analogous to **1** from two fragments by utilization of ethyl 3-*tert*-butylcarbazate (**4**) as the acyclic component (Scheme 1). Treatment of benzoyl chloride **3** with **4** furnished the 3-(2-nitrobenzoyl)carbazate **5** in 56% yield. Catalytic hydrogenation of **5** afforded the cyclization precursor **6**. Attempts to cyclize **6** to **2a**, either thermally or under basic or acidic conditions, were unsuccessful. Apparently, the nitrogen atom closest to the ethoxycarbonyl group of **6** adds sufficient electron density to the carbonyl group as to render it a rather poor electrophile towards intramolecular attack of the aniline nitrogen.

Scheme 1

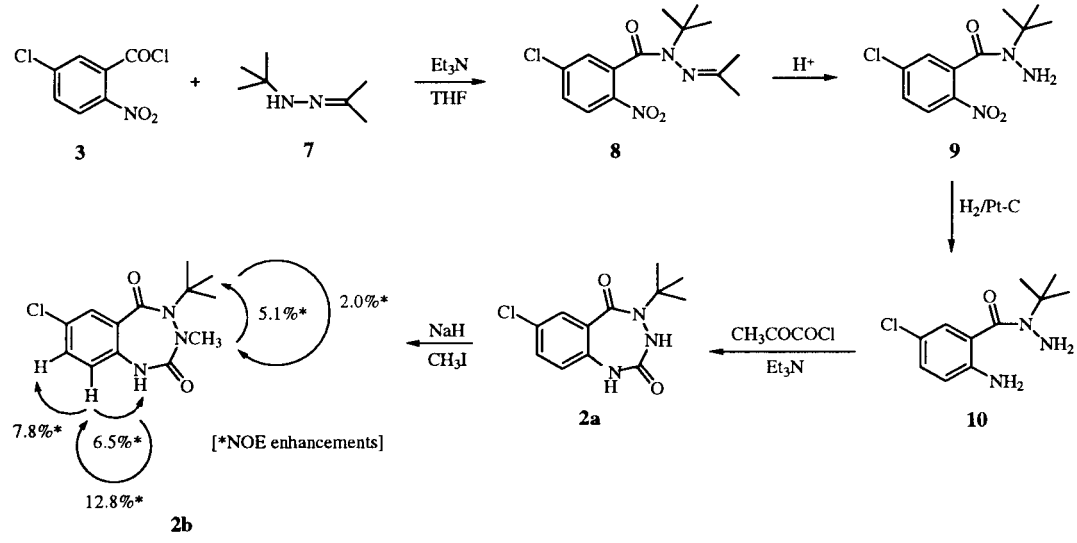


The inability of **6** to cyclize to the desired **2a** necessitated an alternative approach. One strategy, which has been used previously in the preparation of benzotriazepinediones, has been to react an *o*-(aminobenzoyl)hydrazine with a reactive acyl moiety; in effect, tethering the two terminal nitrogen atoms together. Phosgene [2] and ethyl chloroformate [3] have been used for this purpose but yields of less than 35% were reported for the examples cited. In order to utilize this approach to **2a**, preparation of the requisite *o*-(aminobenzoyl)hydrazine intermediate was sought. We envisioned that, in principle, the *o*-(aminobenzoyl)hydrazine could be prepared by reaction of benzoyl chloride **3** with a *tert*-butylhydrazine derivative, followed by nitro reduction of the resultant *o*-(nitrobenzoyl)hydrazine. It was not apparent if *tert*-butylhydrazine would react at the *tert*-butyl-bearing nitrogen atom as desired [10]. To avoid any ambiguity, we initially chose to protect the primary amino nitrogen, thereby forcing the *tert*-butyl-bearing nitrogen to react exclusively.

tert-Butylhydrazine was converted to its acetone hydrazone **7** [11] and reacted with nitrobenzoyl chloride **3** to give the *N*-protected *o*-(nitrobenzoyl)hydrazine **8** in 70% yield (Scheme 2). Acid-catalyzed *N*-deprotection gave **9** in 92% yield. The nitro group of **9** was readily reduced in 79% yield by catalytic hydrogenation, furnishing the desired *o*-(aminobenzoyl)hydrazine **10**. Upon treatment with trichloromethyl chloroformate at room temperature, compound **10** was smoothly transformed into the benzotriazepinedione **2a** in 86% yield.

Preparation of the 3-methyl analog **2b** was then sought. Previous studies [4] have shown that the alkylation of the analogous 4-methylbenzotriazepinedione occurs exclusively

Scheme 2



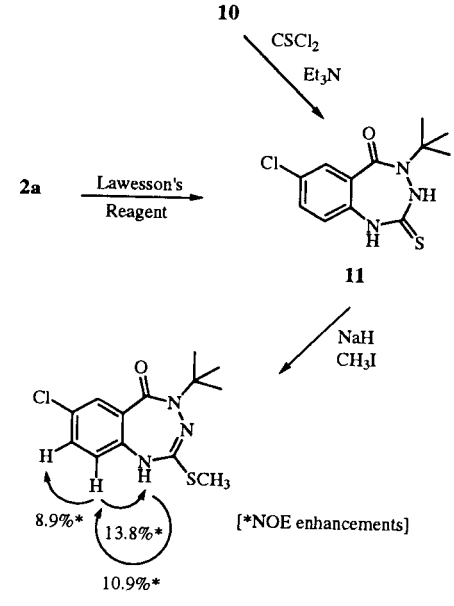
at N-3. The selectivity of N-3 over N-1 was ascribed to the α effect. We questioned whether the bulkier 4-*tert*-butyl group of **2a** would affect the direction of alkylation. Treatment of **2a** with sodium hydride and methyl iodide gave primarily a single compound, isolated in 62% yield. The identity of this compound was confirmed as the 3-methyl compound **2b** by 1D NOE difference spectroscopy. Irradiation of the three nitrogen substituents (hydrogen, methyl and *tert*-butyl) and the C-9 proton indicated the special proximity of the N-H and C-9 protons and the *N*-methyl and *N*-*tert*-butyl groups. A second, less polar compound contaminated with **2b** was also isolated (< 4%), but its structure could not be proved conclusively. Thus, even in the presence of the bulky *tert*-butyl group, alkylation took place predominantly, if not exclusively, at N-3.

When **2a** was heated in the presence of Lawesson's Reagent [12], a single monothione product was obtained in 72% yield, exhibiting carbonyl resonances at 193 and 167 ppm in the ^{13}C nmr (Scheme 3). By subjecting the N-1 and N-3 protons to deuterium exchange, proton-coupled ^{13}C nmr of the product demonstrated that thionation took place at C-2 to afford **11** as the sole product. Compound **11** could also be obtained directly by the cyclization of **10** with thiophosgene in 77% yield, as the product was identical in all respects to that obtained *via* the thionation of **2a**. When compound **11** was treated with sodium hydride and methyl iodide, a single product was isolated which contained a single N-H resonance at 9.24 ppm and a methyl resonance at 2.42 ppm in the ^1H nmr. The remaining N-H had shifted upfield as compared to **11**, where the two N-H resonances were found at 10.85 and 10.00 ppm, respectively. This contrasted with the conversion of **2a** to **2b** where the remaining N-H showed no change upon *N*-methylation. The methyl resonance at 2.42 ppm was considered too far upfield to be due to direct bonding to a nitrogen since it would be expected to occur downfield of 3 ppm. Taken together, these results indicate that alkylation took place on the sulfur. This is not surprising as both thioamides and thioureas alkylate predominantly on sulfur [13]. It only remained to be resolved in which tautomeric form compound **12** existed. Again, 1D NOE difference experiments were helpful in determining the structure of **12** as the NOE effect between the C-9 and the N-1 protons established their special proximity.

The use of *tert*-butylhydrazone **7** allowed for the unambiguous preparation of *o*-(nitrobenzoyl)hydrazine **9**. With the identity of **9** established, compound **3** was treated with *tert*-butylhydrazine to determine if the unprotected hydrazine would also afford compound **9**. A mixture of two products resulted (Scheme 4). The major product, isolated in 65% yield, was identified as **13** as evidenced by the two non-equivalent N-H resonances in the ^1H nmr. A small amount of a second product was also isolated, the identity of which could not easily be determined. The ^1H nmr of this product was highly complex and the mass spectrum of this product exhibited a parent fragment ion of m/z = 231. Interestingly, none of the desired **9** was obtained. The reactivity of *tert*-butylhydrazine contrasts with the propensity of the less bulky methylhydrazine to react primarily at the methyl-bearing nitrogen atom upon reaction of benzoyl chlorides [4] and isatoic anhydrides [3,14].

The reaction of anthranilic acid hydrazides (in which the hydrazide nitrogen atoms are unsubstituted) with urea in decalin at reflux has been reported [4] to give 3-amino-2,4(1*H*,3*H*)-quinazolinediones exclusively while their treatment with 1,1'-carbonyldiimidazole in THF at reflux has been reported [15] to give benzotriazepinediones exclusively. We questioned whether **13**

Scheme 3



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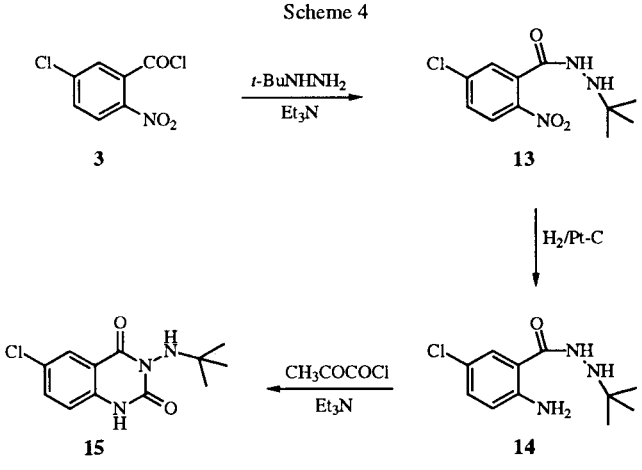
could be converted to the benzotriazopinedione ring system in preference to the 3-amino-2,4-quinazolinedione system under the mild cyclization conditions. To this end, catalytic hydrogenation of **13** afforded the cyclization precursor **14**. When **14** was treated with trichloromethylchloroformate at room temperature, the 3-amino-2,4(1*H*,3*H*)quinazolinedione **15** was isolated as the sole product in 54% yield. Thus, the bulky *tert*-butyl group on the hydrazide β-nitrogen atom directs the cyclization to the quinazolinedione **15** exclusively, even under the mild conditions employed [16].

Scheme 4



The herbicidal activity of the benzotriazepinediones and quinazolinediones reported in this manuscript was significantly less than the analogous benzodiazepinediones reported previously [1].

EXPERIMENTAL

All reactions requiring anhydrous conditions were carried out under an atmosphere of nitrogen. Unless otherwise noted, materials were obtained from commercial suppliers and were used without further purification. Dimethylformamide, tetrahydrofuran and toluene were stored over 4A sieves. Organic layers from aqueous extractions were dried over magnesium sulfate and concentrated *in vacuo*. Melting points are uncorrected. The ^1H and ^{13}C nmr spectra (300 and 75 MHz, respectively) were recorded on a Varian Unity 300 or Varian XL 300 spectrometer. The chemical shifts were measured in ppm using deuteriochloroform or DMSO-d_6 as internal standards. The ir spectra were recorded on a Perkin-Elmer 1600 Series FTIR as Nujol mulls. Chemical ionization mass spectra (ms) were determined on a Finnegan-MAT TSQ4500 mass spectrometer using isobutane as carrier gas and recorded in units of m/z. Elemental analyses were performed by Microlit Laboratories, Caldwell, NJ. Flash chromatography was performed on 230-400 mesh silica gel. Analytical thin-layer chromatography was done with glass-backed silica plates, 250 microns (Analtech).

Ethyl 3-*tert*-Butyl-3-(5-chloro-2-nitrobenzoyl)carbazate (**5**).

To a solution of compound **4** [10] (3.20 g, 20 mmoles) and triethylamine (6.93 ml, 50 mmoles) in tetrahydrofuran (50 ml), cooled to 0°, was added a 1 molar solution of compound **3** in toluene [9] (25 ml, 25 mmoles) during 20 minutes. The resultant heterogeneous reaction mixture was then allowed to warm to ambient temperature and stir overnight. The crude reaction mixture was then partitioned in ethyl acetate and water. The aqueous phase was removed and the organic phase was washed with two portions of 10% hydrochloric acid. The aqueous phases were combined and back-extracted with ethyl acetate. The combined organic layers were then washed sequentially with saturated sodium bicarbonate and saturated sodium chloride, and then dried and concentrated to an amber oil. Trituration in ethyl acetate/hexanes (15/85) gave 3.85 g (56% yield) of compound **5** as a beige powder consisting of a 4.7:1 mixture of rotational isomers as determined by ^1H nmr analysis. A small sample was recrystallized from ethanol/water to give an analytically pure sample as white plates, mp 142-143°; ^1H nmr (DMSO-d_6): δ (major isomer) 9.78 (s, 1H), 8.22 (d, J = 8.7, 1H), 7.69 (dd, J = 2.4, 8.7, 1H), 7.35 (d, J = 2.4, 1H), 3.99-3.80 (m, 2H), 1.43 (s, 9H), 0.91 (t, J = 6.9, 3H), (minor isomer) 9.35 (s, 1H), 8.05 (d, J = 8.7, 1H), 7.90 (dd, J = 2.4, 8.7, 1H), 7.40 (d, J = 2.4, 1H), 3.99-3.80 (m, 2H), 1.42 (s, 9H), 1.20 (t, J = 6.9, 3H); ms: 344 (MH^+).

Anal. Calcd. for $C_{14}H_{18}ClN_3O_5$: C, 48.92; H, 5.28; N, 12.22. Found: C, 48.96; H, 5.28; N, 12.29.

1-*tert*-Butyl-2-isopropylidine-(5-chloro-2-nitrobenzoyl)-hydrazine (**8**).

Using a procedure similar to that used for the preparation of compound **5**, a 1 molar toluene solution of 5-chloro-2-nitrobenzoyl chloride **3** [9] (90 ml, 90 mmoles) and hydrazone **7** [12] (10.0 g, 78.1 mmoles) were reacted to give compound **8**. Flash chromatography (ethyl acetate/hexanes, 15-20%) gave 17.0 g (70% yield) of compound **8** as a yellow solid, mp 81.5-84.5°; ^1H nmr (deuteriochloroform): δ 7.93 (d, J = 9.3, 1H), 7.40-7.36 (m, 2H), 1.79 (s, 3H), 1.70 (s, 3H), 1.49 (s, 9H); ms: 312 (MH^+).

Anal. Calcd. for $C_{14}H_{18}ClN_3O_3$: C, 53.94; H, 5.82; N, 13.48. Found: C, 53.55; H, 5.71; N, 13.37.

1-*tert*-Butyl-(5-chloro-2-nitrobenzoyl)hydrazine (**9**).

Compound **8** (3.65 g, 11.7 mmoles) was stirred in a mixture of ethanol (25 ml) and 10% hydrochloric acid (25 ml) for *ca.* 24 hours. The reaction mixture was then basified with 1 molar sodium hydroxide and the aqueous phase was extracted with ethyl acetate. The organic phase was washed with saturated sodium bicarbonate and saturated sodium chloride, and then dried and concentrated to afford 2.92 g (92% yield) of a pale yellow solid, mp 119.5-120.5°; ^{1}H nmr (deuteriochloroform): δ 8.08 (d, J = 8.8, 1H), 7.40 (dd, J = 2.2, 8.8, 1H), 7.34 (d, J = 2.2, 1H), 3.63 (br s, 2H), 1.55 (s, 9H); ms: 272 (MH^+).

Anal. Calcd. for $C_{11}H_{14}ClN_3O_3$: C, 48.63; H, 5.19; N, 15.47. Found: C, 48.81; H, 5.06; N, 15.27.

1-*tert*-Butyl-(2-amino-5-chlorobenzoyl)hydrazine (**10**).

A solution of compound **9** (2.35 g, 8.67 mmoles) in ethanol (50 ml) was hydrogenated over 5% platinum on carbon (0.47 g) at 50 psi until hydrogen uptake ceased (*ca.* 2 hours). The reaction mixture was then filtered and the catalyst was washed with additional ethanol. The filtrate was concentrated to give a yellow solid. Trituration in ethyl acetate/hexanes (1/9) gave 1.57 g (75% yield) of an off-white solid, mp 113-114°; ^{1}H nmr (deuteriochloroform): δ 7.17 (d, J = 2.7, 1H), 7.07 (dd, J = 2.4, 9.0, 1H), 6.61 (d, J = 9.0, 1H), 4.04 (br s, 4H), 1.47 (s, 9H); ms: 242 (MH^+).

Anal. Calcd. for $C_{11}H_{16}ClN_3O$: C, 54.66; H, 6.67; N, 17.38. Found: C, 54.32; H, 6.57; N, 17.13.

4-*tert*-Butyl-7-chloro-3,4-dihydro-1*H*-1,3,4-benzotriazepine-2,5-dione (**2a**).

A solution comprised of compound **10** (2.32 g, 9.63 mmoles) and triethylamine (2.80 ml, 20.2 mmoles) in toluene (100 ml) was treated with trichloromethylchloroformate (0.58 ml, 4.82 mmoles) in one portion. After stirring the resultant heterogeneous mixture for 3.5 hours at ambient temperature, the crude reaction mixture was diluted with ethyl acetate and then washed sequentially with water and saturated sodium chloride, and then dried and concentrated to give 2.21 g (86% yield) of a yellow solid. A small sample was recrystallized from ethanol to give an analytically pure sample as white plates, mp 267-272°; ^{1}H nmr (DMSO-d_6): δ 9.49 (s, 1H), 8.81 (s, 1H), 7.71 (d, J = 2.4, 1H), 7.47 (dd, J = 2.4, 8.7, 1H), 7.15 (d, J = 8.7, 1H), 1.43 (s, 9H); ^{13}C nmr (DMSO-d_6): δ 166.9 (C=O), 164.3 (C=O), 140.1 (Ar), 131.6 (Ar), 129.5 (Ar), 126.8 (Ar), 126.4 (Ar), 121.1 (Ar), 61.4 (*t*-butyl methine), 27.2 (*t*-butyl methyl); ms: 268 (MH^+).

Anal. Calcd. for $C_{12}H_{14}ClN_3O_2$: C, 53.84; H, 5.27; N, 15.70. Found: C, 54.04; H, 5.06; N, 15.68.

4-*tert*-Butyl-7-chloro-3-methyl-3,4-dihydro-1*H*-1,3,4-benzotriazepine-2,5-dione (**2b**).

A suspension of sodium hydride (0.18 g, 4.37 mmoles, 60% oil dispersion) in dimethylformamide (10 ml) was treated with a solution of compound **2a** (1.11 g, 4.16 mmoles) in dimethylformamide (10 ml) dropwise and the resultant solution was stirred for 20 minutes. Methyl iodide (0.52 ml, 8.32 mmoles) was then added and the reaction was stirred for an additional 1.5 hours. The crude reaction mixture was diluted in ethyl acetate and the organic phase was washed with three portions of water. The combined aqueous phases were back-extracted with ethyl acetate and then the organic layers were combined, dried and concentrated. Flash chromatography (ethyl acetate/hexanes, 15-20%) gave 0.73 g (62% yield) of a white solid, mp 185-187.5°; ir: 1690, 1651 cm^{-1}; ^{1}H nmr (DMSO-d_6): δ 9.46 (s, 1H), 7.73 (d, J = 2.4, 1H), 7.48 (dd, J = 2.4, 8.7, 1H), 7.17 (d, J = 8.7, 1H), 3.06 (s, 3H), 1.42 (s, 9H); ^{13}C nmr (DMSO-d_6): δ 167.4 (C=O), 163.8 (C=O), 140.4 (Ar), 132.1 (Ar), 129.8 (Ar), 126.5 (Ar), 126.0 (Ar), 121.1 (Ar), 62.2 (*t*-butyl methine), 38.8 (N-CH_3), 27.9 (*t*-butyl methyl); ms: 282 (MH^+).

Anal. Calcd. for $C_{13}H_{16}ClN_3O_2$: C, 55.42; H, 5.72; N, 14.91. Found: C, 55.56; H, 5.60; N, 14.79.

4-*tert*-Butyl-7-chloro-2-thio-3,4-dihydro-1*H*-1,3,4-benzotriazepine-2,5-dione (**11**).

Method 1.

A suspension of benzotriazopinedione **2a** (1.00 g, 3.74 mmoles) and Lawesson's Reagent (0.83 g, 2.06 mmoles) [13] in toluene (20 ml) was heated at reflux for 1.5 hours after which time the reaction became homogeneous. After cooling to room temperature, the reaction mixture was diluted with ethyl acetate and washed sequentially with water and saturated sodium chloride, and then the organic layer was dried and concentrated. The crude product was purified by flash chromatography (ethyl acetate/hexanes, 15-20%) affording 0.76 g (72% yield) of compound **11** as a yellow solid, mp 222-224° dec; ir: 1644, 1586, 1541 cm^{-1}; ^{1}H nmr (DMSO-d_6): δ 10.85 (d, J = 1.5, 1H), 10.00 (d, J = 2.1, 1H), 7.74 (d, J = 2.4, 1H), 7.52 (dd, J = 2.4, 8.7, 1H), 7.26 (d, J = 8.7, 1H), 1.43 (s, 9H); ^{13}C nmr (DMSO-d_6): δ 193.1 (C=S), 166.9 (C=O), 140.1 (Ar), 132.0 (Ar), 129.7 (Ar), 127.6 (Ar), 126.9 (Ar), 121.3 (Ar), 62.5 (*t*-butyl methine), 27.3 (*t*-butyl methyl); ms: 284 (MH^+).

Anal. Calcd. for $C_{12}H_{14}ClN_3OS$: C, 50.79; H, 4.97; N, 14.81. Found: C, 51.00; H, 4.98; N, 14.65.

Method 2.

A solution comprised of compound **10** (2.00 g, 8.30 mmoles) and triethylamine (2.41 ml, 17.4 mmoles) in toluene (75 ml) was cooled to 0° and treated with thiophosgene (0.63 ml, 8.30 mmoles) during one minute. After stirring the resultant heterogeneous mixture for 3 hours at ambient temperature, the crude reaction mixture was diluted with ethyl acetate and then washed sequentially with water and sodium chloride. The aqueous phases were back-extracted with ethyl acetate and the organic layers were combined, dried and then concentrated to give a yellow-orange solid. Trituration in ethyl acetate/hexanes (1/9) gave 1.80 g (77% yield) of the desired product as a light-yellow solid, identical to the compound obtained in method 1 by tlc, ^{1}H nmr and ^{13}C nmr.

4-*tert*-Butyl-7-chloro-2-(methylthio)-1*H*-1,3,4-benzotriazepin-5(4*H*)-one (**12**).

A solution of compound **11** (0.90 g, 3.18 mmoles) in dimethylformamide (10 ml) was treated with sodium hydride (0.13 g, 3.34 mmoles, 60% oil dispersion) in one portion. After stirring for 20 minutes, methyl iodide (0.40 ml, 6.36 mmoles) was added to the solution *via* syringe during one minute. After stirring at ambient temperature for 5 hours, the reaction mixture was diluted with ethyl acetate and the organic phase was washed with four portions of water. The aqueous phases were back-extracted with ethyl acetate and the organic layers were combined, washed with saturated sodium chloride, and then dried and concentrated to give an amber oil. Flash chromatography (ethyl acetate/hexanes, 15/85) afforded 0.77 g (82% yield) of compound **12** as a yellow solid. A small sample was recrystallized (methylene chloride/hexanes) to give compound **12** as light yellow needles [18], mp 151-153°; ir:

1740, 1605, 1590 cm^{-1}; ^{1}H nmr (DMSO-d$_6$): δ 9.25 (s, 1H), 7.74 (d, J = 2.5, 1H), 7.43 (dd, J = 2.5, 8.8, 1H), 7.05 (d, J = 8.8, 1H), 2.43 (s, 3H), 1.40 (s, 9H); ^{13}C nmr (DMSO-d$_6$): δ 163.6 (C=O or C=N), 160.8 (C=N or C=O), 143.7 (Ar), 131.9 (Ar), 130.0 (Ar), 125.7 (Ar), 124.3 (Ar), 119.5 (Ar), 59.7 (*t*-butyl methine), 26.8 (*t*-butyl methyl) 13.9 (*S*-methyl); ms: 298 (MH$^+$).

High resolution ms Calcd. for $C_{13}H_{16}ClN_3OS$: 297.0702. Found: 297.0704.

2-*tert*-Butyl-(5-chloro-2-nitrobenzoyl)hydrazine (**13**).

To a solution of *tert*-butylhydrazine (2.00 g, 22.7 mmoles) and triethylamine (7.62 ml, 55.0 mmoles) in tetrahydrofuran (50 ml), cooled to 0°, was added a 1 molar solution of compound **3** in toluene [9] (25 ml, 25 mmoles) *via* an addition funnel. The resultant heterogeneous reaction mixture was then allowed to warm to ambient temperature and stir overnight. The crude reaction mixture was then partitioned in ethyl acetate and water. The aqueous phase was removed and the organic phase was washed with three portions of saturated sodium bicarbonate and sodium chloride. The organic layer was then dried and concentrated to give a dark oil. Flash chromatography (ethyl acetate/hexanes, 15-25%) gave 4.00 g (65% yield) of compound **13** as a yellow solid. Trituration (ethyl acetate/hexanes, 1/9) gave an analytically pure sample consisting of a 6.5:1 mixture of rotational isomers as determined by ^{1}H nmr analysis, mp 126-127°; ir: 3315, 3221, 1642, 1525 cm^{-1}; ^{1}H nmr (DMSO-d$_6$): δ (major isomer) 9.97 (br s, 1H), 8.07 (d, J = 8.8, 1H), 7.78 (dd, J = 2.2, 8.8, 1H), 7.68 (d, J = 2.2, 1H), 4.83 (br s, 1H), 1.06 (s, 9H), (minor isomer) 9.10 (br s, 1H), 8.06 (d, J = 8.8, 1H), 7.77 (dd, J = 2.2, 8.8, 1H), 7.58 (d, J = 2.2, 1H), 4.53 (br s, 1H), 0.74 (s, 9H); ms: 272 (MH$^+$).

Anal. Calcd. for $C_{11}H_{14}ClN_3O_3$: C, 48.63; H, 5.19; N, 15.47. Found: C, 48.57; H, 5.11; N, 15.56.

2-*tert*-Butyl-(2-amino-5-chlorobenzoyl)hydrazine (**14**).

A solution of compound **13** (2.23 g, 8.23 mmoles) in ethanol (50 ml) was hydrogenated over 5% platinum on carbon (0.44 g) at 50 psi until hydrogen uptake ceased (*ca.* 3 hours). The reaction mixture was then filtered and the catalyst was washed with additional ethanol. The filtrate was concentrated to give a yellow solid. Flash chromatography (ethyl acetate/hexanes, 33-40%) gave 1.31 g (66% yield) of compound **14** as a white solid, mp 164-166°; ir: 3420, 3300, 3233, 3100, 1637, 1588 cm^{-1}; ^{1}H nmr (DMSO-d$_6$): δ 9.63 (br s, 1H), 7.46 (d, J = 2.2, 1H), 7.12 (dd, J = 2.2, 8.7, 1H), 6.68 (d, J = 8.7, 1H), 6.34 (br s, 2H), 5.05 (br s, 1H), 1.00 (s, 9H); ms: 242 (MH$^+$).

Anal. Calcd. for $C_{11}H_{16}ClN_3O$: C, 54.66; H, 6.67; N, 17.38. Found: C, 54.79; H, 6.58; N, 17.14.

3-(*tert*-Butylamino)-6-chloro-2,4(1*H*,3*H*)-quinazolinedione (**15**).

To a heterogeneous mixture comprised of compound **14** (0.80 g, 3.32 mmoles) and triethylamine (0.97 ml, 6.97 mmoles) in toluene (30 ml) was added trichloromethylchloroformate (0.20 ml, 1.66 mmoles) *via* dropwise addition over a few minutes. After stirring for 6 hours at ambient temperature, the crude reaction mixture was diluted with ethyl acetate and the organic phase was washed with water. The aqueous washing was then back-extracted with ethyl acetate and the combined organic layers were washed with saturated sodium chloride, and then dried and concentrated a yellow solid. Flash chromatography (ethyl acetate/hexanes, 1/2) gave 0.48 g (54% yield) of compound **15** as a white solid, mp 256.5-258°; ir: 1727, 1663 cm^{-1}; ^{1}H nmr (DMSO-d$_6$): δ 11.54 (br s, 1H), 7.80 (br s, 1H), 7.63 (d, J = 7.8, 1H), 7.15 (d, J = 7.8, 1H), 5.23 (s, 1H), 1.03 (s, 9H), ^{13}C nmr δ 160.6 (C=O), 150.0 (C=O), 137.0 (Ar), 134.1 (Ar), 125.8 (2 Ar), 116.8 (Ar), 114.9 (Ar), 56.1 (*t*-butyl methine), 27.5 (*t*-butyl methyl); ms: 268 (MH$^+$).

Anal. Calcd. for $C_{12}H_{14}ClN_3O_2$: C, 54.04; H, 4.91; N, 15.75. Found: C, 54.08; H, 5.15; N, 15.62.

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