Organotellurium Chemistry. 4. Synthesis and Reactions of Tellurophthalide. The First Alkyltellurenyl Halides

Lars Engman and Michael P. Cava*

Department of Chemistry, University of Pennsylvania, Philadelphia, Pennsylvania 19104

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The first alkyltellurenyl halides were obtained as isolable but unstable compounds from halogenolysis of tellurophthalide (**1c**), a compound obtained in almost quantitative yield from 2-(bromomethyl)benzoyl chloride and sodium hydrogen telluride. The structures of the new compounds were confirmed by transformations to a single benzyl tellurocyanate that was independently synthesized.

Simple aryltellurenyl halides are polymeric and thermally unstable.[1] However, 2-naphthyltellurenyl iodide,[2] the first tellurenyl halide isolated, seems to be reasonably stable, thus constituting an apparent exception to this rule.

The stability of aryltellurenyl halides can be enhanced by complexation with external ligands such as thiourea[3] or by chelation with donor groups already incorporated in the molecule. As an example of the latter effect, *o*-carbonyl-containing groups have been shown, both in solution[4] and in the solid state,[5] to coordinate to the tellurium atom in aryltellurenyl halides.

More recently it has been shown that *o*-nitro[6] and *o*-azo[7] groups may also serve as efficient stabilizing ligands. A similar intramolecular chelation is apparently enhancing the stability of a number of organosulfenyl-containing Te(II) species of the general formula $Te[S(CH_2)_nCOOH]_2$.[8]

Aryltellurenyl halides have been synthesized by halogenolysis of the readily available diaryl ditellurides[1] or by cleavage of aromatic C–Te bonds[9] or aliphatic C–Te bonds[6] by hydrogen halides or bromine, respectively.

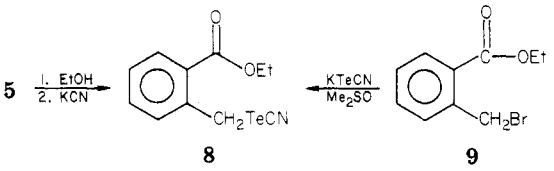
Alkyltellurenyl halides, to the best of our knowledge, have not been described in the literature. They may be expected to be still more unstable than their aryl analogues since any Te–π conjugation offered by the aromatic nucleus is lacking. However, efficient stabilization by suitably positioned chelating groups might be expected to compensate for this effect.

In this paper we report the syntheses of tellurophthalide (**1c**), the first example of a γ-tellurolactone; its halogenolysis has afforded the first examples of isolable alkyltellurenyl halides.

Results and Discussion

Thiophthalide (**1a**)[11] and selenophthalide (**1b**)[12] were both synthesized about 90 years ago. The corresponding tellurium isologue, tellurophthalide (**1c**), however, has remained unknown. We have now found that this yellow crystalline compound is formed in almost quantitative yield from sodium hydrogen telluride and 2-(bromomethyl)benzoyl chloride (**2a**) or 2-(bromomethyl)benzoyl bromide (**2b**), using a phase-transfer technique.[13]

Scheme I



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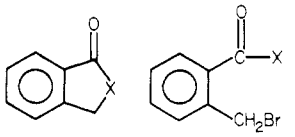

1a, X = S
b, X = Se
c, X = Te

2a, X = Cl
b, X = Br

Tellurophthalide is the first example of a five-membered telluroester; acyclic telluroesters were first prepared by Piette and Renson[14] and more recently further studied by others.[15]

Little appears to be known concerning the stability of the acyl–tellurium bond.[15e] In order to learn more about the behavior of this bond, we have investigated the halogenolysis and several other reactions of tellurophthalide.

We have found that tellurophthalide reacts with equimolar amounts of SO_2Cl_2, Br_2 and I_2, respectively, at −23 °C in CCl_4 to give isolable 1:1 halogen adducts. The products were obtained in reproducibly high yields (81–92%) under ordinary laboratory lighting conditions.

All three compounds are unstable and begin to decompose after a few hours, even when refrigerated. They all melt with decomposition and show carbonyl absorption in the infrared at 1750 cm^{-1}.

Three possible structures (**3**–**5**) must be considered for these products.

For comparison of the analogous reaction of a halogen with a compound containing tellurium bonded only to

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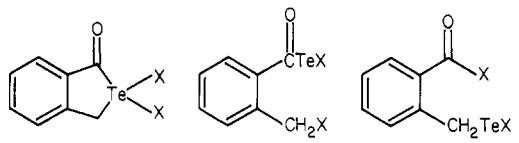
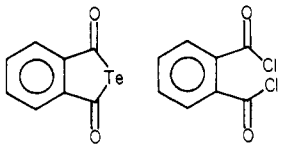


3 4 5a, X = Cl; b, X = Br; c, X = I

carbonyls, tellurophthalic anhydride (**6**)[13] was treated with chlorine at room temperature in CCl_4. Elemental tellurium was immediately precipitated and phthaloyl chloride (**7**) was isolated in quantitative yield.



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This result suggests that structures of the type **3** and **4** are not isolable, and speaks in favor of structure **5**. Conclusive evidence for this structure was obtained by conversion of all three halogen adducts into 2-carbethoxybenzyl tellurocyanate (**8**), by treatment first with ethanol and then with KCN in Me_2SO. Tellurocyanate **8** was independently synthesized in 85% yield from 2-carbethoxybenzyl bromide (**9**) by treatment with KTeCN[16] (Scheme I).

The values of the carbonyl frequencies (1750 cm^{-1}) of **5** are in harmony with the postulated structures, since the tellurium atom is expected to slightly lower the carbonyl stretching (compared to normal acid halides) via intramolecular chelation.[9,15e,17] Tellurophthalide (**1c**) could be regenerated from the tellurenyl bromide **5b** in 45% yield by treatment with aqueous $Na_2S_2O_5$. This reaction probably proceeds via a tellurolate anion which intramolecularly attacks the acid bromide.

When tellurophthalide was treated in CCl_4 with 2 equiv of bromine in the presence of small amounts of either methanol or ethanol, the alkyltellurium tribromides **10a** and **10b** were formed in 62% and 71% yield, respectively. These structures were confirmed by an independent synthesis of compound **10b** from tellurocyanate **8** by treatment with 2 equiv of bromine (Scheme II).

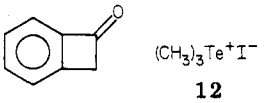
Compounds **10a** and **10b** are most probably formed from compound **5b** by nucleophilic attack of the alcohols at the acyl halide carbonyl group and by further halogen addition to the tellurium atom.

The infrared spectra of several tellurobenzoic acid–tellurophenyl esters have been analyzed in detail by Piette and Renson, [18] who observed a splitting of the carbonyl band attributed to Fermi resonance. Interestingly, the rigid system of tellurophthalide (**1c**) shows the same type of splitting of the carbonyl band (1690 and 1740 cm^{-1}).

The mass spectrum of tellurophthalide shows a base peak at m/e 118, e.g., loss of tellurium. However, all attempts to thermally extrude tellurium from the molecule in order to obtain benzocyclobutenone (**11**) were unsuccessful; *i.e.*, flash vacuum pyrolysis at 500 °C gave only unchanged starting material.

Tellurophthalide also proved to be surprisingly stable photochemically in contrast to simple cyclic telluroesters.[15a] Irradiation of tellurophthalide in benzene at 300 nm afforded mainly unchanged starting material with very little deposition of elemental tellurium.

Treatment of tellurophthalide with organometallic reagents did not yield carbonyl addition products but rather caused destruction of the molecule (PhMgBr gave diphenyl ditelluride). Attempted methylation of tellurophthalide by methyl iodide also resulted in detelluration and the slow separation of colorless prisms of trimethyltelluronium iodide (**12**).



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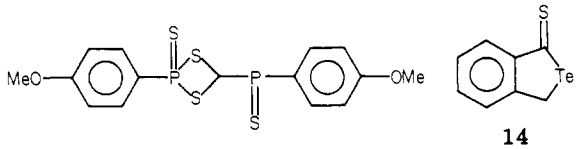
Thionation of tellurophthalide with the dimer of (*p*-methoxyphenyl)thioxophosphine sulfide (**13**), gave the novel tellurothiophalide **14** in 62% yield as surprisingly stable dark green crystals. Work is in progress in our laboratory to explore the chemistry of this unusual organotellurium heterocycle.



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Experimental Section

Melting points were determined on a Thomas-Hoover apparatus and are uncorrected. Mass spectra were recorded with an Hitachi Perkin-Elmer RMH-2 machine. All tellurium-containing mass peaks are reported for ^{130}Te. NMR spectra were obtained with a Bruker WM 250 instrument. They were recorded in $CDCl_3$ solutions containing Me_4Si as internal standard and are reported in δ units. Infrared spectra (KBr unless otherwise stated) were recorded with Perkin-Elmer 137 and 281B instruments. 2-(Bromomethyl)benzoyl bromide,[20] 2-(bromomethyl)benzoyl chloride,[21] 2-carbethoxybenzyl bromide,[20] and the dimer of (*p*-methoxyphenyl)thioxophosphine sulfide[19] were all prepared according to literature methods.

2-Oxo-2,5-dihydrobenzo[*c*]tellurophene (Tellurophthalide) (1c). Sodium borohydride (1.6 g, 42 mmol) was added under N_2 at room temperature to a suspension of tellurium (2.0 g, 16 mmol) in water (40 mL). The reaction mixture was then heated to 40 °C whereupon a vigorous evolution of H_2 started. All tellurium was consumed within 15 min, producing a faintly red aqueous solution. 2-(Bromomethyl)benzoyl chloride (3.7 g, 16 mmol) in toluene (50 mL) containing Adogen 464 [methyltrialkyl(C_8–C_{10})ammonium chloride, 0.25 g] was added rapidly through a dropping funnel to the stirred telluride solution kept at 50 °C. After 30 min the oil bath was removed and the stirring continued for another 2 h.

The dark reaction mixture was then filtered from a small amount of elemental tellurium, diluted with 100 mL of ethyl ether and transferred to a separatory funnel where it was shaken with Na_2CO_3 (5% aqueous, 50 mL). The organic phase was dried ($CaCl_2$) and evaporated to give a dark green oil that crystallized upon standing. To remove trace amounts of finely precipitated elemental tellurium, the material was dissolved in CH_2Cl_2 and passed through a SiO_2 column to yield 3.70 g (96%) of tellurophthalide (**1c**): mp 55–57 °C; IR (CCl_4, 3%) 1690 and 1740 cm^{-1}

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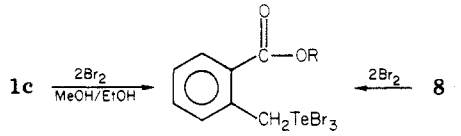
Scheme II



10a, R = CH_3
b, R = C_2H_5

(C=O); NMR δ 4.93 (s, 2 H), 7.22–7.27 (m, 1 H), 7.54–7.57 (several peaks, 2 H), 7.77 (d, 1 H); mass spectrum, *m/e* (relative intensity) M^+, 248 (36), 118 (100), 90 (93), 89 (44). Anal. Calcd for C_8H_6OTe: C, 39.10; H, 2.44; Te, 51.92. Found: C, 39.15; H, 2.44; Te, 51.95.

When 2-(bromomethyl)benzoyl chloride was replaced by 2-(bromomethyl)benzoyl bromide (4.48 g, 16 mmol) under otherwise unchanged reaction conditions, 3.77 g (97%) tellurophthalide was isolated.

[2-(Chlorocarbonyl)benzyl]telluryl Chloride (5a). Sulfuryl chloride (0.33 g, 2.4 mmol) in CCl_4 (6 mL) was added dropwise with stirring to a solution of tellurophthalide (0.60 g, 2.4 mmol) in CCl_4 (15 mL) at −23 °C during 30 min. [2-(Chlorocarbonyl)-benzyl]telluryl chloride (**5a**) is continuously precipitated as a faint yellow solid and filtration afforded 0.65 g (84%) of an unstable material, mp 110–120 °C dec, that slowly decomposed upon storage. All spectra were recorded with freshly prepared material: IR 1750 cm^{-1} (C=O); NMR δ 5.23 (s, 2 H), 7.79 (t, 1 H), 7.66 (d, 1 H), 7.81 (t, 1 H), 8.03 (d, 1 H).

[2-(Bromocarbonyl)benzyl]telluryl Bromide (5b). Bromine (0.13 g, 0.81 mmol) in CCl_4 (5 mL) was added dropwise with stirring to a solution of tellurophthalide (0.20 g, 0.81 mmol) in CCl_4 (5 mL) at −23 °C during 15 min. [2-(Bromocarbonyl)-benzyl]telluryl bromide (**5b**) is continuously precipitated as a yellow solid and filtration afforded 0.27 g (82%) of an unstable material, mp 150–155 °C dec, that slowly decomposed with darkening upon storage. All spectra were recorded with freshly prepared material: IR 1750 cm^{-1} (C=O); NMR δ 5.06 (s, 2 H), 7.47 (t, 1 H), 7.66 (d, 1 H), 7.84 (t, 1 H), 8.05 (d, 1 H).

[2-(Iodocarbonyl)benzyl]telluryl Iodide (5c). Iodine (0.205 g, 0.81 mmol) in CCl_4 (15 mL) was added dropwise with stirring to a solution of tellurophthalide (0.20 g, 0.81 mmol) in CCl_4 (5 mL) at −23 °C during 15 min. [2-(Iodocarbonyl)benzyl]telluryl iodide (**5c**) is continuously precipitated as a red solid, mp 160–170 °C dec, and filtration afforded 0.37 g (91%) of an unstable material that slowly decomposed upon storage. All spectra were recorded with freshly prepared material: IR 1750 cm^{-1} (C=O); NMR δ 5.07 (s, 2 H), 7.46 (t, 1 H), 7.67 (d, 1 H), 7.84 (t, 1 H), 8.05 (d, 1 H).

2-Carbethoxybenzyl Tellurocyanate (8). A mixture of freshly crushed and finely ground tellurium (1.8 g, 14.1 mmol) and powdered potassium cyanide (0.92 g, 14.1 mmol) in dry dimethyl sulfoxide (12 mL) was heated at 100 °C with stirring for 1 h when almost all the Te was dissolved. To the resulting solution, diluted with Me_2SO (15 mL) and cooled to room temperature, was added a solution of 2-carbethoxybenzyl bromide (3.42 g, 14.1 mmol) dropwise during 15 min. After 2 h the resulting pale-yellow solution was rapidly filtered from a small amount of elemental tellurium, poured into water (500 mL) and left overnight. Filtration and drying afforded 3.78 g (85%) of dark, crystalline 2-carbethoxybenzyl tellurocyanate (**8**) in the form of flakes: mp 72–73 °C (CCl_4/hexane); IR 2110 (C≡N), 1660 cm^{-1} (C=O); NMR δ 1.41 (t, 3 H), 4.22 (s, 2 H), 4.36 (q, 2 H), 7.32–7.41 (several peaks, 2 H), 7.54 (t, 1 H), 7.98 (d, 1 H); mass spectrum, *m/e* (relative intensity) 319 (1), 163 (27), 135 (100), 118 (15), 105 (11). Anal. Calcd for $C_{11}H_{11}NO_2Te$: C, 41.70; H, 3.50; N, 4.42. Found: C, 41.68; H, 3.67; N, 4.24.

Tribromo[2-(carbomethoxy)benzyl]tellurium (10a). Bromine (1.3 g, 8.1 mmol) in CCl_4 (15 mL) was added dropwise within 30 min to a cooled (−23 °C, CCl_4/dry ice) solution of tellurophthalide (1.0 g, 4.0 mmol) in CCl_4 (80 mL) containing a small amount of MeOH (0.40 g). After an additional stirring period of 15 min, CH_2Cl_2 (40 mL) was added to the yellow heterogeneous reaction mixture and the cooling bath was removed. After 30 min at room temperature all precipitated material had dissolved and the orange solution was evaporated to give a yellow solid. Recrystallization from CH_3CN afforded 1.3 g (62%) of yellow, highly crystalline tribromo[2-(carbomethoxy)benzyl]-tellurium (**10a**): mp 139–143 °C dec; IR 1620 cm^{-1} (C=O); NMR δ 4.09 (s, 3 H), 5.43 (s, 2 H), 7.37 (d, 1 H), 7.48 (t, 1 H), 7.70 (t, 1 H), 8.07 (d, 1 H). Anal. Calcd for $C_9H_9Br_3O_2Te$: C, 20.93; H, 1.76. Found: C, 20.99; H, 1.77.

Tribromo(2-carbethoxybenzyl)tellurium (10b). Bromine (0.65 g, 4.1 mmol) in CCl_4 (9 mL) was added dropwise to a cooled (−23 °C) solution of tellurophthalide (0.50 g, 2.0 mmol) in CCl_4 (25 mL) containing a small amount of EtOH (0.3 g), during 20 min. After an additional stirring period of 15 min CH_2Cl_2 (10 mL) was added to the yellow heterogeneous reaction mixture and the cooling bath was removed. After 30 min at room temperature all precipitated material had dissolved and the orange solution was evaporated to give a yellow solid. Recrystallization from CH_3CN afforded 0.77 g (71%) of yellow, highly crystalline tribromo(2-carbethoxybenzyl)tellurium (**10b**): mp 130–135 °C dec; IR 1625 cm^{-1} (C=O); NMR: 1.48 (t, 3 H), 4.53 (q, 2 H), 5.42 (s, 2 H), 7.37 (d, 1 H), 7.47 (t, 1 H), 7.69 (t, 1 H), 8.06 (d, 1 H). Anal. Calcd for $C_{10}H_{11}Br_3O_2Te$: C, 22.64; H, 2.09; Br, 45.18; Te, 24.05. Found: C, 22.65; H, 2.13; Br, 45.09; Te, 23.92.

Tribromo(2-carbethoxybenzyl)tellurium from 2-Carbethoxybenzyl Tellurocyanate. To 2-carbethoxybenzyl tellurocyanate (0.22 g, 0.69 mmol) in CCl_4 (20 mL) cooled to −23 °C was added bromine (0.22 g, 1.38 mmol) in CCl_4 (2 mL) dropwise during 20 min. After 15 min CH_2Cl_2 (5 mL) was added and the cooling bath was removed. After 15 min at room temperature the orange homogeneous solution was evaporated to give a yellow solid. Recrystallization from CH_3CN afforded 0.23 g (63%) of tribromo(2-carbethoxybenzyl)tellurium, identical in all respects with the compound described above.

Reduction of [2-(Bromocarbonyl)benzyl]telluryl Bromide (5b) with $Na_2S_2O_5$. [2-(Bromocarbonyl)benzyl]telluryl bromide (237 mg, 0.58 mmol) was added to a separatory funnel containing ethyl ether (25 mL) and $Na_2S_2O_5$ (1.0 g, 5.3 mmol) in water (25 mL). The two phases were shaken until all material was dissolved (a small amount of tellurium is formed). The organic phase was separated, washed with Na_2CO_3 (5% aqueous), dried, and evaporated. Filtration through a small column (SiO_2, CH_2Cl_2) afforded 65 mg (45%) of tellurophthalide (**1c**), identical with the material prepared above.

Conversion of [2-(Bromocarbonyl)benzyl]telluryl Bromide (5b) to 2-Carbethoxybenzyl Tellurocyanate (8). [2-(Bromocarbonyl)benzyl]telluryl bromide (freshly prepared, 0.52 g, 1.28 mmol) was dissolved in EtOH (10 mL) with stirring to produce a dark solution that was added dropwise to a suspension of KCN (0.30 g, 4.6 mmol) in Me_2SO (5 mL). The resulting yellow solution was stirred for 30 min and poured into water (50 mL)/ethyl ether (50 mL). The organic phase was extracted several times with water, dried ($CaCl_2$), and evaporated to give 0.28 g (69%) of 2-carbethoxybenzyl tellurocyanate as an oil that crystallized upon standing, identical in all respects with an authentic sample of **8** (vide infra).

[2-(Chlorocarbonyl)benzyl]telluryl chloride and [2-(iodocarbonyl)benzyl]telluryl iodide were similarly converted into 2-carbethoxybenzyl tellurocyanate in 33% and 44% yield, respectively.

Chlorination of 2,5-Dioxo-2,5-dihydrobenzo[*c*]tellurophene (6). Dry chlorine gas was slowly bubbled through a solution of 2,5-dioxo-2,5-dihydrobenzo[*c*]tellurophene (0.20 g, 0.77 mmol) in CCl_4 (10 mL) kept under N_2. An immediate precipitation of elemental tellurium was observed and the yellow solution turned colorless. The introduction of chlorine was interrupted when some white tellurium tetrachloride, a further oxidation product, could be seen on top of the fluffy precipitate of elemental tellurium. Filtration and evaporation gave a quantitative yield of *o*-phthaloyl chloride (**7**), identical with a commercial sample.

2-Thio-2,5-dihydrobenzo[*c*]tellurophene (14). Tellurophthalide (1.50 g, 6.1 mmol) was refluxed for 2 h in benzene (100 mL) with the dimer of (*p*-methoxyphenyl)thioxophosphine sulfide (1.35 g, 3.3 mmol). The dark-green solution was then evaporated and the residue filtered through a SiO_2 column (CH_2Cl_2). Evaporation and recrystallization from hexane afforded 0.99 g (62%) of compound **14** as a dark-green, highly crystalline compound: mp 96–98 °C; NMR δ 5.14 (s, 2 H), 7.23–7.30 (m, 1 H), 7.50–7.61 (several peaks, 2 H), 8.13 (d, 1 H); mass spectrum, *m/e*

(relative intensity) 264 (5), 134 (48), 130 (14), 81 (100). Anal. Calcd for C_8H_6STe: C, 36.70; H, 2.31; S, 12.25; Te, 48.74. Found: C, 36.47; H, 2.43; S, 12.42; Te, 48.60.

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Registry No. **1c**, 78482-05-0; **2a**, 7115-90-4; **2b**, 40819-28-1; **5a**, 78763-90-3; **5b**, 78763-91-4; **5c**, 78763-92-5; **6**, 69246-89-5; **7**, 88-95-9; **8**, 78763-93-6; **9**, 7115-91-5; **10a**, 78763-94-7; **10b**, 78763-95-8; **13**, 19172-47-5; **14**, 78763-96-9.

Extension of the Nenitzescu Reaction to a Cyclic Enamino Ketone. One-Step Synthesis of 6-Hydroxy-9*H*-pyrimido[4,5-*b*]indole-2,4-dione

Jean-Luc Bernier and Jean-Pierre Hénichart*

INSERM U-16, 59045 Lille, Cédex, France

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A new one-step synthesis of the 6-hydroxypyrimido[4,5-*b*]indole ring involving the condensation of *p*-benzoquinone with 1,3-dimethyl-6-aminouracil has been reported. This procedure, an extension of the Nenitzescu reaction, was compared to a more classical Fischer-type cyclization. In both reactions, intermediates have provided useful mechanistic information. When nitromethane was used as a solvent, this new Nenitzescu-type synthesis conclusively appeared to present some advantages, including simplicity and a relatively good yield.

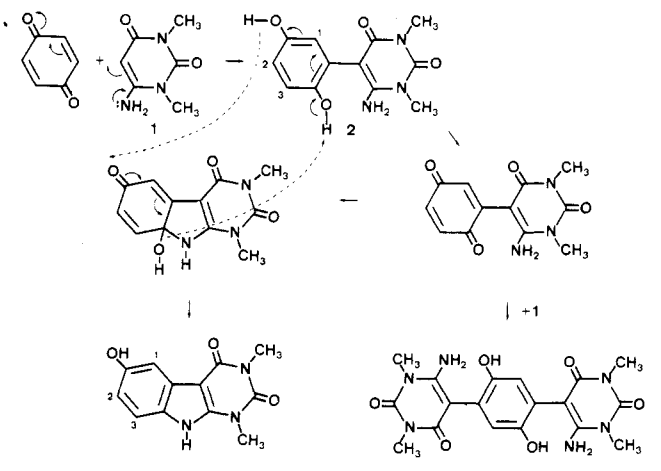
The study of polycyclic DNA-intercalative drugs has been a matter of significant interest for several years. Recently, we have described an approach to a number of 6-hydroxycarbazoles[1] related to the well-known antileukemic 9-hydroxyellipticine.[2] We have also investigated the biological properties of 5-acyl-6-aminouracil derivatives in relation to their structural features.[3]

These initial findings prompted us to include the pyrimidine moiety in a tricyclic system in order to enhance both intercalative and antitumor properties. For this purpose, we have carried out a one-step synthesis of 6-hydroxy-9*H*-pyrimido[4,5-*b*]indole-2,4-dione starting from 1,3-dimethyl-6-aminouracil (1) and *p*-benzoquinone (PBQ) and using either acetic acid or nitromethane as the solvent. In fact, three compounds have been isolated: the hydroquinone **2**, the expected product **3**, and the diadduct **4** (see Scheme I).

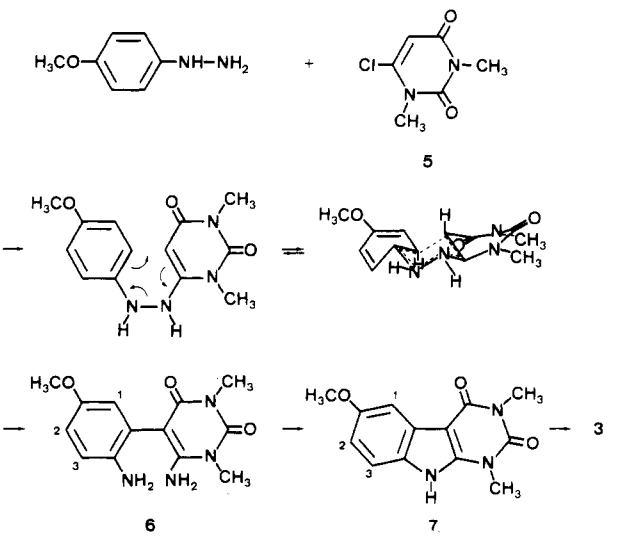
This reaction could be presented as a novel application to the cyclic enamine **1** of the Nenitzescu reaction[4] whose extension to aromatic amines has been recently described.[1a] As demonstrated for classical hydroxyindole synthesis, the reaction presumably proceeds via a Michael addition followed by several steps including an internal oxidation–reduction.[5]

The initial carbon–carbon attack has been clearly demonstrated by the formation of a stable intermediate **2** and

Scheme I



Scheme II



of the diadduct **4**, which is in accordance with previously proposed mechanisms.[6] Furthermore, it is noteworthy

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