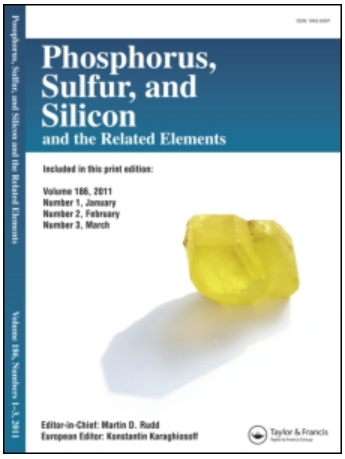

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Synthesis and Reactivity of Mannich Bases. XVIII. Reaction of Dithiocarbamic Acid Salts With Mannich Bases Derived from *Ortho*-Hydroxyacetophenones

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SYNTHESIS AND REACTIVITY OF MANNICH BASES. XVIII. REACTION OF DITHIOCARBAMIC ACID SALTS WITH MANNICH BASES DERIVED FROM *ORTHO*-HYDROXYACETOPHENONES

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(Received April 10, 2003)

The reaction of Mannich bases derived from ortho-hydroxyacetophenones with N,N-dialkyldithiocarbamic acid salts result in the formation of the corresponding dithiocarbamic acid esters via an amine moiety replacement when the process is conducted in cold water. Attempts to carry out the synthesis in refluxing ethanol-water mixture led to the insertion of carbon sulfide at the C—N bond in Mannich bases. N-Aryldithiocarbamic acid salts afforded on reaction with the above-mentioned Mannich bases only bis-(2-(2-hydroxybenzoyl)ethyl)thioethers.

Keywords: Dithiocarbamates; exchange reaction; Mannich bases; ortho-hydroxyacetophenones; S-alkylation

The replacement of the amine group in Mannich bases, which also may be formally regarded as an x-alkylation of a nucleophilic reactant XH by the R—CH_2—moiety of the Mannich base, is one of the most synthetically valuable feature of these compounds' chemistry.[1–3] *S*-Alkylations with Mannich bases provide an easy access to thioethers, thiocarbamic acid esters, sulfones, etc., frequently displaying structures otherwise difficultly to obtain. As it concerns the preparation of dithiocarbamic esters from Mannich bases, the retrosynthetic analysis shows a second possible way, namely the insertion of CS_{21} between the methylene and the amino group in Mannich bases (**b**), besides the replacement of the amine group by a dithiocarbamate anion in an aminomethylation product (**a**) (Scheme 1).

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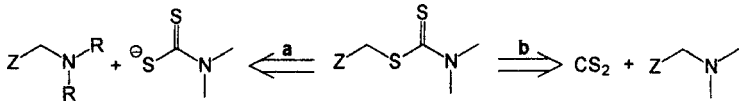
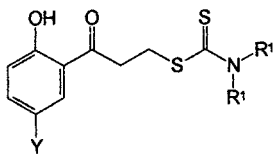


SCHEME 1 Retrosynthetic analysis for the synthesis of dithiocarbamic esters derived from Mannich bases.

The former way usually is employed when Mannich bases are easily available as salts (the case of β-aminoketones) and exceeds the latter route in versatility as it allows the preparation of a wide range of variously N-substituted and N,N-disubstituted dithiocarbamates. Disconnection **b** may be adopted in the case of Mannich bases as free amines (that readily result from phenols, for example) and produces only dithiocarbamic esters that retain the amine group in the initial Mannich base. Both procedures have been scarcely used[4–7] for the preparation of such esters that may act as fungicides[4] or as antioxidizing agents.[8]

Continuing our investigation on the replacement of the amine group in β-aminoketones with nucleophiles,[9–15] this article explores the reaction between Mannich bases derived from *ortho*-hydroxyacetophenones and several dithiocarbamic acid salts. The choice of this particular type of Mannich bases is justified if one takes into account the ability of the resulting dithiocarbamic esters to form with transitional metal cations the complexes **2** ($Me^{II} = Cu^{2+}$, Zn^{2+}, Ni^{2+}, etc), which may exhibit an enhanced potential fiuigitoxic activity when compared to the ligands **1**.



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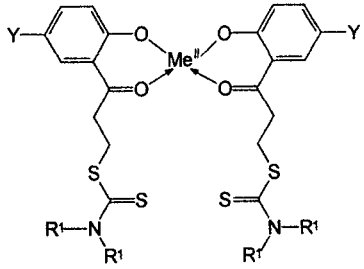
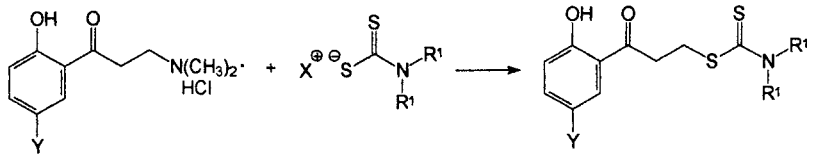


2

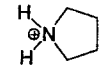
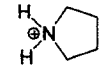
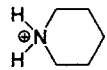
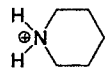
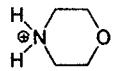
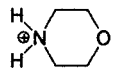
RESULTS AND DISCUSSION

N,N-Dialkyldithiocarbamic acid salts **4a–d** reacted with Mannich bases derived from *ortho*-hydroxyacetophenones **3** and offered easy access to the expected dithiocarbamic acid esters **1a–h**, as described in Scheme 2.

S-Alkylations may proceed either by a nucleophilic substitution mechanism or via a tandem elimination-addition mechanism, as in the case of an amine exchange reaction. In the first approach, the



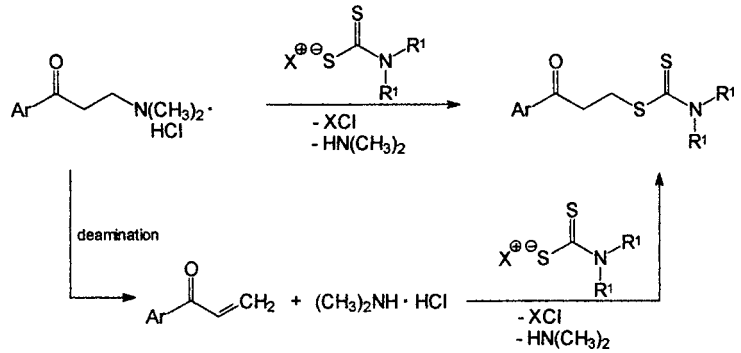
3a,b **4a-d** **1a-h**

Compound	Y	R^1	R^1	X^+
a	H	$-CH_2CH_2CH_2CH_2-$		
b	CH_3	$-CH_2CH_2CH_2CH_2-$		
c	H	$-CH_2CH_2CH_2CH_2CH_2-$		
d	CH_3	$-CH_2CH_2CH_2CH_2CH_2-$		
e	H	$-CH_2CH_2OCH_2CH_2-$		
f	CH_3	$-CH_2CH_2OCH_2CH_2-$		
g	H	$-CH_2CH_3$	$-CH_2CH_3$	Na^+
h	CH_3	$-CH_2CH_3$	$-CH_2CH_3$	Na^+

SCHEME 2 Synthesis of S-(2-(2-hydroxybenzoyl)ethyl)dithiocarbamates from the reaction of Mannich bases derived from *ortho*-hydroxyacetophenones and N,N-dialkyldithiocarbamic acid salts.

nucleophilic dithiocarbamate anion may attack the easily displaceable amino moiety of the Mannich base in a classical SN2 mechanism. The second alternative involves the formation of an α,β-unsaturated ketone after the elimination of the amine hydrochloride, followed by the addition of the dithiocarbamate anion (Scheme 3).

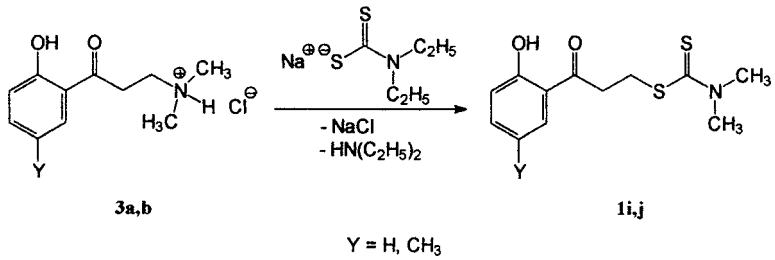
The reaction has been conducted in water at room temperature. By simply adding the solution of the N,N-dialkyldithiocarbamic acid salt **4a–d** to the solution of the Mannich base hydrochloride **3**, an emulsion started to form that later turned into a solid. In most cases, a reaction period of three to four hours offered the necessary time for crystals' formation in a reasonable yield. However, as in the case of



SCHEME 3 Alternative bimolecular nucleophilic substitution and elimination-addition pathways leading to esters **1**.

amine exchange reaction of Mannich bases with piperazines,[13] it has been noticed that the longer the reaction times the better the yields and the purer the reaction products. The yields of the pure esters are dramatically lowered after recrystallization (from 70–80% to 30–40%).

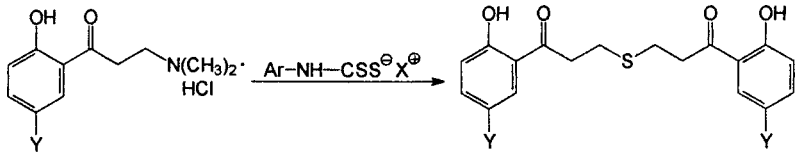
Previous studies have shown that *N*-alkylations with ketonic Mannich bases occur smoothly in a 1:1 (v/v) ethanol-water mixture at reflux when arylamines[9,10] or NH-heterocycles[12,14,15] were employed as nucleophiles. Reaction of 3-(dimethylamino)-l-(2-hydroxy-5-methylphenyl)propan-1-one hydrochloride **3b** and sodium N,N-diethyldithiocarbamate was also attempted under the same conditions. In this case, the reaction product was not the expected S-(2-(2-hydroxy-5-methylbenzoyl)ethyl)-N,N-diethyldithiocarbamate, but S-(2-(2-hydroxy-5-methylbenzoyl)ethyl)-N,N-dimethyldithiocarbamate **1j**, that may have resulted by the insertion of carbon disulfide to the C—N bond in Mannich base (Scheme 4). Moreover, when 1-(2-hydroxyphenyl)-3-(4-morpholinyl)-1-propanone hydrochloride[11] and ammonium N-(2-methylphenyl)dithiocarbamate **4f** were reacted in aqueous ethanol at



SCHEME 4 S-(2-(2-Hydroxybenzoyl)ethyl)dithiocarbamates from the insertion of CS_2 at C—N bond in Mannich bases derived from *ortho*-hydroxyacetophenones.

reflux, the insertion of carbon disulfide occurred to produce a substance presenting the same physical and spectroscopic features as the dithiocarbamic ester **1c**, resulted from the *S*-alkylation of 4-morpholinecarbodithioic acid salt with dimethylamine Mannich base at room temperature. Carbon disulfide was probably generated in situ from the partial decomposition of the dithiocarbamic acid salt on boiling, thus accounting for the modest yields recorded. A similar result was previously noted when β-morpholinopropiophenone hydrochloride was reacted with carbon disulfide in aqueous ammonia.[4]

Ammonium N-phenyldithiocarbamate **4e** gave on treatment with Mannich bases **3a,b** in water at room temperature the symmetrical thioethers **5a,b**, and not the expected dithiocarbamic esters (Scheme 5). Reaction of 3-dimethylamino-1-(2-hydroxyphenyl)propan-1-one hydrochloride **3a** either with ammonium N-(2-methylphenyl)dithiocarbamate **4f** or with triethylammonium N-(2-pyridyl)dithiocarbamate **4g** afforded the same thioether **5a** having two identical 2-hydroxybenzoylethyl) radicals. In a similar manner, 3-dimethylamino-l-(2-hydroxy-5-methylphenyl)propan-l-one hydrochloride **3b** provided access only to bis-[2-(2-hydroxy-5-methylbenzoyl)ethyl]thioether **5b** regardless of the N-aryldithiocarbamic acid salt **4e–g** employed in the reaction.



SCHEME 5 Synthesis of thioeters **5** from Mannich bases derived from *ortho*-hydroxyacetophenones and salts of N-aryldithiocarbamic acids.

IR spectra recorded for all newly synthesized esters **1** and thioethers **5** exhibit a strong $\nu_{C=O}$ peak at 1650 cm^{-1}, corresponding to a carbonyl group involved in a hydrogen bond with the neighbouring phenolic hydroxyl. Several other medium to strong IR absorption bands were also identified and attributed to the dithiocarbamate remainder in esters **1**.

^{1}H- and ^{13}C-NMR spectra confirmed the structure of the esters **1** and thioethers **5**. The two methylene groups always gave clear triplets in all spectra recorded. While the correct signals for the protons in the amine moiety of the dithiocarbamic group were identified in the aliphatic region of the ^{1}H-NMR spectra for compounds **1**, no peak was noticed in

this region of the ^{1}H-NMR spectra of thioethers **5**. The accurate number of signals in the ^{13}C-NMR spectra of substances **1** and **5** were discriminated for all carbon atoms. The signal at about 197 ppm offered evidence for the presence of a new carbon atom from the dithiocarbamate moiety in the structure of esters **1**, whereas this signal was absent in the case of thioethers **5**. Both types of compounds presented a peak above 200 ppm corresponding to the carbon atom of the carbonyl group.

EXPERIMENTAL

Melting points were determined on a Boëtius hot-stage microscope and are uncorrected. IR spectra were taken on a Specord M80 apparatus in KBr pellets. ^{1}H- and ^{13}C-NMR spectra were recorded on a Varian INOVA 300 instrument in $CDCl_3$. All chemical shifts are reported in ppm downfield from tetramethylsilane; the coupling constants (J) are given in Hz.

3-Dimethylamino-1-(2-hydroxyphenyl)propan-1-one hydrochloride **3a**[11] and 3-dimethylamino-1-(2-hydroxy-5-methylphenyl)propan-1-one hydrochloride **3b**[16] were prepared as described. Except for the commercially available sodium N,N-diethyldithiocarbamate trihydrate **4d** (UCB-Belgia), all other dithiocarbamic acid salts **4** were generally prepared from the corresponding amine and CS_2 in the presence of a base. Dithiocarbamic acid salts derived from pyrrolidine, piperidine and morpholine **4a–c** were all synthesized in the same manner,[17] the base used in each of these three cases being the cyclic amine itself. Ammonium N-phenyldithiocarbamate **4e** and ammonium N-(2-methylphenyl)dithiocarbamate **4f** were obtained through the same known procedure,[18] by reacting CS_2 with aniline and *ortho*-toluidine respectively in the presence of ammonium hydroxide. Another literature method[19] was applied for the synthesis of triethylammonium N-(2-pyridy)dithiocarbamate **4g**, when the base employed was triethylamine. All amines used in these syntheses, CS_2 and all other required reagents were commercially available products and were used without prior purification.

Synthesis of Dithiocarbamic Acid Esters 1 Through Amine Moiety Replacement—General Procedure

Mannich base hydrochloride **3** (5 mmol) was dissolved in water (20 mL) and the resulting solution was added to the solution of the N,N-dialkyldithiocarbamic acid salt **4a–d** (5 mmol) in water (20 mL) with good stirring. The esters **1** immediately separated as an emulsion that

soon turned into a solid product. After being stirred for 3–4 h, the reaction mixture was left at room temperature overnight. The dithiocarbamic acid esters were filtered, washed with plenty of water and recrystallized from the appropriate solvent.

S-(3-(2-Hydroxyphenyl)-3-oxopropyl) Pyrrolidine-1-carbodithioate 1a

Yield 0.52 g (35%), m.p. 115–116°C (ethanol). **IR** (KBr, cm^{-1}): 1170, 1290, 1445 and 1495 (–S–(C=S)–N< group); 1640 ($\nu_{C=O}$). **^{1}H-NMR** ($CDCl_3$, δ): 1.96–2.10 (m, 4H, $-CH_2CH_2-$); 3.56 (t, 2H, $J = 6.6$ Hz, $-COCH_2-$); 3.72 (t, 2H, $J = 6.6$ Hz, $-CH_2S-$); 3.64 and 3.94 (t, 2H, $J = 6.5$ Hz, $-N(CH_2-)$); 6.88–6.93 (m, 1H); 6.98 (d, IH, $J_{1,2} = 8.4$ Hz); 7.45–7.50 (m, 1H); 7.81 (dd, 1H, $J_{1,2} = 8$ Hz, $J_{1,3} = 1.3$ Hz); 12.16 (s, 1H, Ar–OH). **^{13}C-NMR** ($CDCl_3$, δ): 24.48 and 26.25 ($-CH_2CH_2-$); 30.13 ($-CH_2S-$); 38.58 ($-CO\underline{C}H_2-$); 50.86 and 55.27 ($-N(CH_2-)_2$); 118.06, 118.64, 119.24, 130.29, 136.72, 162.34 (aromatic carbon atoms); 197.08 (>C=S); 204.32 (>C=O). Anal. calcd. for $C_{14}H_{17}NO_2S_2$ (295): C 56.92, H 5.80, N 4.74; found C 57.06, H 5.97, N 4.59.

S-(3-(2-Hydroxy-5-methylphenyl)-3-oxopropyl) Pyrrolidine-1-Carbodithioate 1b

Yield 0.82 g (53%). m.p. 131–132°C (ethanol). **IR** (KBr, cm^{-1}): 1170, 1290, 1445 and 1490 (–S–(C=S)–N< group); 1645 ($\nu_{C=O}$). **^{1}H-NMR** ($CDCl_3$, δ): 1.98–2.08 (m, 4H, $-CH_2CH_2-$); 2.30 (s, 3H, Ar–CH_3); 3.54 (t, 2H, $J = 6.6$ Hz, $-COCH_2-$); 3.71 (t, 2H, $J = 6.6$ Hz, $-CH_2S-$); 3.64 and 3.94 (t, 2H, $J = 6.5$ Hz, $-N(CH_2-)_2$); 6.88 (d, 1H, $J = 8.5$ Hz); 7.28 (dd, 1H, $J_{1,2} = 8.5$ Hz, $J_{1,3} = 0.7$ Hz); 7.6 (bs, 1H); 12.02 (s, 1H, Ar–OH). **^{13}C-NMR** ($CDCl_3$, δ): 20.67 (Ar–CH_3); 24.47 and 26.24 ($-CH_2CH_2-$); 30.18 ($-CH_2S-$); 38.63 ($-CO\underline{C}H_2-$); 50.85 and 55.27 ($-N(CH_2-)_2$); 118.35, 118.86, 128.28, 129.98, 137.76, 160.41 (aromatic carbon atoms); 196.88 (>C=S); 203.94 (>C=O). Anal. calcd. for $C_{15}H_{19}NO_2S_2$ (309): C 58.22, H 6.19, N 4.53; found C 58.03, H 6.27, N 4.62.

S-(3-(2-Hydroxyphenyl)-3-oxopropyl) Piperidine-1-carbodithioate 1c

Yield 0.37 g (24%), m.p. 103–104°C (ethanol). **IR** (KBr, cm^{-1}): 1165, 1250, 1450 and 1495 (–S–(C=S)–N< group); 1650 ($\nu_{C=O}$). **^{1}H-NMR** ($CDCl_3$, δ): 1.63 (bs, 6H, $-CH_2CH_2CH_2-$); 3.49 (t, 2H, $J = 6.4$ Hz, $-COCH_2-$); 3.65 (t, 2H, $J = 6.6$ Hz, $-CH_2S-$); 3.81 and 4.22 (bs, 2H + 2H, $-N(CH_2-)_2$); 6.81–6.86 (m, 1H); 6.91 (d, 1H, $J_{1,2} = 8.4$ Hz); 7.38–7.43 (m, 1H); 7.73 (dd, 1H, $J_{1,2} = 8$ Hz, $J_{1,3} = 1.3$ Hz); 12.09 (s, 1H, Ar–OH). **^{13}C-NMR** ($CDCl_3$, δ): 24.03, 25.27, 25.73 ($-CH_2CH_2CH_2-$); 30.37 ($-CH_2S-$); 38.15 ($-CO\underline{C}H_2-$); 51.13 and 52.76 ($-N(CH_2-)_2$);

118.17, 118.83, 119.07, 129.90, 136.28, 162.05 (aromatic carbon atoms); 196.73 (>C=S); 204.30 (>C=O). Anal. calcd. for $C_{15}H_{19}NO_2S_2$ (309): C 58.22, H 6.19, N 4.53; found C 58.37, H 6.02, N 4.62.

S-(3-(2-Hydroxy-5-methylphenyl)-3-oxopropyl) Piperidine-1-carbodithioate 1d

Yield 0.53 g (33%), m.p. 135–136°C (ethanol). **IR** (KBr, cm^{-1}): 1180, 1250, 1445 and 1495 (–S–(C=S)–N< group); 1650 ($\nu_{C=O}$). **^{1}H-NMR** ($CDCl_3$, δ): 1.71 (bs, 6H, $-CH_2CH_2CH_2-$); 2.30 (s, 3H, Ar–CH_3); 3.54 (t, 2H, $J = 6.6$ Hz, $-COCH_2-$); 3.72 (t, 2H, $J = 6.6$ Hz, $-CH_2S-$); 3.88 and 4.31 (bs, 2H + 2H, $-N(CH_2-)_2$); 6.89 (d, 1H, $J_{1,2} = 8.5$ Hz); 7.29 (dd, 1H, $J_{1,2} = 8.5$ Hz, $J_{1,3} = 0.7$ Hz); 7.60 (bs, 1H); 12.04 (s, 1H, Ar–OH). **^{13}C-NMR** ($CDCl_3$, δ): 20.69 (Ar–CH_3); 24.44, 25.81 and 26.21 ($-CH_2CH_2CH_2-$); 30.80 ($-CH_2S-$); 38.64 ($-CO\underline{C}H_2-$); 51.49 and 53.04 ($-N(CH_2-)_2$); 118.34, 118.92, 128.24, 130.0, 137.75, 160.38 (aromatic carbon atoms); 196.46 (>C=S); 204.53 (>C=O). Anal. calcd. for $C_{16}H_{21}NO_2S_2$ (323): C 59.41, H 6.54, N 4.33; found C 59.23, H 6.37, N 4.42.

S-(3-(2-Hydroxyphenyl)-3-oxopropyl) Morpholine-4-carbodithioate 1e

Yield 0.36 g (23%), m.p. 125–126°C (ethanol). **IR** (KBr, cm^{-1}): 1145, 1285, 1430 and 1500 (–S–(C=S)–N< group); 1650 ($\nu_{C=O}$). **^{1}H-NMR** ($CDCl_3$, δ): 3.54 (t, 2H, $J = 6.5$ Hz, $-COCH_2-$); 3.73 (t, 2H, $J = 6.6$ Hz, $-CH_2S-$); 3.75 (bs, 4H, $-N(CH_2-)_2$); 3.91 and 4.32 (bs, 2H + 2H, $(-CH_2)O$); 6.86–6.92 (m, 1H); 6.96 (d, 1H, $J_{1,2} = 8$ Hz); 7.43–7.49 (m, 1H); 7.77 (d, 1H, $J_{1,2} = 8$ Hz); 12.10 (s, 1H, Ar–OH). **^{13}C-NMR** ($CDCl_3$, δ): 30.47 ($-CH_2S-$); 38.17 ($-COCH_2-$); 50.21 and 51.35 ($-N(CH_2-)_2$); 66.31 ($-CH_2OCH_2-$); 118.33; 119.01; 119.24; 130.06; 136.42; 162.23 (aromatic carbon atoms); 196.91 (>C=S); 204.44 (>C=O). Anal. calcd. for $C_{14}H_{17}NO_3S_2$ (311): C 53.99, H 5.50, N 4.50; found C 53.87, H 5.57, N 4.60.

S-(3-(2-Hydroxy-5-methylphenyl)-3-oxopropyl) Morpholine-4-carbodithioate 1f

Yield 0.63 g (39%), m.p. 155–156°C (ethanol). **IR** (KBr, cm^{-1}): 1130, 1280, 1430 and 1500 (–S–(C=S)–N< group); 1650 ($\nu_{C=O}$). **^{1}H-NMR** ($CDCl_3$, δ): 2.30 (s, 3H, Ar–CH_3); 3.54 (t, 2H, $J = 6.5$ Hz, $-COCH_2-$); 3.74 (t, 2H, $J = 6.6$ Hz, $-CH_2S-$); 3.75 (bs, 4H, $-N(CH_2-)_2$); 3.93 and 4.34 (bs, 2H+2H, $(-CH_2)O$); 6.88 (d, 1H, $J_{1,2} = 8.5$ Hz); 7.29 (dd, 1H, $J_{1,2} = 8.5$ Hz, $J_{1,3} = 0.8$ Hz); 7.56 (bs, 1H); 11.94 (s, 1H, Ar–OH). **^{13}C-NMR** ($CDCl_3$, δ): 20.65 (Ar–CH_3); 30.59 ($-CH_2S-$); 38.31 ($-CO\underline{C}H_2-$); 50.29 and 51.41 ($-N(CH_2-)_2$); 66.38 ($-CH_2OCH_2-$); 117.76, 119.02,

128.76, 130.43, 137.77, 160.38 (aromatic carbon atoms); 197.35 (>C=S); 204.17 (>C=O). Anal. calcd. for $C_{15}H_{19}NO_3S_2$ (325): C 55.36 H 5.88, N 4.30; found C 55.57, H 5.67, N 4.40.

S-(3-(2-Hydroxyphenyl)-3-oxopropyl) N,N-Diethyldithiocarbamate 1g

Yield 0.82 g (55%), m.p. 81–82°C (ethanol). **IR** (KBr, cm^{-1}): 1210, 1270, 1445 and 1490 (–S–(C=S)–N< group); 1645 ($\nu_{C=O}$). **^{1}H-NMR** ($CDCl_3$, δ): 1.28 (t, 6H, $J = 7.1$ Hz, $-CH_2C\underline{H}_3$); 3.55 (t, 2H, $J = 6.6$ Hz, $-COCH_2-$); 3.72 (t, 2H, $J = 6.6$ Hz, $-CH_2S-$); 4.03 (q, 4H, $J = 7.1$ Hz, $-N(CH_2-)_2$; 6.87-6.92 (m, 1H); 6.99 (d, 1H, $J_{1,2} = 8.4$ Hz); 7.44-7.50 (m, 1H); 7.81 (dd, 1H, $J_{1,2} = 8$ Hz, $J_{1,3} = 1.4$ Hz); 12.13 (s, 1H, Ar–OH). **^{13}C-NMR** ($CDCl_3$, δ): 11.77 and 12.61 ($-CH_2\underline{C}H_3$); 30.75 ($-CH_2S-$); 38.48 ($-CO\underline{C}H_2-$); 46.94 and 49.75 ($-\underline{C}H_2CH_3$);); 118.60, 119.21, 119.63, 130.30, 136.68, 162.46 (aromatic carbon atoms); 196.61 (>C=S); 204.72 (>C=O).). Anal. calcd. for $C_{14}H_{19}NO_2S_2$ (297): C 56.53, H 6.44, N 4.71; found C 56.69, H 6.36, N 4.61.

S-(3-(2-Hydroxy-5-methylphenyl)-3-oxopropyl) N,N-Diethyldithiocarbamate 1h

Yield 0.71 g (46%), m.p. 105–106°C (ethanol). **IR** (KBr, cm^{-1}): 1215, 1280, 1425 and 1500 (–S–(C=S)–N< group); 1650 ($\nu_{C=O}$). **^{1}H-NMR** ($CDCl_3$, δ): 1.28 (t, 6H, $J = 7.1$ Hz, $-CH_2C\underline{H}_3$); 2.31 (s, 3H, Ar–CH_3); 3.53 (t, 2H, $J = 6.6$ Hz, $-COCH_2-$); 3.71 (t, 2H, $J = 6.6$ Hz, $-CH_2S-$); 4.06 (q, 4H, $J = 7.1$ Hz, $-N(CH_2-)_2$; 6.89 (d, 1H, $J_{1,2} = 8.5$ Hz); 7.29 (dd, 1H, $J_{1,2} = 8.5$ Hz, $J_{1,3} = 0.9$ Hz); 7.61 (bs, 1H); 12.08 (s, 1H, Ar–OH). **^{13}C-NMR**($CDCl_3$, δ): 11.80 and 12.62 ($-CH_2\underline{C}H_3$); 20.69 (Ar–CH_3); 30.83 ($-CH_2S-$); 38.59 ($-COCH_2-$); 46.96 and 49.78 ($-\underline{C}H_2CH_3$); 118.36, 118.84, 128.36, 130.03, 137.76, 160.39 (aromatic carbon atoms); 196.22 (>C=S); 204.55 (>C=O). Anal. calcd. for $C_{15}H_{21}NO_2S_2$ (311): C 57.84, H 6.80, N 4.50; found C 58.03, H 6.61, N 4.37.

Thioethers 5 from Mannich Bases Derived from ortho-Hydroxyacetophenones and N-Aryldithiocarbamic Acid Salts 4e–g

Mannich base hydrochloride **3** (5 mmol) was dissolved in water (20 mL) and the resulting solution was added to the solution of ammonium N-phenyldithiocarbamate **4e** (or ammonium N-(2-methylphenyl)dithiocarbamate **4f**, or triethylammonium N-(2-pyridyl)dithiocarbamate **4g**) (5 mmol) in water (20 mL) with good stirring. The solid white thioethers separated immediately from the intitial emulsion. After being stirred for 3–4 h, the reaction mixture was left

at room temperature overnight. The thioethers were filtered, washed with plenty of water and recrystallized from the appropriate solvent.

1-(2-Hydroxyphenyl)-3-[3-(2-hydroxyphenyl)-3-oxopropylthio]propan-1-one 5a

Yield 36–44%, m.p. 107–108°C (ethanol). **IR** (KBr, cm^{-1}): 1650 ($\nu_{C=O}$) **^{1}H-NMR** ($CDCl_3$, δ): 2.96 (t, 4H, $J = 7.2$ Hz, $-CH_2S-$); 3.31 (t, 4H, $J = 7.2$ Hz, $-COCH_2-$); 6.86–6.91 (m, 2H); 6.96 (d, 2H, $J_{1,2} = 8.3$ Hz); 7.42–7.48 (m, 2H); 7.72 (dd, 2H, $J_{1,2} = 8.1$ Hz, $J_{1,3} = 1.1$ Hz); 12,10 (s, 2H, Ar—OH). **^{13}C-NMR** ($CDCl_3$, δ): 26.40 ($-CH_2S-$); 38.39 ($-CO\underline{C}H_2-$); 116.52, 119.00, 119.07, 129.67, 136.53, 162.31 (aromatic carbon atoms); 204.07 (>C=O). Anal. calcd. for $C_{18}H_{18}O_4S$ (330): C 65.43, H 5.49; found C 65.23, H 5.59.

1-(2-Hydroxy-5-methylphenyl)-3-[3-(2-hydroxy-5-methylphenyl)-3-oxopropylthio]propan-1-one 5b

Yield 37–54%, m.p. 109–110°C (ethanol). **IR** (KBr, cm^{-1}): 1650 ($\nu_{C=O}$). **^{1}H-NMR** ($CDCl_3$, δ): 2.27 (s, 6H, Ar—CH_3); 2.94 (t, 4H, $J = 7.2$ Hz, $-CH_2S-$); 3.29 (t, 4H, $J = 7.2$ Hz, $-COCH_2-$); 6.84 (d, 2H, $J_{1,2} = 8.4$ Hz); 7.25 (d, 2H, $J_{1,2} = 8.4$ Hz); 7.48 (s, 2H); 11.91 (s, 2H, Ar—OH). **^{13}C-NMR** ($CDCl_3$, δ): 20.48 (Ar—CH_3); 26.41 ($-CH_2S-$); 38.40 ($-CO\underline{C}H_2-$); 118.29, 118.75, 128.14, 129.36, 137.62, 160.27 (aromatic carbon atoms); 203.96 (>C=O). Anal. calcd. for $C_{20}H_{22}O_4S$ (358): C 67.01, H 6.19; found C 66.81, H 6.27.

Insertion of CS_2 at the C–N Bond in Mannich Bases Derived from ortho-Hydroxyacetophenones

Mannich base hydrochloride **3** (5 mmol) and sodium N,N-diethyldithiocarbamate trihydrate **4d** (1.125 g, 5 mmol) were refluxed for 1 h in 12 mL 1:1 (v/v) ethanol-water mixture. The reaction mixture was cooled to room temperature and set aside. The clear supernatant was removed and the remaining oily product was stirred with a little cold ethanol until crystallization occurred. The solid was filtered off and recrystallized from the appropriate solvent to give pure esters **1i** and **1j**.

S-(3-(2-Hydroxyphenyl)-3-oxopropyl) N,N-Dimethyldithiocarbamate 1i

Yield 0.16 g (12%), m.p. 131–132°C (ethanol). **IR** (KBr, cm^{-1}): 1155, 1285, 1380 and 1495 ($-S-(C=S)-N<$ group); 1650 ($\nu_{C=O}$). **^{1}H-NMR** ($CDCl_3$, δ): 3.36 and 3.56 (bs, 3H + 3H, $-N(CH_3)_2$); 3.55 (t, 2H, $J = 6.4$ Hz, $-COCH_2-$); 3.70 (t, 2H, $J = 6.6$ Hz, $-CH_2S-$); 6.87-6.92 (m, 1H);

6.98 (d, 1H, $J_{1,2} = 8.4$ Hz); 7.44-7.50 (m, 1H); 7.79 (dd, 1H, $J_{1,2} = 8$ Hz, $J_{1,3} = 1.5$ Hz); 12.10 (s, 1H, Ar—OH). **^{13}C-NMR** ($CDCl_3$, δ): 31.14 (—CH_2S—); 38.32 (—CO$\underline{C}H_2$—); 41.69 and 45.58 (—N(CH_3)$_2$); 118.61, 119.22, 119.64, 130.23, 136.70, 162.46 (aromatic carbon atoms); 196.89 (>C=S); 204.57 (>C=O). Anal. calcd. for $C_{12}H_{15}NO_2S_2$ (269); C 53.50, H 5.61, N 5.20; found C 53.54, H 5.43, N 5.27.

S-(3-(2-Hydroxy-5-methylphenyl)-3-oxoprophyl) N,N-Dimethyldithiocarbamate 1j

Yield 0.47 g (30%), m.p. 150–151°C (acetone). **IR** (KBr, cm^{-1}): 1180, 1290, 1380 and 1500 (—S—(C=S)—N< group); 1650 ($\nu_{C=O}$). **^{1}H-NMR** ($CDCl_3$, δ): 2.24 (s, 3H, Ar—CH_3); 3.30 and 3.50 (bs, 3H + 3H, —N(CH_3)$_2$); 3.46 (t, 2H, $J = 6.5$ Hz, —$COCH_2$—); 3.63 (t, 2H, $J = 6.6$ Hz, —CH_2S—); 6.82 (d, 1H, $J_{1,2} = 8.5$ Hz); 7.22 (dd, 1H, $J_{1,2} = 8.4$ Hz, $J_{1,3} = 1.9$ Hz); 7.52 (s, 1H); 11.90 (s, 1H, Ar—OH). **^{13}C-NMR** ($CDCl_3$, δ); 20.89 (Ar—CH_3); 31.44 (—CH_2S—); 38.62 (—CO$\underline{C}H_2$—); 41.91 and 45.80 (—N(CH_3)$_2$); 118.56, 119.30, 128.57, 130.16, 137.98, 160.59 (aromatic carbon atoms); 197.17 (>C=S); 204.63 (>C=O). Anal. calcd. for $C_{13}H_{17}NO_2S_2$ (283): C 55.09, H 6.05, N 4.94; found C 54.94, H 6.13, N 4.87.

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