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THE REACTION OF *t*-BUTYL HYPOCHLORITE WITH THIOCARBONYL COMPOUND - A CONVENIENT METHOD FOR THE >C=S → >C=O TRANSFORMATION

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Abstract - The reaction of *t*-butyl hypochlorite with different thiocarbonyl compounds has been studied. Primary thioamides 1a-c give 1,2,4-thiadiazole derivatives. N-Phenylthiourea 4a gives 5-imino-4-phenyl-3-phenylamino-4,5-dihydro-1,2,4-thiadiazoline 15. Secondary and tertiary thioamides 2a-d, N-methyl-2-thiopyrrolidinone 3, N,N'-dicyclohexylthiourea 4b, N,N,N'-trimethylthiourea 4c, 5-ethyl-5-phenylthiobarbituric acid 5, xanthione 7a, Michler's ketone 7b, thiocoumarin 8, O-ethylthiobenzoate 9, O,O-diphenylthiocarbonate 10, di-*p*-tolyl and o-phenylene trithiocarbonates 11 and 12 have all afforded the oxygen analogues. N,N-Dimethyl-S-phenyldithiocarbonate 6 produces a mixture of di-, tri-, and tetrasulfides. A mechanism for the >C=S → >C=O transformation is suggested in accordance with the Hard and Soft Acids and Bases (HSAB) principle.

The transformation of thiocarbonyl compounds to their corresponding oxygen analogues has received considerable attention during recent years. Different methods are known, including sodium nitrite and N-nitrosamines in aqueous acid solution,[1,2] potassium-*t*-butoxide,[3] sodium ethoxide,[3] sodium hydroxide under conditions of phase transfer catalysis,[3] DMSO/acids,[4,5] DMSO/I_2,[6] bis-(*p*-methoxyphenyl) telluroxide,[7] benzene seleninic anhydride,[8] diaryl- and dimethyl selenoxide[9,10] and Ag^+ in dioxane/water.[11,12] Recently, trimethylphosphide and iron pentacarbonyl have also been used for this transformation.[13]

In recent papers[1,2,14] the HSAB principle[15] was introduced for an understanding of the >C=S → >C=O transformation, assuming that the borderline (soft) ^+NO species attacks the soft sulfur of the thiocarbonyl group,[15] and by subsequent hydrolysis the carbonyl compound is produced. As a continuation of this work, we feel prompted to study reactions of other soft acids with thiocarbonyl compounds. It was thus decided to investigate *t*-butyl hypochlorite (*t*-BuOCl), a source of Cl^+, the borderline soft acid.[16] It should be noticed that *t*-BuOCl is of relatively high stability and easy to prepare.[17]

Literature search revealed that in a recent patent[18] some thioureas have been transformed into their corresponding oxygen analogues using *t*-BuOCl. N-Bromosuccinimide converts the same substrates mainly to the corresponding carbodiimides beside small yield of urea derivatives.[19]

This paper presents the transformation of thiocarbonyl compounds into the corresponding oxygen analogues using *t*-BuOCl in anhydrous tetrachloromethane for a variety of thiocarbonyl compounds. Mechanisms for the formation of 1,2,4-thiadiazoles and for the >C=S → >C=O trans-

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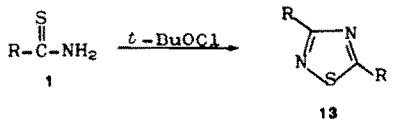
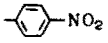
formation are presented.

RESULTS AND DISCUSSION

Primary thioamides 1a-c react with *t*-BuOCl in anhydrous CCl_4 to give 1,2,4-thiadiazole derivatives 13a-c of which 13a and c are known[20,21] and are identical in all aspects with authentic samples. High yields of 13a and b are found

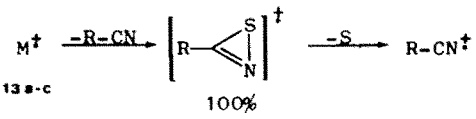


1 13

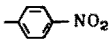
a: R = Ph
b: R = 
c: R = CH_3

(> 93%), whereas 13c is isolated in 52% yield (Table I).

In M.S. the molecular ions are always observed and the loss of nitrile followed by sulfur expulsion are also typical fragmentations.



13a-c 100%

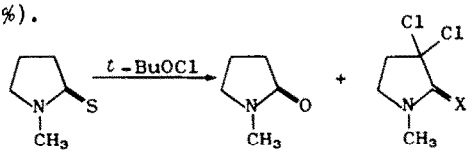
a: R = Ph
b: R = 
c: R = CH_3

The ^1H NMR spectrum of 13a shows the shifts of the aromatic hydrogens centered at δ 7.5, 8, and 8.33 in the ratio 3:1:1, respectively. All other spectroscopic data are also consistent with the structures[22] of 13a, 13b and 13c.

For the formation of 13 from 1 it is suggested that the first step is a soft-soft interaction between Cl^+ and the thiocarbonyl group (Scheme 1), and different mechanisms for the subsequent formation of 13 are then envisaged (*e.g.* Routes A and/or B). It should be noted that the nitrile (RCN) is always observed in these reactions.

The reaction of secondary and tertiary thioamides 2a-d with *t*-BuOCl affords their oxygen analogues (Table II).

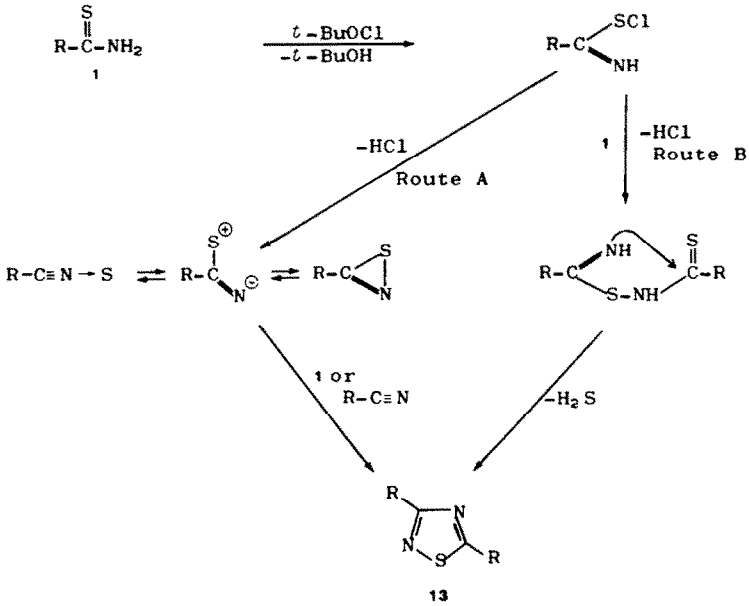
The thiolactam N-methyl-2-thiopyrrolidinone 3 gives the known oxygen analogue in 42% yield (Table II) besides the known 3,3-dichloro derivatives 14a[23] (10%) and 14b (7%).



3 14

a: X = O
b: X = S

Scheme 1



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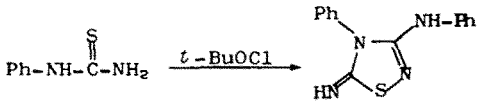
M.S. for 14a shows the molecular ion (M^+, 50%) at *m/e* 167, 169, and 171 with the isotopic ratio of two chlorine atoms, *m/e* 132 (M^+-Cl$^\cdot$, 100%), and *m/e* 110 (M^+-CH_3NCO, 40%).

The structural proofs of 14b are based on precise mass measurement for M^+, 183 (Exp.) and other spectroscopic analyses: MS shows *m/e* 183, 185, 187 (M^+ 41%) with isotopic ratio of 2 chlorine atoms, *m/e* 148 (M^+-Cl, 100%) and *m/e* 105 (36%). ^{1}H NMR ($CDCl_3$) shows peaks at 2.8-3.1 (2H, t) H4, 3.25 (3H, s) for the methyl group hydrogens, and 3.5-3.8 (2H, t) H5. The IR spectra show peaks assigned to thioamide $\underset{S}{\geqslant}C-N\lessdot$ (1525 cm^{-1}, s) and $>C=S$ (1175 cm^{-1}).[24]

Some thiourea derivatives were subjected to this study. Thus, N-phenylthiourea 4a reacts with *t*-BuOCl to give the known 5-imino-4-phenyl-3-phenylamino-4,5-dihydro-1,2,4-thiadiazoline 15 [25,26] in 46% yield. Both N,N'-dicyclohexylthiourea

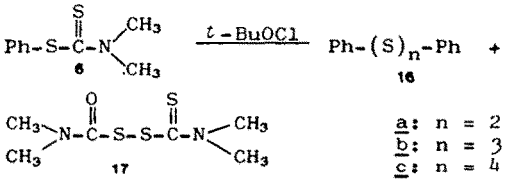


4a 15

4b and N,N,N'-trimethylthiourea 4c afford the oxygen analogues (Table II). N,N,N',N'-Tetramethylthiourea gives a complicated mixture which has not been identified.

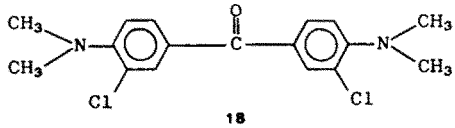
5-Ethyl-5-phenylthiobarbituric acid 5 reacts with *t*-BuOCl to give its oxygen analogue in low yield (Table II), while it is stated that under other conditions the N-chlorinated derivatives can be isolated.[27]

The reaction of N,N-dimethyl-S-phenyldithiocarbamate 6 with *t*-BuOCl produces a mixture of 51% diphenyldisulfide 16a besides traces of tri- and tetrasulfides 16b and c, and dimethylcarbamoyldimethylthiocarbomoyl disulfide 17 (17% yield).[28,29]



MS for 16b shows peaks at *m/e* 250 (M^+), 218 (M^+-S), 141 (Ph-S-S$^+$), and 109 (Ph-S$^+$). MS for 16c shows peaks at *m/e* 282 (M^+, 3%), 250 (M^+-S, 21%) 218 (M^+-2S, 91%), 186 (M^+-3S, 5%, *m/e* 141 (Ph-S-S$^+$, 45%), and 109 (Ph-S$^+$, 100%). MS for 17 shows peaks at *m/e* 224 (M^+, 4%), 192 (M^+-S, 25%), 88 (Me_2NCS^+, 56%), and 72 (Me_2NCO^+, 100%). ^{1}H NMR ($CDCl_3$) for 17 shows peaks at 3 (6H, s) $2CH_3$ attached to N-CO, 3.44 (3H, s), and 3.5 (3H, s) $2CH_3$ attached to N-CS splitted due to hindered rotation around the N-C bond. Its IR shows peaks assigned to N-H stretching (3330 cm^{-1}), C=O (1665 cm^{-1}) and $>N-\underset{|}{C}=S$ (1500 cm^{-1}).[23,28]

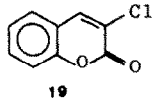
Two thioketones have been investigated: Xanthione 7a gives the oxygen analogue in quantitative yield, whereas Michler's thioketone 7b produces its oxygen analogue in 60% yield (Table II), besides 3,3'-dichloro-4,4'-bis(dimethylamino)-benzophenone 18 in 30% yield.



18

The structural proofs of 18 are based on precise mass measurement of M^+ 336, IR, NMR, and MS (Exp.)

Thiocoumarin 8 produces 64% of coumarin (Table II) and 20% of 3-chlorocoumarin 19. O-Ethyl thiobenzoate 9 on treatment with *t*-BuOCl gives excellent yield of ethyl benzoate (Table II), while



19

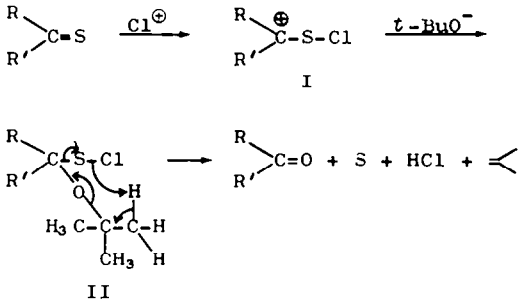
the reaction of both ethyl dithiobenzoate and dithiobutyrolactone with *t*-BuOCl give complicated reaction mixtures.

The reaction of thiocarbonates with *t*-BuOCl is not simple. O,O-Diphenyl thiocarbonate 10 produces the oxygen analogue (38%, Table II) and phenol (33%). Similarly, di-*p*-tolyl-trithiocarbonate 11 gives the oxygen analogue in low yield (33%, Table II) besides unidentified products. O-Phenylene trithiocarbonate 12 yield 55% of the oxygen analogue (Table II).

In order to elucidate the $>S \rightarrow >O$ transformation the reaction of xanthione, 7a was performed in the presence of a free

radical inhibitor: hydroquinone; the reaction is found to give the same yield as before. Furthermore, ESR analyses of the reactions of 2d and 3 with *t*-BuOCl did not indicate the presence of radicals.

The first step in the reaction is thus suggested to be the attack of the soft chlorinium ion Cl^+ on the soft sulfur in the thiocarbonyl function under the formation of the intermediate I. Subsequent attack of *t*-BuO^- gives II. The product is then formed through an intramolecular rearrangement according to the following tentative scheme:



In the reaction mixture elemental sulfur and HCl are detected. The presence of isobutylene is shown by bubling the gas into a solution of HBr in acetic acid and the presence of *t*-butyl bromide is proven by GLC.

EXPERIMENTAL

^{1}H NMR spectra were recorded at 60 MHz on a Varian EM360 spectrometer. TMS was sed as internal standards. ESR spectra were recorded on a Varian E3 EPR spectrometer. IR spectra were recorded on a Bechman IR-18 spectrometer. MS were recorded at a Micromass 7070F spectrometer operating at 70 eV using direct inlet. Microanalyses were carried out by Løvens Kemiske Fabrik, DK-2750 Ballerup (Microanalytical Lab.). The starting compounds were prepared according to known methods or were commercially available.

The >C=S → >C=O Transformation

General Procedure. If not otherwise stated, *t*-BuOCl solution (10 mmole in 5 ml dry CCl_4) is added dropwise to a solution of 10 mmole >C=S compound in 10 ml dry CCl_4 while stirring under nitrogen atmosphere at room temp. The reactions were monitored by TLC.

After the appropriate time, the reaction mixture is evaporated on silica gel and separated by column chromatography using CH_2Cl_2 as eluent followed by 2% $MeOH/CH_2Cl_2$. Always elemental sulfur S_8 was separated as the first fraction except in the case of thiocarbamates 6. where no sulfur was separated. In case of thioamides and thiourea derivatives the reaction mixture is neutralized at first with $NaHCO_3$ solution and extracted with CH_2Cl_2. The organic layer is dried with anh. $MgSO_4$, evaporated and then subjected to the column chromatography. Tables I and II indicate the reactions and yields. The products are subjected to spectroscopic analyses and mp measurements.

3,3'-Dichloro-N-methyl-2-thiopyrrolidinone 14b:

M^+ = 182.967 (Calc. 182.968).

The reaction of N,N-dimethyl-S-phenyl dithiocarbonate 6 with *t*-BuOCl

As the general procedure. Reaction time 2 hrs at r.t. Diphenyldisulfide 16a identical with authentic 16a, is isolated in 51%. Traces of diphenyltetrasulfide 16c, in all respects identical with authentic 16c, is also isolated besides of 16b, the diphenyltrisulfide (from MS and TLC). Compound 20[28,29] was isolated in 19% yield.

3,3'-Dichloro-4,4'-bis(dimethylamino-)benzophenone 18:

Waxy. M^+ = 336.079 (Calc. 336.03). ^{1}H NMR ($CDCl_3$): 2.9 (12H, s) $-CH_3$, 6.9 and 7.03 (2H, s), 5,5'H, 7.47-7.8 (4H, m), 2,2',6,6'H. MS: 336 (M^+, 100%), 301 (17%), 182 (43%, 167 (17%). IR: 1650 cm^{-1} >C=O.

TABLE I. Reaction of primary thioamides 1a-c with *t*-BuOCl under formation of 1,2,4-thiodiazoles 13a-c

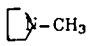
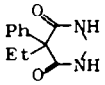
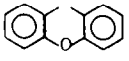
Thioamide	Reaction time (min)	Product	mp (°C)	Yield (%)
1a	5	13a	89 (lit.90)[20]	98
1b	5	13b [a]	210-211	93
1c	5 [b]	13c	(liquid) [c]	52

[a] Analyses. Found: C 50.93, H 2.62, N 16.93, S 9.71. Calc.: C 51.22, H 2.46, N 17.06, S 9.77 %

[b] Exothermic

[c] B.p. 140-145 °C.[21]

TABLE II. Experimental data for the $R^1-\overset{S}{\overset{\|}{C}}-R^2 \rightarrow R^1-\overset{O}{\overset{\|}{C}}-R^2$ transformation

Starting	R^1	R^2	React.time (hrs)	React.temp. (°C)	Yield (%)
2a	Ph	NH-Ph	3	40	95
2b	Ph-CH_2	NH-CH_2-Ph	1	40	87
2c	Ph	$N(CH_3)_2$	1	40	88
2d [b]	Ph	-N⟨O⟩	1	40	94
3			1/2	25	42 [c]
4b [a]	$C_6H_{11}NH$	$HN-C_6H_{11}$	1/6	25	81
4c [a]	$(CH_3)_2N$	$HN-CH_3$	1/2	22	40
5 [a,b]			8	40	10
7a [b]			1/6	25	100
7b [b]	*p*-$(CH_3)_2NC_6H_4$	$C_6H_4N(CH_3)_2$-*p*	5	25	60 [c]
8 [b]			1/2	25	64 [c]
9	Ph	$O-C_2H_5$	2	40	93
10	Ph-O	O-Ph	2	25	38 [c]
11 [b]	*p*-$CH_3C_6H_4S$	$S-C_6H_4CH_3$-*p*	4	25	33
12			2	25	55

[a] Few drops of absolute ethanol were added to increase the solubility.
[b] Excess (50%) of *t*-BuOCl was used.
[c] By-products have also been isolated and characterized (Text).

3-Chlorocoumarin 19:

Mp. 121 °C (lit.122-3).[27] ^{1}H NMR ($CDCl_3$): δ 7.72 (1H,s) vinylic H, 7.50-6.95 (4H,m) Ph. MS: 180 (M^+,100%), 152 (48%), 123 (38%), and 89 (55%).

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✱ NB! Correction - please read on p.1, Abstract, line 8, 'Michler's thioketone' instead of 'Michler's ketone'.

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