New Mechanism for the Reaction of Amines with Zinc Dithiocarbamates

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ABSTRACT: This article reports a detailed reinvestigation of the reaction of bis(dialkyldithiocarbamato)zinc(II) (ZDAC) with amines. The reaction of primary amines with bis(dimethyldithiocarbamato)zinc(II) (ZDMC) results in the formation of a 1,1,3-trisubstituted thiourea, a 1,3-disubstituted thiourea, dimethylammonium dimethyldithiocarbamate (DMADC), ZnS, and H_2S. The ratio of formation between the two thiourea products strongly depends on the reaction conditions chosen. A new mechanism is proposed, which involves the formation of an amine–dithiocarbamic intermediate, from which the two most important products, a 1,1,3-trisubstituted and a 1,3-disubstituted thiourea, are formed. Also, direct transformation of the 1,1,3-trisubstituted thiourea into the 1,3-disubstituted thiourea via nucleophilic attack of the primary amine onto the thiocarboxy of the 1,1,3-trisubstituted thiourea was found to occur, catalyzed by $ZnCl_2$. The reaction of primary amines with ZDACs is catalyzed by elemental sulfur, which has been attributed to sulfur insertion in the zinc–ligand ring of the ZDAC, resulting in a higher reactivity of the ZDAC complex. Finally, when ZDACs are reacted with a secondary amine, no thiourea products are formed and only a mixture of zinc dithiocarbamates is obtained. © 2000 John Wiley & Sons, Inc. J Appl Polym Sci 79: 1074–1083, 2001

Key words: zinc dithiocarbamates; amines; thioureas; sulfur; catalysis

INTRODUCTION

Recently, a new curing system was developed for unsaturated rubbers,[1] in particular for *cis*-1,4-polybutadiene (BR). This system involves the reaction of a cyclic disulfide such as 1-oxa-4,5-dithiacycloheptane in the presence of bis(dimethyldithiocarbamato)zinc(II) (ZDMC) and a primary amine, resulting in the formation of organosulfur crosslinks (Scheme 1). Preliminary results from model studies using *cis,cis,cis*-1,5,9-cyclododecatriene (*ccc*-1,5,9-CDT), a model compound for BR,

as well as from NMR studies involving BR, indicate that the crosslinks are formed via an addition mechanism.

At present, the crosslinking mechanism of the ZDMC/primary amine/cyclic disulfide curing system is largely unknown, since it is not clear which species acts as a hydron (H^+) donor to furnish the required hydrogen for this crosslink formation. However, a clue for the mechanism may be derived from the fact that optimum cure is obtained when 1 equiv of a cyclic disulfide is reacted with 1 equiv of ZDMC and 2 equiv of a primary amine. This stoichiometry would suggest that the mechanism of crosslinking depends to some degree upon the interaction of these species. Indeed, it is known that primary amines may react with zinc dialkyldithiocarbamates to yield both 1,1,3-trisubstituted and 1,3-disubstituted thiourea products.[2] A mechanism was proposed[2] which in-
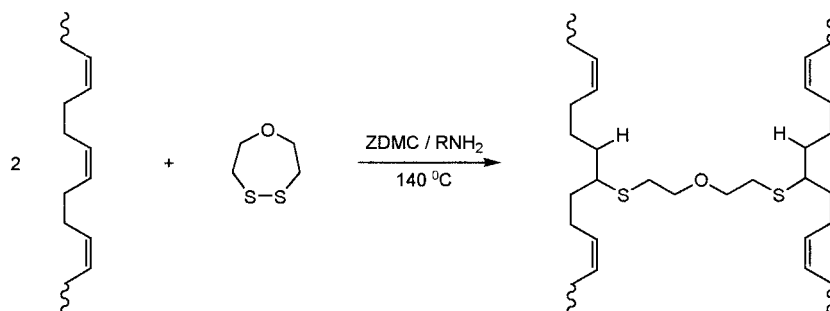
Scheme 1   Formation of a bis(alkyl) crosslink via the reaction of BR with 1-oxa-4,5-dithiacycloheptane in the presence of ZDMC and a primary amine.[1]

volves the degradation of an amine– bis(dialkyl-dithiocarbamato)zinc(II) (ZDAC) complex in one single step, as shown in Scheme 2.

Although this mechanism does explain the formation of the observed products, it may be regarded less likely, since single-step reactions leading to the formation of more than two reaction products are highly uncommon.[3] Thus, in view of the essential involvement of the ZDMC–primary amine combination in the crosslinking of rubber by cyclic disulfides, as well as the interaction of amines with ZDACs, in general, it was decided to investigate the ZDAC–amine interaction in more detail.

This article reconfirms the formation of a 1,1,3-trisubstituted thiourea, a 1,3-disubstituted thiourea, dimethylammonium dimethyldithiocarbamate (DMADC), ZnS, and H_2S, when ZDMC and primary amines are reacted and proposes a new mechanism for the reaction of amines with ZDACs. This new mechanism involves the formation of an amine–dithiocarbamic intermediate from which the two most important products, a 1,1,3-trisubstituted thiourea and a 1,3-disubstituted thiourea, are formed in the case of the reaction of a primary amine with ZDACs. On the other hand, when a ZDAC is reacted with a secondary amine, only a mixture of zinc–dithiocar-
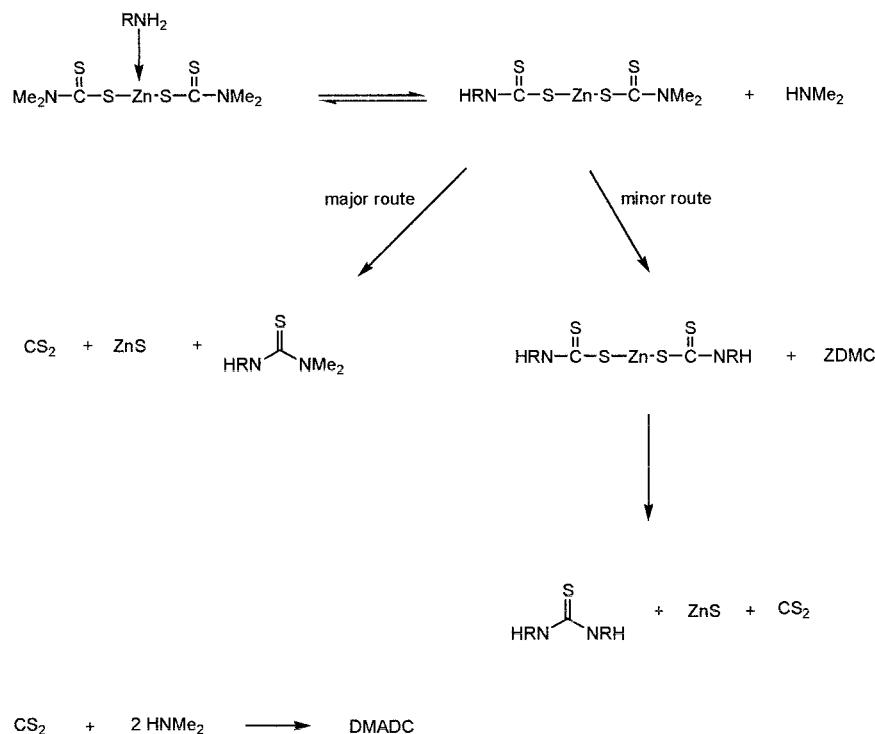
Scheme 2   Mechanism for the reaction of primary amines with ZDACs reproduced after gelling.[2]

bamate complexes is obtained and no thiourea products are formed. Tertiary amines were found not to react with ZDACs at all. An important finding appears to be that the reaction of primary amines with ZDACs is catalyzed by elemental sulfur.

EXPERIMENTAL

General

ZDMC (Aldrich, 98%) and bis(diethyldithiocarbamato)zinc(II) (ZDEC; Aldrich, 98%) were recrystallized from reagent-grade chloroform (J.T. Baker) prior to use. Reagent-grade toluene (J.T. Baker), reagent-grade dichloromethane (J.T. Baker), acetonitrile (Rathburn, HPLC grade), *n*-hexylamine (Aldrich, 99%), zinc chloride (Merck, 98%), zinc nitrate [$Zn(NO_3)_2 \cdot 6H_2O$, J. T. Baker, 99.3%], and sodium *N,N*-dibenzyldithiocarbamate (NDBC, Aldrich, 97%) were used without further purification. For reactivity experiments, stock solutions of $0.050M$ ZDAC and $0.110M$ *n*-hexylamine, dimethylamine (DMA), or triethylamine in toluene were prepared. The stock solutions were stored at -20^0C under argon.

The reactivity experiments were performed in 30-mL tailor-made Schlenk-type reaction vessels[4] equipped with Teflon valves and screw caps with Teflon inserts. Reversed-phase HPLC analyses were performed using a Gynkotek M480 ternary gradient pump equipped with a Gastorr Model GT-103 on-line degassing device, Marathon XT autoinjector, Alltech Nucleosil 100 C18 5μ stainless-steel RP-HPLC column thermostated at 30°C, and a Gynkotek HPLC UVD 320S photodiode-array detector. Methanol (Biosolve Ltd., HPLC grade) was used as the mobile phase at a volumetric flow rate of 0.45 mL min^{-1}. Data acquisition and management were performed with the Gynkosoft chromatography data system installed on a PC. ^{1}H-NMR spectra were recorded in CDCl$_3$ on a Bruker WM-300-MHz spectrometer operating at 300.13 MHz. ^{13}C-NMR spectra were recorded at 75.48 MHz. Chemical shifts are given in ppm (δ) relative to CHCl$_3$ as an internal standard for ^{1}H-NMR data and relative to CDCl$_3$ for ^{13}C-NMR data. The singlet, doublet, triplet, and multiplet peaks in the NMR spectra are abbreviated as s, d, t, and m, respectively.

Elemental analyses were performed at the Microanalytical Laboratory of the University College of Dublin or at the Leiden Institute of Chemistry (LIC). TLC analysis was carried out on DC-Alufolien (Merck, Silica gel 60 F$_{254}$) with detection by UV light. Column chromatography was performed using a Merck Kieselgel 60 (0.040–0.063 mm). A 1/1 v/v mixture of petroleum ether 40–60 (PE) and diethyl ether was used as the mobile phase. These solvents were of technical grade and were distilled prior to use. For the mathematical analyses of the results, curve fits were performed using nonlinear regression. All data including the quantification of the two thiourea products by RP HPLC could be described by one-site binding hyperbolas. These functions do not describe the kinetics of the reaction, but give an impression of the thiourea product formation in time. The vertical I beams represent the standard error measurements (SEM).

Products from the Reaction of ZDMC with *n*-Hexylamine

A solution of 2.00 mL of *n*-hexane, 0.223 g (2.20 mmol) of *n*-hexylamine, and 0.306 g (1.00 mmol) of ZDMC was stirred for 1 h at 140^{0}C in a sealed vessel, after which the reaction mixture was filtered and the solvent was removed *in vacuo*. The residue was analyzed using X-ray powder diffraction and was identified as zinc sulfide (ZnS) after comparison of the measured pattern with the data from the JCPDS–International Center for Diffraction Data.[5,6] Column chromatography of the filtrate by elution with a 1/1 v/v mixture of PE/diethyl ether gave *N*-hexyl-*N'*,*N'*-dimethylthiourea (hdmtu) **1** as a yellow oil ($R_f = 0.21$) in a yield of 64.0% (0.121 g, 0.640 mmol).

^{1}H-NMR (CDCl$_3$): $\delta = 0.83$ (t, 3H, CH$_3$), 1.26 (m, 6H, CH$_2$), 1.56 (m, 2H, NHCH$_2$C$\underline{H}_2$), 3.21 [m, 6H, N(C$\underline{H}_3$)2], 3.56 (m, 2H, NHC$\underline{H}_2$), 5.40 (s, 1H, NH). ^{13}C-NMR: $\delta = 13.64, 22.16, 26.22, 28.99, 31.14, 40.06, 45.94, 181.08$.

ANAL. Calcd for **1** (C$_9$H$_{20}$N$_2$S) (188.3): C, 57.4%; H, 10.73%; N, 14.87%; S, 17.02%. Found: C, 57.40%,; H, 10.70%; N, 14.87%; S, 17.02%.

N,N'-dihexylthiourea (dhtu) **2** was obtained as a yellow solid (R$_f$ = 0.89) in a yield of 17.2% (0.0420 g, 0.172 mmol).

^{1}H-NMR (CDCl$_3$): $\delta = 0.90$ (t, 6H, CH$_3$), 1.32 (m, 12H, CH$_2$), 1.60 (m, 4H, NHCH$_2$C$\underline{H}_2$), 3.38 (m, 4H, NHC$\underline{H}_2$), 5.62 (s, 2H, NH). ^{13}C-NMR: δ = 13.83, 22.38, 26.44, 28.88, 31.30, 44.33, 181.20.

ANAL. Calcd for **2** (C$_{13}$H$_{28}$N$_2$S) (244.4): C, 63.88%; H, 11.55%; N, 11.46%; S, 13.12%. Found: C, 63.80%; H, 11.73%; N, 11.14%; S, 12.83%.

DMADC **3** was removed as a white solid sublimate from the reaction vessel.

^{1}H-NMR (CDCl$_3$): δ = 2.78 (s, 3H, CH$_3$), 3.58 (s, 3H, CH$_3$), 8.12 (s, 1H, NH).

Thiourea Products from the Reaction of ZDEC with *n*-Hexylamine

A 3.00-mL solution of 0.70*M* ZDEC and 1.54*M* *n*-hexylamine in toluene was heated for 1 h at 140°C, after which the reaction mixture was filtered and the solvent was removed *in vacuo*. Column chromatography of the filtrate by elution with a 3/2 v/v mixture of PE/diethyl ether gave *N*-hexyl-*N'*,*N'*-diethylthiourea (hdetu) **4** as a yellow oil (R_f = 0.39) in a yield of 62.0% (0.563 g, 2.60 mmol).

^{1}H-NMR (CDCl$_3$): δ = 0.89 (t, 3H, CH$_3$), 1.21 (m, 6H, CH$_2$), 1.47 (t, 2H, NCH$_2$CH$_2$), 1.64 (m, 6H, NHCH$_2$CH$_3$), 3.49 (t, 2H, NCH$_2$CH$_2$), 3.70 (q, 4H, NCH$_2$CH$_3$), 5.84 (s, 1H, NH). ^{13}C-NMR: δ = 13.18, 16.85, 21.77, 28.41, 30.72, 40.94, 45.97, 48.39.

N,*N'*-Dihexylthiourea (dhtu) **2** was obtained as a yellow solid (R_f = 0.92) in a yield of 34.8% (0.178 g, 0.73 mmol).

Synthesis of Bis(dibenzyldithiocarbamato)zinc(II) (ZBEC) 5

To a boiling solution of 0.252 g (0.847 mmol) of Zn(NO$_3$)$_2$ in 20 mL of absolute ethanol, a boiling solution of 0.500 g (1.69 mmol) of NDBC in 20 mL of absolute ethanol was added. The mixture was allowed to cool slowly to room temperature. The complex **5** was obtained as a white precipitate, which was filtered and recrystallized from acetonitrile to give colorless, needle-shaped crystals (0.303 g, 0.497 mmol, 58.4%).

^{1}H-NMR: δ = 5.06 [s, 8H, N(CH$_2$)$_2$], 7.36 (m, 20H, C$_{arom}$H).

ANAL. Calcd for **5** (C$_{14}$H$_{28}$N$_2$S$_4$Zn) (610.22): C, 59.05%; H, 4.62%; N, 4.59%; S, 21.02%. Found: C, 58.45%; H, 3.85, N, 4.82%; S, 21.34%.

Thiourea Products from the Reaction of ZBEC with *n*-Hexylamine

A 3.00-mL solution of 0.70*M* ZBEC and 1.54*M* *n*-hexylamine in toluene was heated for 1 h at 140°C, after which the reaction mixture was filtered and the solvent was removed *in vacuo*. Column chromatography of the filtrate by elution with a 3/2 v/v mixture of PE/diethyl ether gave *N*-hexyl-*N'*,*N'*-dibenzylthiourea (hdbtu) **6** as a yellow oil (R_f = 0.35) in a yield of 63.8% (0.911 g, 2.67 mmol).

^{1}H-NMR (CDCl$_3$): δ = 1.02 (t, 3H, CH$_3$), 1.35 (m, 6H, CH$_2$), 3.51 (m, 2H, NHCH$_2$CH$_2$), 5.65 (t, 2H, NHCH$_2$CH$_2$), 4.88 (s, 4H, NCH$_2$C$_6$H$_{13}$), 6.25 (s, 1H, NH), 7.20 (m, 10H, C$_6$H$_5$). ^{13}C-NMR: δ

= 13.44, 21.91, 25.75, 28.36, 30.84, 45.89, 53.41, 126.49, 127.16, 128.02, 135.66, 182.21.

N,*N'*-dihexylthiourea (dhtu) **2** was obtained as a yellow solid (R_f = 0.71) in a yield of 36.0% (0.184 g, 0.76 mmol).

## Synthesis of Bis(hexyldithiocarbamato)zinc(II) 7

First, sodium hexyldithiocarbamate was synthesized according to a procedure for sodium diethyldithiocarbamate described by Bögemann et al.,[7] using 40 mL of demineralized water, 8.01 g of NaOH, 20.24 g of *n*-hexylamine, and 12.3 mL of carbon disulfide. Equal amounts of these reactants were added a second time after 15 min of stirring. The orange, viscous solution formed, containing sodium hexyldithiocarbamate, was dissolved in absolute ethanol. To this mixture, a solution of 0.200 mol (59.51 g) Zn(NO$_3$)·6H$_2$O in 200 mL of demineralized water was added, to give **7** as a white precipitate in a yield of 70.4% (58.86 g, 0.141 mol) after decanting the water/absolute ethanol mixture and recrystallization from methanol.

^{1}H-NMR: δ = 0.90 (t, 6H, CH$_3$), 1.31 (m, 12H, CH$_2$), 1.64 (m, 4H, NHCH$_2$CH$_2$), 3.49 (m, 4H, NHCH$_2$), 7.79 (s, 2H, NH). ^{13}C-NMR: δ = 13.99, 22.48, 26.45, 28.29, 31.34, 49.65, 225.01.

Reactivity Experiments

When a reactivity experiment was performed in an argon atmosphere, the vessel was first evacuated three times and filled with argon, whereas all samples during the experiment were taken under the outstream of argon gas. When a catalytic amount of elemental sulfur (S$_8$) was required for the reaction, 2.00 mL of a 0.4997-m*M* stock solution of S$_8$ in dichloromethane was added to the reaction vessel with a magnetic stirrer bar. Dichloromethane was removed by immersing the open vessel in the thermostated oil bath, when necessary under the outstream of argon or dioxygen. A 2.00-mL stock solution of ZDAC with *n*-hexylamine in toluene or a solution of 0.100 mmol (0.0418 g) of **7** with 0.220 mmol of *n*-hexylamine in 2.00 mL of toluene was added to the reaction vessel containing a magnetic stirrer bar. After 5 min of stirring, a 50-μL sample was taken for HPLC analysis and the vessel was closed. The vessel was partly immersed in a 110°C thermostated oil bath of a large volume equipped for magnetic stirring. During 4 h, every 30 min the vessel was taken out of the oil bath and the reaction was quenched by rapid cooling using liquid
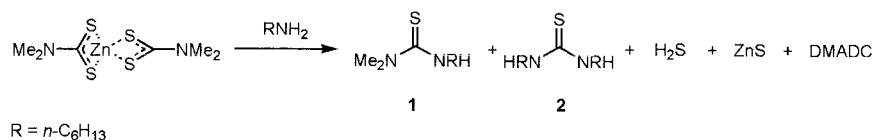
Scheme 3   Overall reaction of *n*-hexylamine with ZDMC.

dinitrogen. When the vessel had reached room temperature, a 50-μL sample was taken. Pressure effects due to decrease of the liquid volume were neglected. The 50-μL samples were diluted with methanol (HPLC grade) to 5.00 mL and analyzed using RP HPLC. All these reactions were performed in duplicate. Additional reactivity experiments for the reaction of ZDMC with an excess of *n*-hexylamine, as well as the reactions of secondary and tertiary amines with ZDACs, were carried out in an argon atmosphere and were not performed in duplicate. For the reactions of 1.0 equiv of ZDMC with 4.0 or 24.0 equiv of *n*-hexylamine, 0.0223 g or 0.2214 g, respectively, of extra *n*-hexylamine was added to 2.00 mL of the stock solution of ZDMC and *n*-hexylamine in toluene.

Reaction of 1 with *n*-Hexylamine

A vessel was charged with a solution of 0.132 g (0.0701 mmol) of **1** and 0.0707 g (0.0698 mmol) of *n*-hexylamine in 2.00 mL of toluene. The procedure followed was the same as that described for the reactivity experiments. For 4 h, 50-μL samples were taken every 30 min. The reaction was performed at 110°C in an argon atmosphere. The reaction was also carried out in the presence of a catalytic amount (2 mol %) of S_8 and in the presence of a catalytic amount (2 mol %) of $ZnCl_2$.

RESULTS AND DISCUSSION

Reaction of Amines with ZDACs

Heating a homogeneous, colorless solution containing 1.0 equiv of ZDMC and 2.2 equiv of *n*-hexylamine in toluene for 1 h at 140°C in air initially results in the formation of a yellow-colored, transparent reaction mixture. After 30 min, dihydrogen sulfide (H_2S) is formed, as noticed from its smell. A yellow-colored precipitate subsequently forms in the reaction mixture and a white solid is deposited in the neck of the reaction vessel. Using ^{1}H-NMR spectroscopy, the white solid was identified as DMADC.[8] Filtering the reaction mixture allowed identification of the yellow-colored residue as zinc sulfide (ZnS) by X-ray

powder diffraction.[5,6] Using TLC and subsequent column chromatography, the filtrate was found to contain two products, namely, a yellow oil, hdmtu (**1**), and a yellow solid, dhtu (**2**). Both thiourea products were characterized by ^{1}H-NMR spectroscopy, ^{13}C-NMR spectroscopy, as well as elemental analysis. The overall reaction is depicted in Scheme 3.

Having established that hdmtu and dhtu are formed as the main organic products of the reaction between ZDMC and *n*-hexylamine, the kinetics of this reaction were investigated by measuring the rate of formation of the thiourea products under various conditions. The rate of reaction of *n*-hexylamine with ZDMC in toluene may be expressed in terms of the half-life ($t_{1/2}$ values), as shown in Table I. This table also lists the product ratio of the thioureas in the final mixture.

First, a mixture of ZDMC and *n*-hexylamine was heated in an argon atmosphere to prevent interference of the reaction by H_2O, O_2, or CO_2 present in air, whereas the temperature was set at 110°C to ensure a sufficiently moderate rate of reaction. The reaction was followed in time by quantitation of both thiourea products in the samples using RP HPLC (Fig. 1).

It is easily seen that initially the symmetric 1,3-disubstituted product, dhtu, is formed more slowly than is the asymmetric 1,1,3-trisubstituted product, hdmtu, whereas toward the end of the reaction, it becomes more abundant. This suggests that ZDMC is first transformed into hdmtu, which is subsequently converted into dhtu. To test this hypothesis, pure hdmtu was reacted with

Table I   Observed $t_{1/2}$ Values and Ratios of Formation Between the Thiourea Products for the Reaction of *n*-Hexylamine with ZDMC Under Argon in the Absence and in the Presence of S_8 and Under O_2
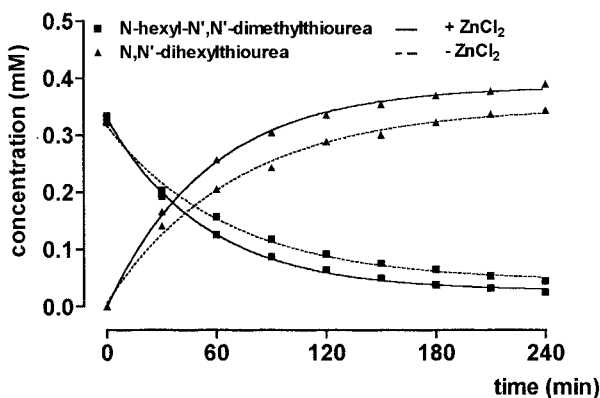
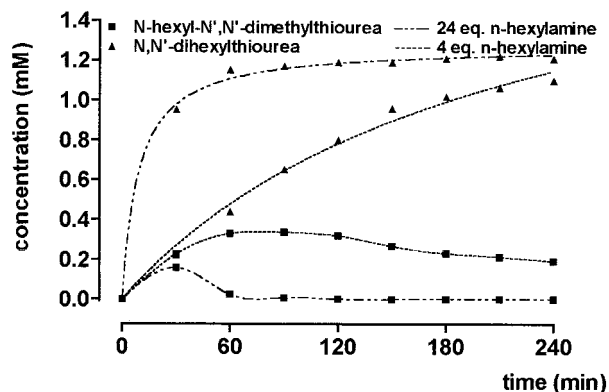| Atmosphere	$t_{1/2}$ (min)	**1:2**
Argon	59	1:1.36
Argon + 1 mol % S_8	20	1:0.49
O_2	29	1:0.50
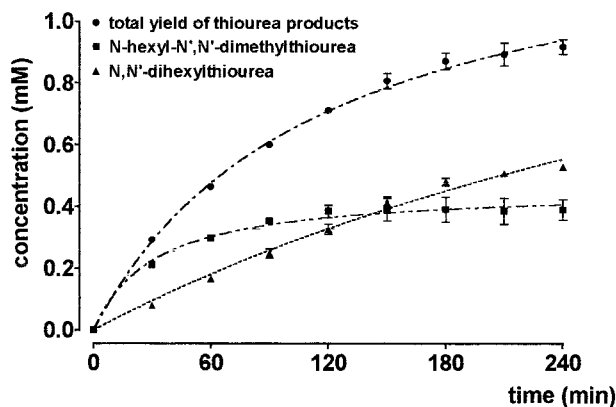
Figure 1 Reaction of n-hexylamine with ZDMC in an argon atmosphere followed in time via quantification of the thiourea products by RP HPLC.

Figure 3 Influence of the concentration of n-hexylamine on the formation of the thiourea products.

n-hexylamine. Indeed, after 4 h, an almost complete conversion of hdmtu into dhtu was observed (Fig. 2). Interestingly, the addition of a catalytic amount of zinc chloride ($ZnCl_2$) resulted in a faster reaction. Therefore, $ZnCl_2$ can be regarded as a moderately active catalyst for this reaction, presumably due to activation of the C=S moiety, as a result of its coordination to zinc. A similar catalytic influence may be expected from the ZnS formed during the reaction of primary amines with ZDMC.

Furthermore, when the reaction of ZDMC is performed in the presence of an excess of n-hexylamine, initially, hdmtu is formed, whereas toward the end of the reaction, the concentration of hdmtu decreases, or even becomes zero, depending on the amount of added n-hexylamine (Fig. 3). This observation supports the suggestion that hdmtu acts as a precursor for the formation of dhtu.

Because common vulcanization reactions are performed in the presence of elemental sulfur,[9] the influence of elemental sulfur on the reaction of primary amines with ZDMC was also investigated. Surprisingly, it was observed that the reaction proceeds much faster in the presence of elemental sulfur. In Figure 4, the development of the total concentration of thiourea products in time is plotted for the reaction of ZDMC with n-hexylamine in the absence, as well as in the presence, of only 1 mol % of elemental sulfur.

Thus, even addition of a catalytic amount of elemental sulfur results in a significant decrease of $t_{1/2}$, as shown in Table I. From these experiments, it is concluded that elemental sulfur is a catalyst for the reaction of ZDMC with n-hexylamine.

Quite interestingly, the addition of a catalytic amount (1 mol %) of elemental sulfur to the reaction mixture also induces a change in the ratio of the two formed thiourea products (Table I). In the

Figure 2 $ZnCl_2$ as a moderate catalyst for the reaction of hdmtu with n-hexylamine.
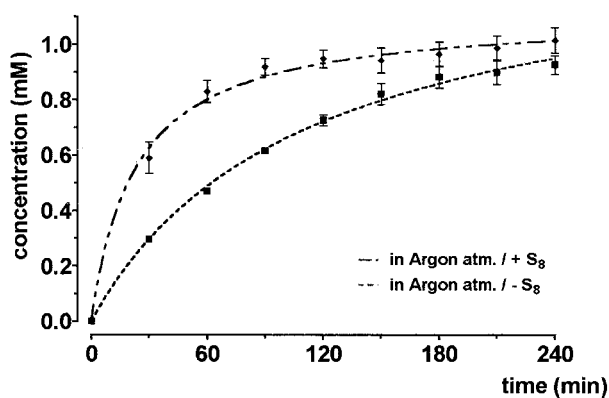
Figure 4 Catalytic effect of elemental sulfur on the reaction of n-hexylamine with ZDMC.

presence of elemental sulfur, hdmtu is formed much faster and is eventually also the most abundant product. Apparently, the transformation of hdmtu into dhtu becomes less important when elemental sulfur is available. Finally, when the reaction of ZDMC with *n*-hexylamine is performed in the presence of O$_2$, a significant decrease in $t\frac{1}{2}$ and a change in the ratio of the two formed thiourea products are also observed (Table I).

To determine whether the formation of an asymmetric 1,1,3-trisubstituted and a symmetric 1,3-disubstituted thiourea has a general value for the interaction of zinc dialkyldithiocarbamates with primary amines, experiments of ZBEC and ZDEC with *n*-hexylamine were also performed in an argon atmosphere. As expected, hdbtu, hdetu, and dhtu were formed from ZBEC and ZDEC. These products were characterized using ^{1}H-NMR spectroscopy and ^{13}C-NMR spectroscopy. Similar to the reaction of *n*-hexylamine with ZDMC, these reactions proceed significantly faster in the presence of a catalytic amount (1 mol %) of elemental sulfur. Also, the product ratio between both thiourea compounds changes in favor of the asymmetric 1,1,3-trisubstituted thiourea. On the other hand, when ZDMC is reacted with a secondary amine, for example, DMA, no thiourea products are formed. Tertiary amines were found not to react at all with ZDACs.

DISCUSSION OF THE OBSERVATIONS

In 1973, Gelling proposed a mechanism for the reaction of primary amines with ZDAC, assuming an amine-exchange reaction followed by thermolysis (Scheme 2).[2] Such a reaction indeed explains the products that are obtained, but the proposed mechanism seems less likely, since it requires a complex between ZDAC and a primary amine to dissociate in one single reaction step to form the several products. Furthermore, based on such a mechanism, it appears to be anomalous that secondary amines react with a zinc–dithiocarbamate complex to induce an exchange of amine substituents. Tertiary amines are believed not to form adducts with zinc dithiocarbamates at vulcanization temperatures.[2]

Based on the experiments described above, a new mechanism for the reaction of amines with ZDACs can be proposed, which is not only in good agreement with all presently available observations, including the observed catalysis by elemental sulfur, but which also confirms common mech-anistic insights in organic reactions. This mechanism is summarized in Scheme 4 for the reaction of a primary amine with ZDMC.

To explain the initial formation of a 1,1,3-trisubstituted thiourea, a conventional nucleophilic attack of the primary amine onto the thiocarboxy atom is proposed, resulting in the formation of an amine–dithiocarbamic intermediate (step **A**). From this intermediate, there are three possibilities for the reaction to proceed: First, ZDMC can be regenerated by loss of the primary amine, since the formation of the intermediate is reversible (step **A′**). A second possibility is that (dimethyldithiocarbamato)(hydrogensulfido)zinc(II) acts as a leaving group, leading to the formation of a 1,1,3-trisubstituted thiourea (step **B**). In fact, this reaction closely resembles that of a common esterification reaction,[3] except that the leaving group is now hydrogen sulfide instead of hydroxide. In this case, the expulsion of HS$^-$ is aided by coordination to (dimethyldithiocarbamato)zinc(II). The third possibility is that DMA acts as a leaving group, as a result of which an (alkyldithiocarbamato)(dimethyldithiocarbamato)zinc(II) complex is obtained (step **C**). From this complex, in a second reaction cycle, a 1,3-disubstituted thiourea may be formed, when the alkyldithiocarbamato ligand reacts with the primary amine (step **D**). This reaction scheme and the results presented above (Fig. 2) suggest that the 1,3-disubstituted thiourea cannot be formed only via the reaction of the primary amine with a 1,1,3-trisubstituted thiourea (step **G**), but also through a nucleophilic attack of the primary amine on the bis(alkyldithiocarbamato)zinc(II) complex (step **D** or **F**). The formation of DMADC during the reaction of a primary amine with ZDMC can now be explained by the decomposition of (dimethyldithiocarbamato)(hydrogensulfido)-zinc(II) [HS—Zn(dmtc)], which gives dimethyldithiocarbamic acid (Hdmtc) and ZnS. DMADC results from the reaction of Hdmtc with DMA or when two Hdmtc molecules combine, splitting off CS$_2$ (Scheme 5).[8]

The present mechanism (Schemes 4 and 5) also yields a viable explanation for the intriguing acceleration of the reaction of a primary amine with a ZDAC observed upon the addition of a catalytic amount (1 mol %) of elemental sulfur. It has been generally assumed that sulfur atoms can be incorporated into the zinc–ligand bond of common accelerators such as bis(mercaptobenzothiazolato)zinc(II) (ZMBT) and ZDMC as depicted in Scheme 6 for ZDMC.[9–11] Recently, in the case of ZDMC, this assumption was proven by quantum-chemical calculations and mass spectrometry.[12,13]
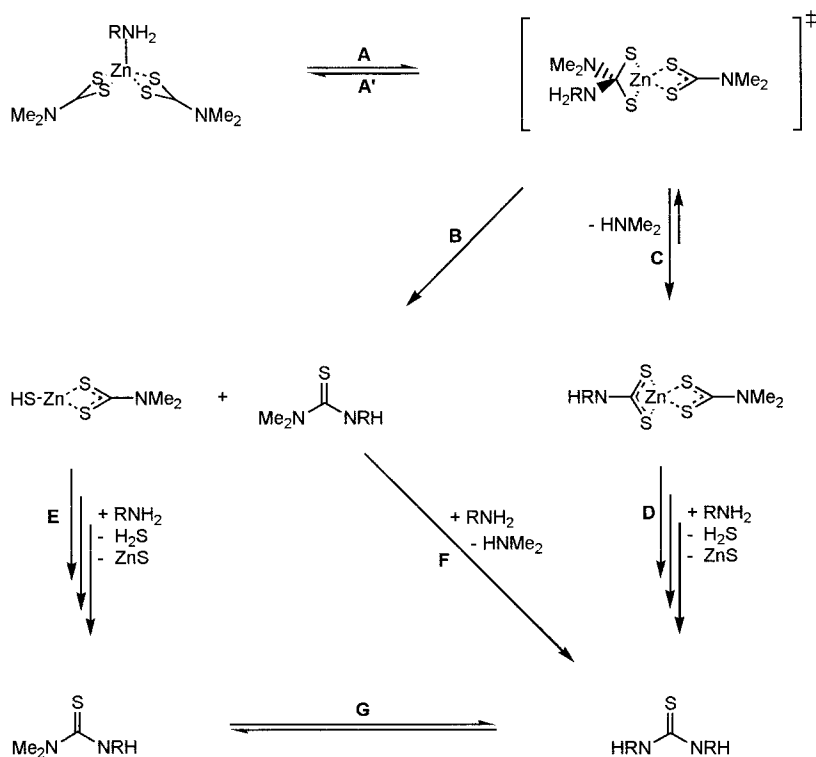
**Scheme 4**   Proposed mechanism for the reaction of primary amines with ZDMC.

The incorporation of additional sulfur atoms in the zinc–dithiocarbamate ring yields a bis(tri-thiocarbamato)zinc(II) species. It was calculated that the negative charge of the dithiocarbamate ligand is no longer evenly distributed over the S—C—S bonds.[12] Instead, this charge becomes concentrated on the inserted sulfur atom, which means that the electron density on the thiocar-bonyl carbon atom has decreased, rendering it more reactive for nucleophilic attack by the primary amine. As a result of sulfur insertion, also, the S—Zn—S bite angle increases from 77.7° in ZDMC to 96.1° in the bis(dimethyltrithiocar-

bamato)zinc(II) complex.[12] The four coordinating sulfur atoms around zinc now approach a tetra-hedral coordination sphere. This geometry is especially favorable in the transition state after nucleophilic attack, since it allows a more efficient stabilization of the negative charges by the zinc atom, as depicted in Scheme 6. A final effect of sulfur insertion might be that, as a result of tet-rahedral "shielding" of zinc by the sulfur atoms, only a small amount of primary amine is coordinated to zinc. This would imply that a larger amount of primary amine is available for nucleophilic attack on the thiocarboxy atom.
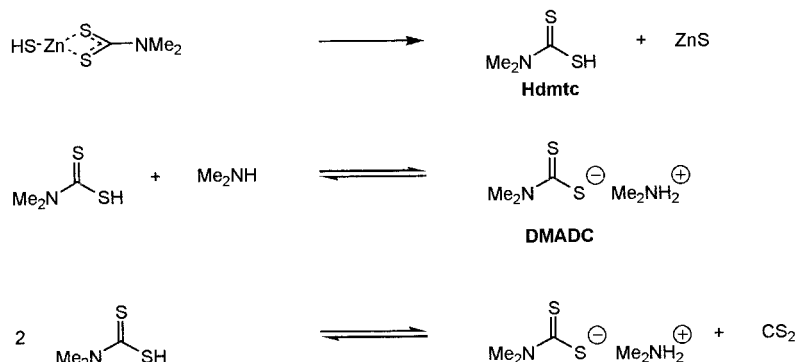
Scheme 5   DMADC formation from Hdmtc.[8]
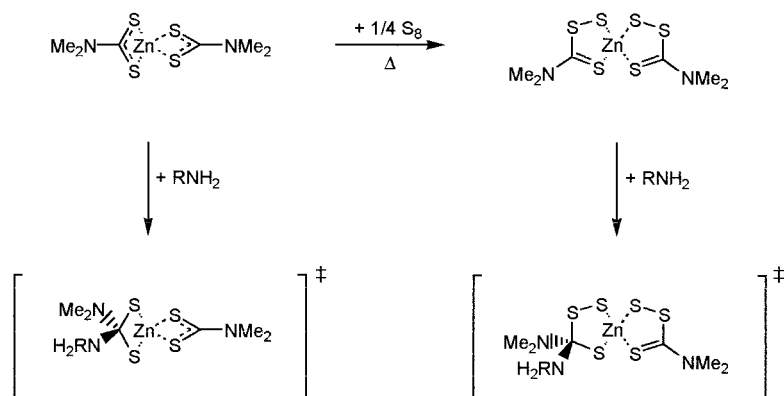
Scheme 6 Sulfur insertion in ZDMC in relation to amine binding.

As was mentioned above, in the presence of elemental sulfur, the product ratio between the two thiourea compounds also changes. This suggests that due to sulfur insertion into ZDAC the indirect transformation of the 1,1,3-trisubstituted thiourea into the 1,3-disubstituted thiourea proceeds more slowly than does the direct formation of the 1,1,3-trisubstituted thiourea from the zinc dialkyldithiocarbamate. The amount of 1,3-disubstituted thiourea formed via the reaction of the primary amine with a zinc dialkyldithiocarbamate is assumed to be negligible. However, in the presence of elemental sulfur, the reaction of the primary amine with a zinc dithiocarbamate will be catalyzed, preferentially resulting in the formation of the 1,1,3-trisubstituted thiourea. Now, since the direct transformation of the 1,1,3-trisubstituted thiourea into the 1,3-disubstituted thiourea has become less important, the 1,1,3-trisubstituted thiourea is formed as the most abundant product during the reaction of a primary amine with a ZDAC.

The proposed mechanism also provides an explanation for the sole formation of zinc dithiocarbamate mixtures when ZDAC is reacted with a secondary amine. With this nucleophile, contrary to primary amines, no thiourea products are produced. A viable explanation lies in the proton transfer from the incoming nucleophile to the leaving group, either DMA or HS—Zn(dmtc), which is the crucial step in this mechanism. Thus, the proton must be positioned suitably for interaction with the lone pair of the neighboring sulfur or nitrogen atom. When the incoming nucleophile is a primary amine, two protons are available, and interaction may occur undisturbed with either sulfur or nitrogen. However, when the nucleophile is a secondary amine, two specific orientations are required for the proton to interact

with either sulfur or nitrogen as depicted in Scheme 7.

From this scheme, it can be seen that in the orientation leading to the thiourea product—when the hydrogen is in close proximity to the lone pair of the sulfur—an unfavorable steric interaction is present with the alkyl substituents of the DMA group (Scheme 7, **1**). A similar interaction is absent when the proton interacts with the lone pair of the DMA substituent (Scheme 7, **2**), rendering the reaction path to the substituted ZDACs the only viable one.

CONCLUSIONS

The kinetic study of the reaction of amines with ZDACs has provided more insight into the mechanism of this reaction. Based on the experimental results, a new mechanism is proposed, which is in very good agreement with all observations. This mechanism involves a conventional nucleophilic attack of an amine on the carbon atom of the thiocarboxy group of a ZDAC, resulting in the formation of an amine–dithiocarbamic intermediate, from which either, in the case of primary amines, thiourea products are obtained or, in the case of secondary amines, a mixture of ZDACs is formed. Tertiary amines were found not to react with ZDACs. Furthermore, elemental sulfur was found to catalyze this reaction, which may be explained by sulfur insertion into the zinc–ligand bond, rendering a more reactive zinc–dithiocarbamate complex. Finally, the ratio of formation between the two thiourea products was found to depend on the experimental conditions chosen.
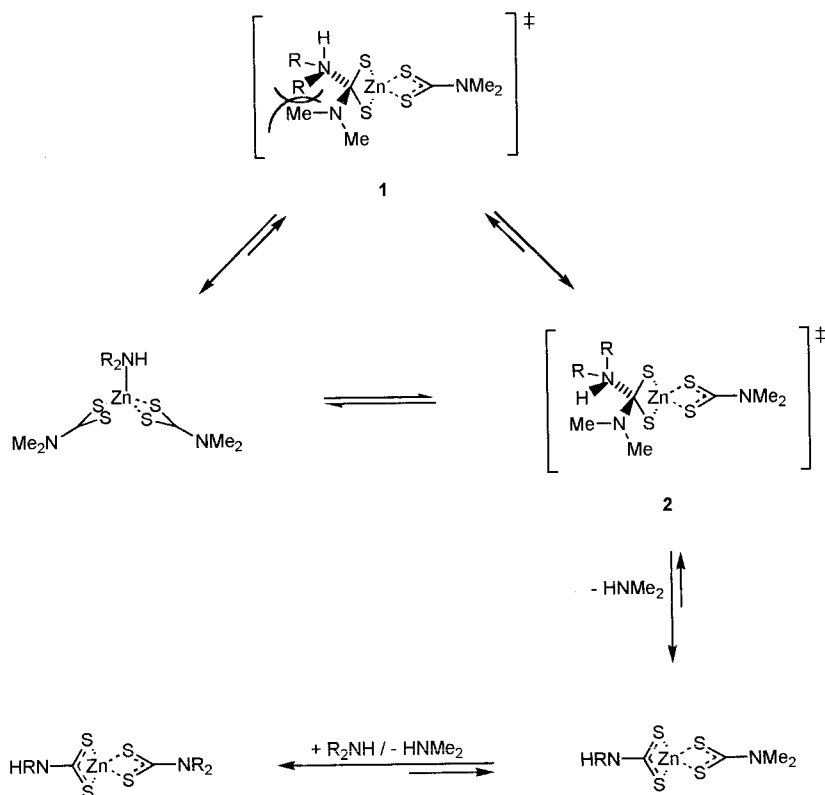
Scheme 7   Reaction of a secondary amine with ZDMC.

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