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The (*E*)/(*Z*)-Ratio in the Reaction of 5-(2-Aryl-2-oxoethyl)-2-thioxo-4-oxo-1,3-thiazolidines with Bromine

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Summary. 3-Aryl-, 3-benzyl-, and 3 *H*-5-(2-aryl-2-oxoethyl)-2-thioxo-4-oxo-1,3-thiazolidines **3a–h** react with bromine in acetic acid solution to give mixtures of the respective 5-aroylmethylene (*E*) and (*Z*) diastereomeric derivatives **5** and **6**. They contain more than 85% of the (*E*)-diastereomers along with some pure isomers. The intermediacy of the 5-bromo derivatives **4** is proven and a plausible route of the reaction is presented. Structures of compounds **3–6** are evidenced by analytical and spectral data.

Keywords. (*E*)- and (*Z*)-3-Aryl-, 3-Benzyl-, and 3 *H*-5-Aroylmethylene-2-thioxo-4-oxo-1,3-thiazolidines; (*E*)- and (*Z*)-5-Aroylmethylene-2,4-dioxo-1,3-thiazolidines; Bromine; Configurational assignment.

Das Verhältnis von (*E*)- und (*Z*)-Isomeren bei der Reaktion von 5-(2-Aryl-2-oxomethyl)-2-thioxo-4-oxo-1,3-thiazolidinen mit Brom

Zusammenfassung. 3-Aryl-, 3-Benzyl- und 3 *H*-5-(2-Aryl-2-oxoethyl)-2-thioxo-4-oxo-1,3-thiazolidine **3a–h** reagieren mit Brom in essigsaurer Lösung zu Gemischen der entsprechenden diastereomeren 5-Arylmethylen-Derivate ((*E*) und (*Z*)) **5** und **6**. Sie enthalten mehr als 85% des (*E*)-Diastereomeren. Die intermediäre Natur der 5-Brom-Derivate **4** wird bewiesen; ein Reaktionsweg wird vorgeschlagen. Die Strukturen der Verbindungen **3–6** werden durch analytische und spektroskopische Daten abgesichert.

Introduction

Following our interest in the chemistry of 4-thiazolidinones [1–5], we wanted to investigate the problem of the (*E*)/(*Z*)-ratio of the 5-aroylmethylene derivatives produced in the reaction of 5-(2-aryl-2-oxoethyl)-2-thioxo-4-oxo-1,3-thiazolidines **3** with bromine. The wide use of thiazolidinones as pharmaceuticals and agrochemicals [6] and the well known relation between biological activity and configuration have prompted us to concentrate on the problem of the product (*E*)/(*Z*)-ratios. The reaction was first reported by *Nagase* [7] in 1974, but since that time no further work has been reported.

Results and Discussion

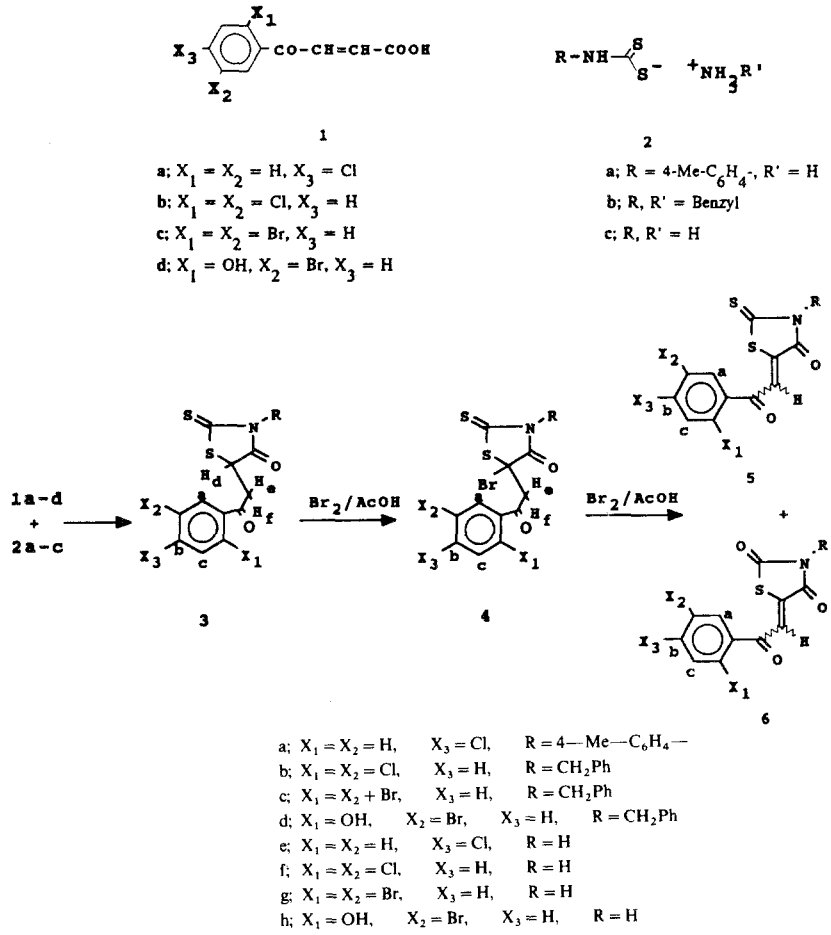
A series of compounds **3** bearing a variety of substituents at different positions of the aroyl moiety as well as at the 3-position of the hetero ring were synthesized and treated with bromine in acetic acid solution.

The structure of **3a–h** which were prepared by a method similar to that of *Nagase* [7] by treating 3-aroylacrylic acids **1a–d** with a variety of dithiocarbamates **2a–c** is evidenced by analytical, IR, and ^{1}H NMR spectral data. The ^{1}H NMR spectrum of **3b** showed long range couplings between benzyl methylene protons and the methine proton at the 5-position of the hetero ring and the neighbouring methylene protons. A support for this phenomenon followed from the lack of such couplings in the spectrum of the 3-unsubstituted derivative **3f**. Moreover, the EI mass spectra of compounds **3b,d** showed the expected molecular ion peaks and exhibited a common fragmentation pattern. The preferred bond rupture takes place between the aroyl carbonyl and the neighbouring methylene groups.

3-Aryl- (**3a**) and 3-benzyl- (**3b–d**) substituted derivatives reacted with bromine in acetic acid solutions to give mixtures of the (*E*)- and (*Z*)-diastereomers of the 5-aroylmethylene-2-thioxo-4-oxo-1,3-thiazolidines **5** in the majority of cases studied. The 3-unsubstituted derivatives, however, afforded (*E*, *Z*)-mixtures of the 2,4-dioxo-analogues **6**. **3b** and **3g** seemed to be exceptions, as the first yielded a mixture of **5b** and **6b** and the latter afforded **5g** instead of **6g**. Fractional recrystallization of the crude products yielded (*E*,*Z*)-mixtures along with pure isomers. The results are represented in Table 1 which shows also the total percentages of the (*E*)-diastereomers. The structures of **5** and **6** are based on microanalytical, IR and ^{1}H NMR spectral data. Compounds **6** are characterized by the coupled carbonyl pattern extending to 1745 cm^{-1}, whereas compounds **5** absorb at relatively lower values, usually below 1715 cm^{-1}. The structures of (*E*,*Z*)-**5b**, (*E*,*Z*)-**5g**, and **6b** are further supported by EI-MS, showing the molecular ion peaks and similar fragmentation. The preferred bond rupture takes place between the 1,2- and 3,4-bonds of the hetero ring. The base peak of **5b** and **6b** is the fragment of $m/e = 91$, whereas that of **5g** is the isotopic peak at $m/e = 263$.

Formation of the 2,4-dioxo-compounds **6e**, **f**, and **h** upon treating the 3-unsubstituted derivatives **3e**, **f** and **h** with bromine was as expected [1]. Conversion of the thioxo to oxo groups in similar systems is faster in the 3-unsubstituted compounds as compared with the 3-substituted counterparts. However, formation of **5g** rather than the expected **6g** could be attributed to the insolubility of **5g** in the reaction mixture as it precipitated instantaneously upon addition of bromine.

Scheme 1 illustrates the conversion of **3** into **5** and **6** *via* successive bromination at the 5-H atom of the hetero ring followed by dehydrobromination. The first step is evident from the isolation of the 5-bromo-3-(4-methylphenyl)-2-thioxo-4-oxo-1,3-thiazolidine **4a** from the reaction mixture. Moreover, another 5-bromo-derivative has been reported [8] to be formed upon treating 2-carbethoxymethylene-3-methyl-4-oxo-1,3-thiazolidine with bromine. The intermediacy of **4a** is further supported chemically as it is easily converted into **5a** *via* a *trans* dehydrobromination step, either by heating for 2 minutes or by leaving in acetic acid solution for a longer period of time.



a; $X_1 = X_2 = H$, $X_3 = Cl$, $R = 4\text{—}Me\text{—}C_6H_4\text{—}$
b; $X_1 = X_2 = Cl$, $X_3 = H$, $R = CH_2Ph$
c; $X_1 = X_2 + Br$, $X_3 = H$, $R = CH_2Ph$
d; $X_1 = OH$, $X_2 = Br$, $X_3 = H$, $R = CH_2Ph$
e; $X_1 = X_2 = H$, $X_3 = Cl$, $R = H$
f; $X_1 = X_2 = Cl$, $X_3 = H$, $R = H$
g; $X_1 = X_2 = Br$, $X_3 = H$, $R = H$
h; $X_1 = OH$, $X_2 = Br$, $X_3 = H$, $R = H$

Scheme 1

Table 1. Data of compounds **3**, **5**, and **6** obtained from **3a–h** with bromine

Starting compd. **3**	Total yield (%)	Product(s)	Yield (%)	(E)-diastereomer (%)	Total (E)-diastereomer (%)[a]
a	93.8	(*E*, *Z*)-**5a**	90.0	90.0	90.0
b	93.0	(*E*, *Z*)-**5b**	10.5	85.0	uncertain
		6b	78.9	-	
c	94.5	(*E*)-**5c**	91.5	100.0	93.2
		(*E*, *Z*)-**5c**	8.5	20.0	
d	94.5	(*E*, *Z*)-**5d**	92.7	95.0	95.5
		(*E*, *Z*)-**5d**	4.9	60.0	
e	96.2	(*E*, *Z*)-**6e**	88.4	85.0	88.0
		(*Z*)-**6e**	9.6	-	
f	93.7	(*E*)-**6f**	90.0	100.0	96.0
		(*E*, *Z*)-**6f**	10.0	60.0	
g	95.0	(*E*, *Z*)-**5g**	95.0	95.0	95.0
h	94.5	**6h**	94.5	-	uncertain

[a] % of (*E*)-**5** and/or (*E*)-**6**

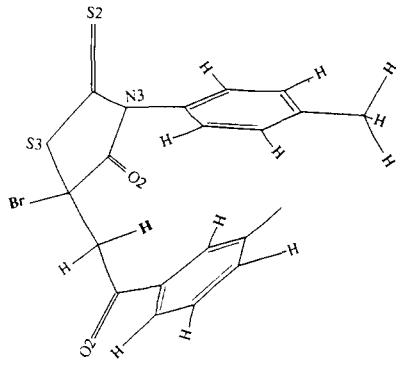


Fig. 1. Energy optimized molecular model of **4a**

The structure of **4a** was evidenced by ^{1}H NMR spectroscopy. The ABX pattern of the $-CH-CH_2-CO-$moiety of **3a** collapsed into two doublets with a coupling constant consistent with a geminal rather than a vicinal coupling.

Configurational assignment of compounds **5** and **6** is based exclusively on ^{1}H NMR spectroscopy by comparing the obsrved chemical shift values of the exocyclic olefinic protons with incremented values [9]; the olefinic protons of the (*E*)-diastereomers are relatively shielded as compared to their (*Z*)-counterparts.

Formation of larger proportions of the (*E*)-isomers could be explained in terms of the larger contribution of the 1-diastereomers of the 5-bromo-derivatives **4** in the reaction mixture, a conclusion which was derived from molecular modeling [10]. Fig. 1 shows the energy optimized form of **4a** which is rotated globaly in such a way to show the elimination requirement for hydrogen bromide. As the H and Br atoms acquire the antiperiplanar conformation, the (*E*)-diastereomer is produced. A similar conclusion was reached for the 3-benzyl and the 3-H-5-bromo derivatives.

Thus, we could conclude that the reaction of **3** with bromine in acetic acid solutions yields mixtures of (*E*)- and (*Z*)-diastereomers of the 5-aroylmethylene derivatives **5** and **6** in which the former constitute more than 85%, irrespective of type and position of substituents. The 3-unsubstituted compounds afford mainly the 2,4-dioxo compounds **6**, whereas the 3-substituted analogues give the 2-thioxo-4-oxo derivatives **5** in most cases.

Experimental

All melting points are uncorrected. Infrared spectra were measured on a Unicam SP 1200 spectrometer as KBr discs. ^{1}H NMR spectra were recorded on a Varian Gemini 200 MHz instrument; chemical shifts (δ; ppm) relative to tetramethylsilane. Mass spectra were recorded on a Shimadzu GC MS QP-200 Spectrometer at 70 eV. The term acetic acid used herein refers to 90% acetic acid (v/v). Elemental analyses gave satisfactory results. The following compounds were synthesized as described previously: 3-(4-chlorobenzoyl)acrylic acid (**1a**) [11], ammonium dithiocarbamate (**2c**) [12], benzylammonium benzyldithiocarbamate (**2b**) [13], and ammonium 4-methylphenyldithiocarbamate (**2a**) [14].

3-Aroylacrylic Acids **1b–d**

To a mixture of 9.4 g maleic anhydride (100 mmol) and 4-bromoanisole (25 ml, 134 mmol), 1,4-dichlorobenzene (20 g, 136 mmol), or 1,4-dibromobenzene (25 g, 106 mmol), anhydrous aluminium chloride (300 mmol) was added and the mixture was stirred for 45 min at room temperature in the first

case and in an oil bath adjusted at 80 °C for the latter ones. The cold dark brown viscous complex was decomposed by slow addition of acidified water and the whole mixture was steam distilled and left to cool. The precipitated solid was filtered off, dried, and recrystallized from the indicated solvent.

3-(2,5-Dichlorobenzoyl)-acrylic acid (**1b**; $C_{10}H_6Cl_2O_3$): yield, 85%; m.p., 165–167 °C (benzene); IR, ν = 3200–3400 br (OH), 1715, 1675 (C=O) cm^{-1}. *3-(2,5-Dibromobenzoyl)-acrylic acid* (**1c**; $C_{10}H_6Br_2O_3$): yield, 87%; m.p., 187–190 °C (benzene–methanol); IR, ν = 3200–3400 (OH), 1715, 1675 (C=O) cm^{-1}. *3-(2-Hydroxy-5-bromobenzoyl)-acrylic acid* (**1d**; $C_{10}H_7BrO_4$): yield, 70%; m.p., 193–195 °C (benzene, methanol); IR, ν = 3200–3400 br (OH), 1715, 1675 (C=O) cm^{-1}.

Synthesis of **3a–h**

A solution of **2a–c** (11 mmol) in methanol (15 ml) was added to a solution of **1a–d** (10 mmol) in methanol (10 ml). The mixture was stirred at room temperature for 1 h, then acidified wit 3 ml conc. HCl, left at room temperature for 30 min, and diluted with water. The solid or viscous oil thus obtained was isolated and purified.

5-[2-(4-Chlorphenyl)-2-oxoethyl]-3-(4-methylphenyl)-2-thioxo-4-oxo-1,3-thiazolidine (**3a**; $C_{18}H_{14}ClNO_2S_2$): yield, 85%; m.p. 139–141 °C (benzene–methanol); IR, ν = 3030 (=CH), 2880–2900 (C–H), 1715, (C=O aroyl group), 1670 (C=O hetero ring) cm^{-1}; ^1H NMR (δ, $CDCl_3$): 4.74 (dd, $J_{d,e}$ = 8.2Hz, $J_{d,f}$ = 4.0Hz, 1H, H_d), 3.71 (dd, $J_{e,f}$ = 18.0Hz, 1H, H_e), 4.10 (dd, 1 H, H_f), 7.93, 7.50 (each d, J = 8.0Hz, 4H, ArCO), 7.36, 7.16 (each d, J = 8.0Hz, 4H, *tolyl H*), 2.41 (s, 3H, Me). *5-[2-(2,5-Dichlorophenyl)-2-oxoethyl]-3-benzyl-2-thioxo-4-oxo-1,3-thiazolidine* (**3b**; $C_{18}H_{13}Cl_2NO_2S_2$): yield, 90%; m.p., 198–199 °C (methanol); IR, ν = 3040 (=CH), 2915, 2905 (C–H), 1715 (C=O, aroyl group), 1685 (C=O, hetero ring) cm^{-1}; ^1H NMR (δ, $CDCl_3$): 4.60 (apparent dt, $J_{d,e}$ = 9.8 Hz, $J_{d,f}$ = 3.2 Hz, $J_{\text{long range}}$ = 2.8 Hz, 1H, H_d), 4.05 (apparent dt, $J_{e,f}$ = 18.8Hz, 1H, H_e), 3.57 (ddd, $J_{\text{long range}}$ = 2.8Hz, 1H, H_f), 7.59 (m, 1H, H_a), 7.39–7.49 (m, 2H, H_b, H_c), 5.29, 5.17 (d of ABq, $J_{A,B}$ = 18.8 Hz, $J_{\text{long range}}$ = 2.8 Hz, 2H, $\underline{CH_2}$-Ph), 7.27–7.39 (m, 5H, $CH_2\underline{Ph}$); EI-MS (*m/e*): 409 (13.7) $[M^{\cdot+}]$, 236 (63.5) $[M^{\cdot+}-\text{aroyl}\cdot]^+$, 148 (62.9) $[M^{\cdot+}-\text{aroyl}\cdot-CH_3CSCHO]^+$, 173 (22.9) $[\text{aroyl}]^+$, 145 (10.2) $[\text{aroyl}-CO]^+$, 149 (30.9) $[M^{\cdot+}-\text{aroyl}-CH_2-\underline{CH-S-CO}]^{\cdot+}$, 91 (100) $[M^{\cdot+}-\text{aroyl-}CH_2-\underline{CH-S-CO}-SCN\cdot]^+$. *5-[2-(2,5-Dibromophenyl)-2-oxoethyl]-3-benzyl-2-thioxo-4-oxo-1,3-thiazolidine* (**3c**; $C_{18}H_{13}Br_2NO_2S_2$) reaction of **1c** with **2b** afforded a viscous oil which solidified upon trituration with light petroleum (b.p. 40–60 °C) followed by diethyl ether. The crude product was recrystallized from diethyl ether to give **3c**; yield, 75%; m.p. 120–122 °C; IR, ν = 3040 (=CH), 2915 (C–H), 1715 (C=O, aroyl group), 1685 (C=O, hetero ring) cm^{-1}. *5-[2-(2-Hydroxy-5-bromophenyl)-2-oxoethyl]-3-benzyl-2-thioxo-4-oxo-1,3-thiazolidine* (**3d**; $C_{18}H_{14}BrNO_3S_2$): reaction of **1d** with **2b** yielded a viscous oil which solidfied after warming in diethyl ether. The crude product was recrystallized from dilute methanol to give **3d**; yield, 78%; m.p., 138–140 °C; IR, ν = 3600 (O–H), 3040 (=CH), 2915 (C–H), 1720 (C=O, aroyl group), 1690 (C=O, hetero ring) cm^{-1}; EI-MS (*m/e*): 435 (10) $[M^{\cdot+}]$, 236 (23.3) $[M^{\cdot+}-\text{aroyl}\cdot]^+$, 148 (21.3) $[M^{\cdot+}-\text{aroyl}\cdot-CH_3CSCHO]^+$, 200 (5.2) $[\text{aroyl}]^+$, 172 (24.1) $[\text{aroyl}-CO]^+$, 149 (6.3) $[M^{\cdot+}-\text{aroyl-}CH_2\underline{CH-S-CO}]^{\cdot+}$ and 91 (100) $[M^{\cdot+}-\text{aroyl-}CH_2\underline{CH-S-CO}-SCN\cdot]^+$. *5-[2-(4-Chlorophenyl)-2-oxoethyl]-2-thioxo-4-oxo-1,3-thiazolidine* (**3e**; $C_{11}H_8ClNO_2S_2$): yield, 90%; m.p., 186–188 °C (toulene); IR, ν = 3180 (N–H), 3080 (=CH), 2860–2980 (C–H), 1710 (C=O, aroyl group), 1670 (C=O, hetero ring) cm^{-1}. *5-[2-(2,5-Dichlorophenyl)-2-oxoethyl]-2-thioxo-4-oxo-1,3-thiazolidine* (**3f**; $C_{11}H_7Cl_2NO_2S_2$): yield, 85%; m.p., 189–191 °C (methanol); IR, ν = 3180 (N–H), 3090 (=CH), 2980–2860 (C–H), 1710 (C=O, aroyl group), 1670 (C=O, hetero ring) cm^{-1}; ^1H NMR (δ, *DMSO*): 4.92 (dd, $J_{d,e}$ = 8.2 Hz, $J_{d,f}$ = 4.0 Hz, 1H, H_d), 4.00 (dd, $J_{e,f}$ = 19.2Hz, 1H, H_e), 3.83 (dd, 1H, H_f), 7.94 (d, $J_{a,b}$ = 2.0Hz, 1H, H_a), 7.69 (dd, $J_{b,c}$ = 8.6Hz, 1H, H_b), 7.63 (d, 1H, H_c), 13.28 (br s, 1H, excangeable H). *5-[2-(2,5-Dibromophenyl)-2-oxoethyl]-2-thioxo-4-oxo-1,3-thiazolidine* (**3g**; $C_{11}H_7Br_2NO_2S_2$): the viscous oil obtained after dilution of the reaction mixture of **1c** and **2c** with water was extracted with chloroform and the dried extract (sodium sulfate) was left to stand at room temperature overnight. The residual oil (50% yield) failed to solidify both by digestion in diethyl ether and by trituration with light petroleum (b.p. 40–60°) and was purified by chromatography on silica gel eluting with a mixture of light petroleum (b.p. 40–60°)-chloroform

(10:1 v/v); IR (neat), $\nu = 3200$ (NH), 3025 (C=CH), 2980 (C–H), 1725 br (C=O, aroyl and hetero ring) cm^{-1} *5-[2-(2-Hydroxy-5-homophenyl)-2-oxoethyl]-2-thioxo-4-oxo-1,3-thiazolidine* (**3h**; $C_{11}H_8BrNO_3S_2$): yield, 85% m.p. 198–200 °C (toluene); IR, $\nu = 3180$, 3100 (NH), 3000 (C=CH), 2970, 2870 (C–H), 1715 br (C=O, aroyl and hetero ring) cm^{-1}. *5-Bromo-5-[2-(4-chlorophenyl)-2-oxoethyl]-3-(4-methylphenyl)-2-thioxo-4-oxo-1,3-thiazolidine* (**4a**; $C_{18}H_{13}BrClNO_2S_2$); 0.8 g Br_2 (5 mmol) was added dropwise to a solution of 1.9 g **3a** (5 mmol) in 30 ml acetic acid at room temperature. The crude product (4.0 g) soon precipitated (m.p. 180–188 °C). It was dissolved in cold chloroform and reprecipitated by addition of light petroleum (b.p. 40–60°) to give a mixture of **4a** and the dehydrogenated product **5a**. However, few crystals of **4a** (m.p. 186–188 °C) were obtained by hand picking from the residue obtained upon cooling a solution of the crude product (2.0 g) in a mixture of chloroform light petroleum (b.p. 40–60°) (10:1 v/v) in the refrigerator. ^1H NMR (δ, $CDCl_3$): 2.42 (s, 3H, Me), 4.15, 4.54 (ABq, $J = 18.8$ Hz, 2H, H_e, H_f), 7.38, 7.31 (each d, $J = 7.4$ Hz, 4H, 4-tolyl), 7.91, 7.50 (each d, $J = 7.6$ Hz, 4H, aroyl group).

Reactions of **3a–h** *with Bromine*

A solution of 1.8 g Br_2 (11 mmol) in 10 ml acetic acid was added dropwise to a solution of 10 mmol **3a–h** and the mixture was heated on a water bath for 10 min and left to cool. The precipitate was filtered off, dried, washed with diethyl ether, and fractionated from the indicated solvent.

(E)- and (Z)-5-(4-Chlorophenylmethylene)-3-(4-methylphenyl)-2-thioxo-4-oxo-1,3-thiazolidine (**5a**; $C_{18}H_{12}ClNO_2S_2$): the crude product obtained from **3a** (3.5 g, 93.8%; m.p., 255–258 °C) was recrystallized from glacial acetic acid to afford (*E*)- + (*Z*)-**5a** containing 90% of the (*E*)-diastereomer; m.p., 258–260 °C (glacial acetic acid); IR, $\nu = 3030$ (=CH), 2950 br (C–H), 1715 (C=O, aroyl group, 1670 (C=O hetero ring) cm^{-1}; ^1H NMR (δ, $CDCl_3$): 8.20, 7.95 (each s, =CH, 1H, (*Z*)- and (*E*)-diastereomers), 8.05, 7.54 (each d, $J = 7.6$ Hz, 4H, aroyl group), 7.37, 7.15 (each d, $J = 7.4$ Hz, 4H, tolyl group), 2.42 (s, 3H, Me). *(E)- and (Z)-5-(2,5-Dichlorobenzoylmethylene)-3-benzyl-2-thioxo-4-oxo-1,3-thiazolidine* (**5b**; $C_{18}H_{11}Cl_2NO_2S_2$) *and its 2,4-dioxo analogue* (**6b**; $C_{18}H_{11}Cl_2NO_3S$): the crude product (3.8 g, 93%) obtained from **3b** (m.p. 95–100 °C) was dissolved in 10 ml glacial acetic acid diluted with water (1 ml) and left at room temperature overnight. The precipitated orange clusters (0.4 g, 10.5%) were filtered off and recrystallized from methanol to give (*E*)- + (*Z*)-**5b** containing 85% of the (*E*)-isomer; m.p., 113–114 °C; IR, $\nu = 3050$ (=CH), 2900 br (C–H), 1710 br (C=O, aroyl and hetero ring) cm^{-1}; ^1H NMR (δ, $CDCl_3$): 7.75, 7.74 (each s, =CH, 1H, (*Z*)- and (*E*)-isomers), 7.62 (m, 1H, H_a), 7.50–7.28 (m, 7H, H_b, H_c, CH_2Ph), 5.35 (br s, 2H, CH_2Ph); EI-MS (*m/e*): 407 (7.2) $[M^{\cdot+}]$, 258 (4.1) $[M^{\cdot+} - PhCH_2\text{-}NCS]^{\cdot+}$, 230 (3.3) $[M^{\cdot+} - PhCH_2\text{-}NCS - CO]^{\cdot+}$, 173 (33.7) $[M^{\cdot+} - PhCH_2 - NCS - CO - HC{-}S{-}C\cdot]^+$, 145 (16.4) $[M^{\cdot+} - PhCH_2 - NCS - CO - HC{-}S{-}C\cdot - CO]^{\cdot+}$, 149 (15.3) $[M^{\cdot+} - aroyl - CH{=}C{-}S{-}CO]^{\cdot+}$, 91 (100) $[M^{\cdot+} - aroyl - CH{=}C{-}S{-}CO - NCS\cdot]^{\cdot+}$, 363 (22.7) $[M^{\cdot+} = C{-}S]^{\cdot+}$. An additional quantity of (*E*)- + (*Z*)-**5b** (0.4 g, 10.5%) was obtained when the mother liquor was concentrated to 5 ml. The residue obtained by evaporating the solution to dryness was recrystallized from dilute acetic acid to give **6b**: yield, 78.9% m.p., 110–112 °C; IR, $\nu = 3050$ (=CH), 2915 br (C–H), 1750, 1730, 1685 (coupled C=O of the hetero ring and aroyl C=O groups) cm^{-1}; ^1H NMR (δ $CDCl_3$): 7.96 (br s, =CH, 1H), 7.60 (m, 1H, H_a), 7.50–7.27 (m, 7H, H_b, H_c, CH_2Ph), 4.90 (br s, 2H, CH_2Ph); EI-MS (*m/e*) 391 (4.2) $[M\cdot]^+$, 258 (3.0) $[M^{\cdot+} - PhCH_2 - NCO]^{\cdot+}$, 230 (2.0 $[M^{\cdot+} - PhCH_2 - NCO - CO]^{\cdot+}$, 173 (40.1) $[M^{\cdot+} - PhCH_2 - NCO - CO - HC{-}S{-}C\cdot]^+$, 145 (16.4) $[M^{\cdot+} - PhCH_2 - NCO - CO - HC{-}S{-}C\cdot - CO]^{\cdot+}$, 133 (3.4) $[M^{\cdot+} - aryoyl - CH{=}C{-}S{-}CO]^{\cdot+}$, 91 (100) $[M^{\cdot+} - aroyl - CH{=}C{-}S{-}CO - NCS\cdot]^{\cdot+}$ and 363 (22.7) $[M^{\cdot+} - CO]^{\cdot+}$. *(E)- and (Z)-5-2-(2,5-Dibromobenzoylmethylene)-3-benzyl-2-thioxo-4-oxo-1,3-thiazolidine* (**5c**; $C_{18}H_{11}Br_2NO_2S_2$): the crude product (4.7 g; 94.5%; m.p. 165–167 °C) obtained from **3c** was dissolved in 20 ml glacial acetic acid and left at room temperature for 12 h. The precipitated orange crystals (4.3 g; 91.5%) were filtered off and recrystallized from glacial acetic acid to give (*E*)-**5c**: m.p., 118–120 °C; IR, $\nu = 3050$ (=CH), 2920 br (C–H), 1720, 1685 (C=O aroyl and hetero ring) cm^{-1}; ^1H

NMR (δ, $CDCl_3$): 7.72 (s, 1H, =CH), 7.87 (d, $J_{a,b} = 1.8$ Hz, 1H, H_a), 7.60 (dd, $J_{b,c} = 8.0$ Hz, 1H, H_b), 7.47 (d, 1H, H_c), 7.44 (dd, $J = 8.0$ Hz, $J = 1.8$ Hz, 2H, CH_2Ph), 7.27–7.36 (m, 3H, CH_2Ph), 5.34 (br, s, 2H, CH_2Ph). The mother liquor was evaporated and the precipitated orange crystals (0.4 g, 8.5%) were recrystallized from glacial acetic acid to give (*E*)- + (*Z*)-**5c** containing 20% of the (*E*)-isomer: m.p., 190–195 °C; IR, same as (*E*)-**5c**; ^{1}H NMR (δ, $CDCl_3$): 8.30, 7.72 (each s, 1H, =CH, (*Z*)- and (*E*)-isomers), 7.90–7.80 (m, 2 H, H_a, H_b), 7.62–7.20 (m, H_c, Ph), 5.34 (br s, 2H, CH_2Ph). *(E)- and (Z)-5-(2-Bromo-5-hydroxybenzoylmethylene)-3-benzyl-2-thioxo-4-oxo-1,3-thiazolidine* (**5d**; $C_{18}H_{12}BrNO_3S_2$): the crude product (4.1 g, 94.5%; m.p. 160–170 °C) was dissolved in 15 ml glacial acetic acid and left at room temperature for 12 h. The precipitated orange crystals (3.8 g, 92. 7%) were filtered off and recrystallized from glacial acetic acid to afford (*E*)- + (*Z*)-**5d** containing 95% of the (*E*)-isomer: m.p., 190–191 °C; IR, $\nu = 3600$–2800 br (O–H and C–H), 1720, 1690 (C=O, aroyl and hetero ring) cm^{-1}; ^{1}H NMR (δ, *DMSO*): 8.35, 8.21 (each s, 1H, =CH), (*Z*)- and (*E*)-isomers), 8.23, 7.88 (each d, $J = 2.6$ Hz, 1H, H_a), 7.68 (dd, $J_{b,c} = 9.0$ Hz, 1H, H_b), 7.11 (d, 1H, H_c), 7.34 (br s, 5H, CH_2Ph), 9.08 (br s, 1H, exchangeable H). The mother liquor was concentrated to 5 ml and the golden yellow crystals thus obtained (0.2 g, 4.9%) were recrystallized from glacial acetic acid to give another fraction of (*E*)- + (*Z*)-**5d** containing 60% of the (*E*)-diastereomer: m.p., 170–172 °C; IR and ^{1}H NMR: same as above.

(E)- and (Z)-5-(4-Chlorobenzoylmethylene)-2,4-dioxo-1,3-thiazolidine (**6e**; $C_{11}H_6ClNO_3S$): the crude product (2.6 g, 96.2%; m.p. 250–255 °C) was recrystallized from glacial acetic acid (15 ml) and the precipitated orange crystals were recrystallized from the same solvent to give (*E*)- + (*Z*)-**6e** containing 85% of the (*E*)-diastereomer (2.3 g, 88.4%): m.p., 260–262 °C; IR, $\nu = 3190$ (N–H), 3050 (=CH), 2790 br (C–H), 1750, 1700, 1690 br (C=O, aroyl and hetero ring) cm^{-1}; ^{1}H NMR (δ, *DMSO*): 8.14, 7.95 (each s, =CH, 1H, (*Z*)- and (*E*)-isomers), 8.21, 8.23 (each d, $J = 8.6$ Hz, 2H, chlorobenzoyl H), 7.68 (d, $J = 8.6$ Hz, 2H, chlorobenzoyl H), 12.89 (exchangeable H). The mother liquor was concentrated to 5 ml and the yellow crystals precipitated (0.25 g, 9.6%) were recrystallized from glacial acetic acid to give (*Z*)-**6e**: m.p., 250–252 °C; IR, $\nu = 3190$ (N–H), 3050 (=CH), 2790 br (C–H), 1750, 1700 br (C=O, aroyl and hetero ring) cm^{-1}; ^{1}H NMR (δ, *DMSO*): 8.1 (s, =CH, 1 H), 8.21, 7.68 (each d, 4H, aroyl H), 12.89 (exchangeable H). *(E)-5-(2,5-Dichlorobenzoylmethylene)-2,4-dioxo-1,3-thiazolidine* (**6f**; $C_{11}H_5Cl_2NO_3S$) *and (E)- + (Z)-***6f**: The crude product (3.0 g, 93.7%; m.p. 190–195 °C) was recrystallized from 10 ml glacial acetic acid to give yellowish brown crystals of (*E*)-**6f** (2.7 g, 90%) at first, then (*E*)- + (*Z*)-**6f** containing 60% of the (*E*)-diastereomer (0.3 g, 10%) from the mother liquor. (*E*)-**6f**: m.p., 196–198 °C (glacial acetic acid); IR, $\nu = 3100$ br (N–H), 2960 br (C–H), 1735, 1685 br (C=O, aroyl and hetero ring) cm^{-1}; ^{1}H NMR (δ, $CDCl_3$): 7.68 (s, =CH, 1H), 7.63 (d, $J_{a,b} = 2.2$ Hz, H_a), 7.47–7.40 (m, 3H, H_a, H_b, H_c), 13.25 (exchangeable H). *(E)- + (Z)-***6f**: m.p., 165–167 °C (methanol-water); IR, $\nu = 3100$ br (N–H), 2950 br (C–H), 1745, 1700 br (C=O, aroyl and hetero ring) cm^{-1}; ^{1}H NMR (δ, $CDCl_3$): 7.91, 7.84 (each s, =CH, 1H, (*Z*)- and (*E*)-diastereomers), 7.63 (d, $J_{a,b} = 2.2$ Hz, H_a), 7.52–7.40 (m, 2H, H_b, H_c), 13.25 (exchangeable H). *(E)- and (Z)-5-(2,5-Dibromobenzoylmethylene)-2-thioxo-4-oxo-1,3-thiazolidine* (**5g**; $C_{11}H_5Br_2NO_2S_2$): the crude product (3.9 g, 95%; m.p., 222–224 °C) was recrystallized from glacial acetic acid (15 ml) to give (*E*)- + (*Z*)-**5g** containing 95% of the (*E*)-diastereomer in yellowish brown crystals: m.p., 222–224 °C; IR, $\nu = 3160$ (N–H), 3060 (=CH), 2900 (C–H), 1710, 1690 br (C=O, aroyl and hetero ring) cm^{-1}; ^{1}H NMR (δ, *DMSO*): 8.53, 8.00 (each s, =CH, 1H, (*Z*)- and (*E*)-isomers) 8.10, 8.00 (each d, $J_{a,b} = 1.0$ Hz, 1 H, H_a, (*E*)- and (*Z*)-isomers), 7.80, 7.73 (partially splitted ABq, $J_{b,c} = 8.2$Hz, 2H, H_b, H_c), 13.35 (exchangeable H); EI-MS (*m/e*): 405 (6.5) [M·$^+$], 346 (7.6) [M·$^+$ – H-NCS]·$^+$, 318 (3.5) [M·$^+$ – H-NCS – CO]·$^+$, 261 (45.5) [M·$^+$ – H-NCS – CO – HC–S–C·]$^+$, 263 (261 + 2), 233 (15.8) [M·$^+$ – H–NCS – CO – HC–S–C· – CO]$^+$, 59 (34.5) [M·$^+$ – aroyl – CH=C–S–CO]·$^+$ and 361 (11) [M·$^+$ – CS]·$^+$. *5-(2-Hydroxy-5-bromobenzoylmethylene)-2,4-dioxo-1,3-thiazolidine* (**6h**; $C_{11}H_6BrNO_4S$): the crude product (3.1 g, 94.5%; m.p. 246–248 °C) was recrystallized from glacial acetic acid to give **6h**: m.p., 246–248 °C; IR, $\nu = 3150$ br (N–H), 3050 (=CH), 2850 br (C–H), 1750, 1700 br (C=O, aroyl and hetero ring) cm^{-1}; ^{1}H NMR (δ, $CDCl_3$): 7.87 (br s, 1H, =CH), 7.82 (br s, 1H, H_a), 7.40 (dd, $J_{b,c} = 9.2$ Hz, $J_{a,b} = 2.0$ Hz, 1H, H_b), 6.78 (d, 1H. H_c), 11.65, 12.40 (each br s, 2H, exchangeable H).

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