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The Reaction of Dimethyl *N*-Benzoylcarbonimidodithioates with Amines

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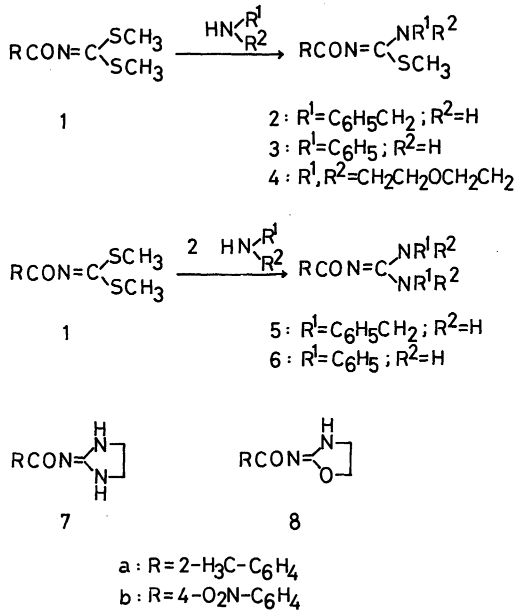
Synopsis. 1-Substituted 3-benzoyl-2-methylisothioureas and 1,3-disubstituted 2-benzoylguanidines were synthesized from dimethyl *N*-benzoylcarbonimidodithioates and amines. From ethylenediamine and 2-aminoethanol, imidazolidine and oxazolidine derivatives were obtained respectively.

In recent years, α-oxoketene dithioacetals have been widely used for the preparation of heterocycles and intermediates in organic synthesis. However, relatively few studies have been reported on the reactions of the corresponding aza-analog *N*-acylcarbonimidodithioic acid dithioesters. In our continuing study of the reactions of amides with carbon disulfide,[1,2)] we have previously reported the general synthesis of dimethyl *N*-aroylcarbonimidodithioates from aromatic amide, carbon disulfide, and sodium hydride.[3)] The dithioesters reacted with hydrazine hydrate to give 3-aryl-5-methylthio-1*H*-1,2,4-triazoles in good yields.[3)] Augustin *et al.* reported the syntheses of dimethyl *N*-cinnamoyl- and *N*-aroylcarbonimidodithioates, and their reactions with nucleophilic compounds.[4—7)] Recently Potts *et al.* used diethyl *N*-benzoylcarbonimidodithioates and the potassium enolates of methyl ketones to prepare *N*-acyl-β-enamino ketones.[8)]

In this note, we wish to report the reactions of dimethyl *N*-benzoylcarbonimidodithioates **1** obtained from 2-methyl- and 4-nitrobenzamides with several amines. When equimolar mixtures of **1** and amines (benzylamine, aniline, and morpholine) were heated in ethanol, 1-substituted 3-benzoyl-2-methylisothioureas **2**—**4** were obtained in good yields. Two moles of the amines (benzylamine and aniline) gave 1,3-disubstituted 2-benzoylguanidines **5** and **6**. For the latter reactions it was necessary to heat in boiling xylene. Although early reports[9,10)] described the preparation of compounds of these types (**2**—**6**), the method reported here is more convenient. From ethylenediamine and 2-aminoethanol, the cyclized compounds, 2-(benzoylimino)imidazolidines **7** and 2-(benzoylimino)oxazolidine **8** respectively, were obtained.



1

2: $R^1=C_6H_5CH_2$; $R^2=H$
3: $R^1=C_6H_5$; $R^2=H$
4: $R^1,R^2=CH_2CH_2OCH_2CH_2$

1

5: $R^1=C_6H_5CH_2$; $R^2=H$
6: $R^1=C_6H_5$; $R^2=H$

7

8

a: $R=2\text{-}H_3C\text{-}C_6H_4$
b: $R=4\text{-}O_2N\text{-}C_6H_4$

These results are similar to those of the reaction of α-oxoketene dithioacetals with amines[11)] and offer new possibilities in preparing heterocycles.

Experimental

1-Substituted 3-Benzoyl-2-methylisothioureas (2—4). *General Procedure.* A mixture of dimethyl *N*-benzoylcarbonimidodithioate (**1**, 0.002 mol),[3)] amine (benzylamine, aniline, or morpholine; 0.0022 mol), and ethanol (30—40 ml) was refluxed for 1—3 h. The solvent was then removed, and the residual solid was recrystallized.

*1-Benzyl-2-methyl-3-(2-methylbenzoyl)isothiourea (**2a**)*: Recrystallized from ethanol; IR (KBr) 3160 m (NH) and 1590 *vs.* cm^{-1} (C=O); UV (EtOH) λ_{max} 244sh (log ε 4.13), 249 (4.15), 255 (4.15), 262sh (4.22), and 282 nm (4.47); ^{1}H NMR (CCl$_4$) δ=2.55 (s, 3H, CH$_3$), 2.58 (s, 3H, CH$_3$), 4.55 (d, 2H, CH$_2$), 7.2—8.5 (m, 9H, C$_6$H$_4$ and C$_6$H$_5$), and 11.77 (br s, 1H, NH); MS *m/z* 298 (M$^+$).

*1-Benzyl-3-(4-nitrobenzoyl)-2-methylisothiourea (**2b**)*: Recrystallized from ethanol; IR (KBr) 3250 w (NH) and 1580 *vs.* cm^{-1} (C=O); MS *m/z* 329 (M$^+$).

*2-Methyl-3-(2-methylbenzoyl)-1-phenylisothiourea (**3a**)*: Recrystallized from hexane–ethanol; IR (KBr) 1605 *vs.* cm^{-1} (C=O); MS *m/z* 284 (M$^+$).

*2-Methyl-3-(4-nitrobenzoyl)-1-phenylisothiourea (**3b**)*: Recrystallized from ethanol; IR (KBr) 1615 m cm^{-1} (C=O); MS *m/z* 315 (M$^+$).

*4-[2-Methylbenzoylimino(methylthio)methyl]morpholine (**4a**)*: Recrystallized from ethanol; IR (KBr) 1604 s cm^{-1} (C=O); UV (EtOH) λ_{max} 240 (log ε 4.27) and 281 nm (4.23); MS *m/z* 278 (M$^+$).

*4-[Methylthio(4-nitrobenzoylimino)methyl]morpholine (**4b**)*: Recrystallized from ethanol; IR (KBr) 1630 s cm^{-1} (C=O); MS *m/z* 309 (M$^+$).

1,3-Disubstituted 2-Benzoylguanidines (5 and 6). *General Procedure.* A mixture of **1** (0.002 mol), amine (benzylamine or aniline; 0.0044 mol), and xylene (30—40 ml) was refluxed for 5 h. In the case of **6a**, ethanol was used as the solvent. The solvent was removed, and the residual solid was recrystallized.

*1,3-Dibenzyl-2-(2-methylbenzoyl)guanidine (**5a**)*: Recrystallized from ethanol; IR (KBr) 3295 *vs.* (NH) and 1615 *vs.* cm^{-1} (C=O); MS *m/z* 357 (M$^+$).

*1,3-Dibenzyl-2-(4-nitrobenzoyl)guanidine (**5b**)*: Recrystallized from hexane–ethanol; IR (KBr) 3398 s (NH) and 1612 s cm^{-1} (C=O); MS *m/z* 388 (M$^+$).

*1,3-Diphenyl-2-(2-methylbenzoyl)guanidine (**6a**)*: Recrystallized from ethanol; IR (KBr) 3380 m, 3250 s (NH), and 1680 *vs.* cm^{-1} (C=O); UV (EtOH) λ_{max} 234sh (log ε 4.33) and 278 nm (4.42); MS *m/z* 329 (M$^+$).

Table 1. Yields and analytical data

Compound	Yield	Mp	Molecular	Found (Calcd) (%)			
	%	θ_m/°C	formula	C	H	N	S
2a	97	71—72	$C_{17}H_{18}N_2OS$	68.40 (68.43)	6.14 (6.08)	9.50 (9.39)	10.44 (10.75)
2b	83	120—121	$C_{16}H_{15}N_3O_3S$	58.48 (58.35)	4.68 (4.59)	12.73 (12.76)	9.80 (9.73)
3a	66	71—72	$C_{16}H_{16}N_2OS$	67.43 (67.58)	5.73 (5.67)	9.59 (9.85)	11.12 (11.28)
3b	85	153—154[a)]	$C_{15}H_{13}N_3O_3S$	57.25 (57.13)	4.18 (4.16)	13.37 (13.33)	10.25 (10.17)
4a	87	91—92	$C_{14}H_{18}N_2O_2S$	60.66 (60.41)	6.52 (6.52)	10.10 (10.06)	11.26 (11.52)
4b	55	152—154	$C_{13}H_{15}N_3O_4S$	50.46 (50.48)	4.90 (4.89)	13.56 (13.58)	10.05 (10.37)
5a	78	146—147	$C_{23}H_{23}N_3O$	77.13 (77.28)	6.50 (6.49)	11.70 (11.76)	
5b	77	154—156	$C_{22}H_{20}N_4O_3$	67.73 (68.03)	5.29 (5.19)	14.26 (14.42)	
6a	57	134—135	$C_{21}H_{19}N_3O$	76.49 (76.57)	5.87 (5.81)	12.76 (12.76)	
6b	84	145—147	$C_{20}H_{16}N_4O_3$	66.52 (66.66)	4.56 (4.48)	15.46 (15.55)	
7a	96	162—163	$C_{11}H_{13}N_3O$	65.05 (65.01)	6.43 (6.45)	20.90 (20.68)	
7b	94	252—253[b)]	$C_{10}H_{10}N_4O_3$	51.31 (51.28)	4.49 (4.30)	23.93 (23.92)	
8b	63	236—238	$C_{10}H_9N_3O_4$	51.05 (51.07)	3.90 (3.86)	17.93 (17.87)	

a) Lit,[7)] mp 148—150 °C. b) Decomp.

*1,3-Diphenyl-2-(4-nitrobenzoyl)guanidine (**6b**)*: Recrystallized from ethanol; IR (KBr) 3375 m (NH) and 1600 s cm^{-1} (C=O); MS m/z 360 (M$^+$).

*Imidazolidines **7** and Oxazolidine **8*** were prepared from ethylene diamine and 2-aminoethanol respectively as has been described for the preparation of **2**—**4**.

*2-(2-Methylbenzoylimino)imidazolidine (**7a**)*: Recrystallized from ethanol; IR (KBr) 3340 s (NH) and 1600 *vs.* cm^{-1} (C=O); UV (EtOH) λ_{max} 244 nm (log ε 4.48); MS m/z 203 (M$^+$).

*2-(4-Nitrobenzoylimino)imidazolidine (**7b**)*: Recrystallized from *N,N*-dimethylformamide–ethanol; IR (KBr) 3310 s (NH) and 1620 *vs.* cm^{-1} (C=O); MS m/z 234 (M$^+$).

*2-(4-Nitrobenzoylimino)oxazolidine (**8b**)*: Recrystallized from *N,N*-dimethylformamide; IR (KBr) 3290 s (NH) and 1620 *vs.* cm^{-1} (C=O); MS m/z 235 (M$^+$).

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