A study of the Willgerodt–Kindler reaction to obtain thioamides and α-ketothioamides under solvent-less conditions

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Abstract: In this paper, the results obtained in the synthesis of thioamides and α-ketothioamides by a modification of the Willgerodt–Kindler reaction, under solvent-free and noncatalyst conditions using IR energy as a source of activation, are presented. The use of IR energy in these reactions has been shown to lead to a mixture of thioamide and α-ketothioamide as the main products in most cases, with the latter predominating. The yields of α-ketothioamides from most of these reactions are better than those reported previously. To the best of our knowledge, this is the first time that IR energy has been applied to promote the Willgerodt–Kindler reaction.

Key words: Willgerodt–Kindler modification, α-ketothioamides, solvent-less conditions, IR energy, noncatalyst.

Résumé : Dans ce travail, on rapporte les résultats obtenus lors de la synthèse de thioamides et de α-cétothioamides, par le biais d'une modification de la réaction de Willgerodt–Kindler dans des conditions qui n'impliquent aucun solvant et aucun catalyseur et qui utilisent l'énergie infrarouge comme source d'activation. On a démontré que l'utilisation de l'infrarouge dans ces réactions conduit, dans la plupart des cas, à des mélanges contenant comme produits principaux un thioamide et un α-cétothioamide et que ce dernier est prédominant. Les rendements en α-cétothioamides, pour la plupart des réactions, sont meilleurs que ceux rapportés antérieurement. Au meilleur de nos connaissances, c'est la première fois que l'énergie de l'infrarouge a été utilisée pour la promotion de la réaction de Willgerodt–Kindler.

Mots-clés : modification de la réaction de Willgerodt-Kindler, α-cétothioamides, conditions expérimentales sans solvant, énergie infrarouge, sans catalyseur.

[Traduit par la Rédaction]

Introduction

Thioamides are among the most extensively studied chalcogen-containing compounds. They are known to demonstrate biological activity,[1] are used as synthetic intermediates in organic chemistry,[2] have been found in natural products, and have many applications in materials science and industrial processes.[3] They are also employed as insecticides[4] because they are well tolerated by plants and have low toxicity in higher animals, and they are used in medical applications, for example, in tuberculosis treatment,[5] as painkillers,[6] and as antioxidants.[7]

Currently, it is possible to find several methods for the synthesis of thioamides, most of which employ Lawesson's reagent.[8] However, there are also publications concerning the Willgerodt–Kindler method for the generation of these compounds,[9] but this method has some limitations, i.e., long reaction times are required and low yields are achieved. This reaction is characterized by the use of alkyl aryl ketones or aldehydes, elemental sulfur, and amines, with morpholine being the most commonly used amine. When ketones are used in this methodology, the carbonyl group is reduced to a methylene group and the terminal methyl group is oxidized to a thiocarbonyl group (**I**, Scheme 1).

Previous studies using thermal energy for the activation of reactions have yielded some unexpected results, with the most common problem being the failure to reduce the carbonyl group in the alkyl aryl ketone used, leading to the formation of the α-ketothioamide **II** as a reaction byproduct. Dauben and Rogan,[10] Harris et al.[11] Harrowven and Lucas,[12] and Liu et al.[13] encountered this problem and generated **II** in yields of 3%–20% when using reaction times of 8–24 h. In

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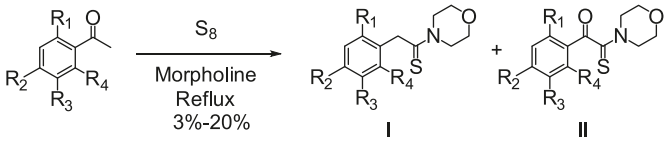
Scheme 1. General reaction conditions for the synthesis of thioamides. Dauben and Rogan:[10] Acetophenone (2.0 g, 12.3 mmol), elemental sulfur (0.40 g, 12.3 mmol), morpholine (1.08 g, 12.3 mmol); R_1 = Me, R_2 = Me, R_3 = H, R_4 = Me; yield (**II**) = 20%; 8 h. Harris et al.:[11] Acetophenone (5.0 g, 20.4 mmol), elemental sulfur (1.0 g, 31.25 mmol), morpholine (2.82 g, 32.4 mmol); R_1 = OC_6H_5, R_2 = H, R_3 = Cl, R_4 = H; yield (**I**) = 46%, **II** not isolated; 20 h. Harrowven and Lucas:[12] Acetophenone (23.3 g, 142 mmol), elemental sulfur (6.8 g, 213 mmol), morpholine (18.5 g, 213 mmol); R_1 = OMe, R_2 = Me, R_3 = H, R_4 = H; yield (**I**) = 57%, yield (**II**) = 10%; 24 h. Liu et al.:[13] Acetophenone (12.2 g, 100 mmol), elemental sulfur (4.8 g, 150 mmol), morpholine (11.3 g, 130 mmol); R_1 = R_2 = R_3 = R_4 = H; yield (**I**) = 66%, yield (**II**) = 3%; 20 h.



these reports, the reactions were performed at reflux, in the absence of solvent, employing acetophenones, elemental sulfur, and morpholine. However, the methodology developed in these studies cannot be considered to be a general synthetic route to α-ketothioamides **II**, because this unexpected product of the Willgerodt–Kindler reaction was only generated in isolated cases.

Other published routes to α-ketothioamides have employed α-chloroketones,[14] α-oxonitryl,[15] thioacetomorpholides,[16] pinacolone (3,3-dimethyl-2-butanone),[17] α-chlorosulfonyl and trisulfane intermediates,[18] or *N*,*N*-(dialkyl)aroylmethylamines.[19] However, like the Willgerodt–Kindler reaction, these methodologies are not general for the synthesis of α-ketothioamides. The reaction conditions employed are also dangerous or require expensive reagents and long reaction times. In general, thermal energy is used as the activation source for the Willgerodt–Kindler reaction. The use of alternative energy sources such as ultrasound[20] and microwaves[21] has recently been explored, and microwave activation has attracted particular attention. To the best of our knowledge, however, the use of IR energy as an activation source for the Willgerodt–Kindler reaction has not yet been reported. IR energy has been demonstrated to be useful in organic synthesis,[22] and has been used in the synthesis of 1,3,5-trioxanes from aldehydes,[23] in the Biginelli[24] and Knoevenagel[25] reactions, and for the synthesis of diindolylmethanes[26] and 3,4-dihydro-2(1*H*)-pyridones.[27] When investigating the synthesis of ε-caprolactam from cyclohexanone and hydroxylamine using bentonic clay under solvent-less conditions, we explored the use of several energy sources for activation of the reaction and found that IR energy performed better than thermal, microwave, or ultrasound energies.[28]

Results and discussion

We set out to explore the use of IR energy for the activation of the Willgerodt–Kindler reaction, employing acetophenone, elemental sulfur, and morpholine. After extensive experimentation, we found that a stoichiometric ratio for the starting materials of 1:1:1, solvent-less conditions, and irradiation with IR energy at a wavelength of 1100 nm (near-IR) for 1 h at 100 °C[29] were optimal conditions for the generation of the corresponding α-ketothioamide. In this way, the desired product was obtained exclusively in 56% yield.

This result encouraged us to study the reaction using other acetophenones and amines, to establish this method as a general route to synthesize α-ketothioamides **3** (Scheme 2).

We found that, under these conditions, this reaction ensured that the α-ketothioamides **3a**–**3h** (Table 1) were generated as the main products in most cases, and the yields were higher than those obtained (3%–20%) by other synthetic methods previously reported in the literature. The Willgerodt–Kindler products **4a**–**4h** were also detected in yields ranging from 0%–42% as a second product. Thus, with the methodology employed in this work, the outcome of the Willgerodt–Kindler reaction can be regarded as unclassical.

The products **3a**–**3h** were obtained in yields close to or higher than 50%, although when 2-methylpiperidine was used as the amine, a yield of only 20% was obtained, which may be attributed to steric factors. In entries 1–5 of Table 1, the products were synthesized from unsubstituted acetophenone, and the amine used was either morpholine, piperidine, or methylated regioisomers of the latter.

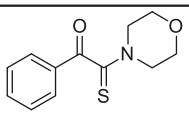
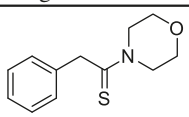
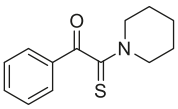
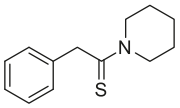
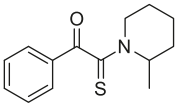
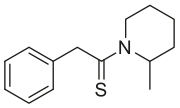
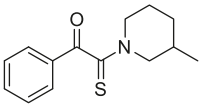
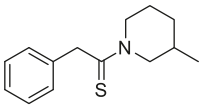
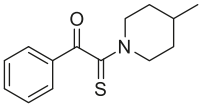
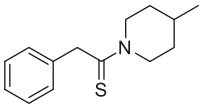
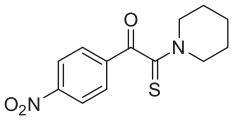
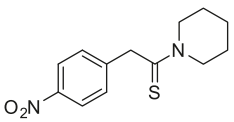
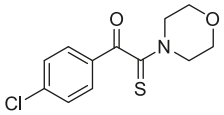
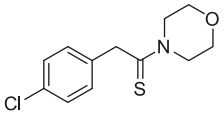
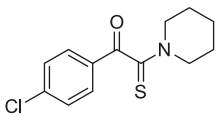
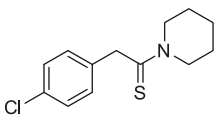
When the reaction was carried out with *p*-chloroacetophenone, a crystalline product was formed, and a single crystal could be used for X-ray diffraction study[30] (Fig. 1).

It is important to mention that the low yields of **3** shown in entries 7 and 8 in Table 1 were due to a competitive S_NAr reaction resulting in the formation of *p*-morpholino- or *p*-(1-piperidinyl)acetophenone[31] in yields of 20% and 19%, respectively, along with the corresponding thioamides from the Willgerodt–Kindler reaction, compounds **4g** and **4h** (Scheme 2; Table 1).

We also studied the reactions leading to the synthesis of **3a**–**3h** at room temperature, to determine the influence of temperature and energy source on their outcomes. The reactions were monitored for 48 h by TLC, and the conversion percentages were measured by gas chromatography coupled with mass spectrometry (Table 2). More than 50% of the acetophenone remained unreacted in some cases (Table 2, entries 7 and 8), and the behavior of these reactions was similar when IR energy was used. These results clearly demonstrated that the reactions proceeded better when activated with IR energy than when conducted at room temperature, and established the importance of IR energy in the synthesis of α-ketothioamides **3**. The formation of **4a**–**4h** was detected and the results are summarized in Table 2.

To compare the use of thermal conditions and IR energy for the synthesis of α-ketothioamides, we performed the reactions to obtain **3a** and **3b** under reflux conditions. After 5 h of reaction, with hourly monitoring by TLC, no formation of the corresponding α-ketothioamides could be detected. This behavior is consistent with the reported results by Liu et al.[13] for the reaction employing acetophenone, elemental sulfur, and morpholine at reflux temperature (83–85 °C), whereby **3** was obtained in just 3% yield after 20 h of reaction. In contrast, in the present study, the same compound (Table 1, entry 1) was obtained in 56% yield in a reaction time of 1 h. Moreover, Carmack et al.[32] reported similar reaction conditions to those used in the present paper (100 °C, elemental sulfur, morpholine, and solvent-less conditions) for

Table 1. Obtained results from the Willgerodt–Kindler reaction employing IR energy.

Entry	α-Ketothioamide	Yield(%)[a]	Willgerodt–Kindler product	Yield (%)[a]	Time (min)
1	 **3a**	56; 3;[13] 58;[b,14] 94[c,16]	 **4a**	Not formed; 50–81[21a]	60
2	 **3b**	50; 22;[b,14] 11[19]	 **4b**	39	60
3	 **3c**	20; 26[19]	 **4c**	Not formed	150
4	 **3d**	67	 **4d**	Not formed	60
5	 **3e**	48	 **4e**	Trace	60
6	 **3f**	54	 **4f**	Not formed	30
7	 **3g**	19; 83[c,16]	 **4g**	42; 40–55[21a]	60
8	 **3h**	12; 10[19]	 **4h**	11	60

[a]Purified product.

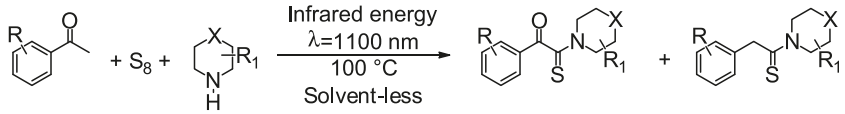
[b]From the linear synthesis (three steps); yield is for the last step.

[c]From the linear synthesis (two steps); yield is for the last step.

the reaction of linear and cyclic aliphatic ketones, using thermal energy, and obtained only the Willgerodt–Kindler product and carbonyl group isomerization products. Considering all of these results, it is proposed that IR energy is responsible for the synthesis of **3** as the principal product, and not the thermal heating that comes from the lamp employed in this work (see the Supplementary data).

The use of IR energy gives very efficient heat transfer similar

Scheme 2. Synthesis of thioamides from acetophenones, elemental sulfur, and heterocyclic amines.

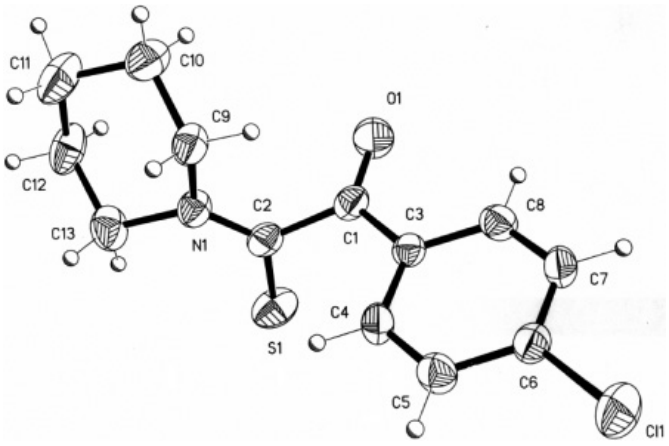


1a-1c **2a-2e** **3a-3h** 12%-67% **4a-4h** 0%-42%

1a H
1b *p*-NO_2
1c *p*-Cl

2a X=O, R_1=H
2b X=CH_2, R_1=H
2c X=CH_2, R_1=2-Me
2d X=CH_2, R_1=3-Me
2e X=CH_2, R_1=4-Me

Fig. 1. ORTEP for 1-(4-chlorophenyl)-2-piperidin-1-yl)-2-thioxo-ethanone (**3h**).



to that provided by microwave irradiation because both are electromagnetic waves and the behavior is comparable. The main effect produced by IR energy is thus an overheating in the reaction mixture that favors the formation of **3**. Mechanistically, we are in agreement with the reaction mechanism proposed by Darabi et al.[33]

Conclusion

In summary, we have described a new methodology for the synthesis of α-ketothioamides as the principal products, employing a multicomponent reaction activated by IR energy under solvent-less conditions. As far as we are aware, this is the first report of the use of IR energy for activation of the Willgerodt–Kindler reaction. We have established the utility of this method for the generation of α-ketothioamides, a reaction that could not previously be reliably accomplished by the Willgerodt–Kindler protocol when thermal energy was used. In all cases reported in this study, the α-ketothioamides were produced in yields ranging from moderate to good, depending on the substituents on the acetophenone aromatic ring.

This new methodology can be considered as a useful addition to the synthetic organic chemistry tool kit, as, to the best of our knowledge, no method has hitherto been reported to give α-ketothioamides in a one-pot reaction in yields better than those reported here.

Experimental section

General

All reagents were from Sigma-Aldrich and used from its commercial presentation, ^{1}H and ^{13}C NMR spectra were recorded by use of $CDCl_3$ or acetone-d_6 in Varian Mercury 200 and 300 MHz instruments, chemical shifts were reported in ppm from TMS with the solvent resonance as the internal standard, and coupling constants (*J*) are given in hertz, where s was assigned to single, d for doublet, t for triplet, m for multiple, and br for broad signals. The GC–MS analyses were conducted with gas chromatograph model 6850 and mass spectrometer 5975C by Agilent Technologies, employing a J&W HP-5MS capillary column. GC conditions: capillary column (30 m × 0.25 mm i.d., 0.25 μm film), helium as carrier gas at a constant flow velocity of 35 cm/s, and injector temperature 250 °C. MS data were reported as *m/z* (relative intensity). HRMS were recorded in an MStation JMS-700 JEOL at 70 eV. Melting points were obtained on a Fisher-Johns apparatus and are uncorrected. Analytical TLC was performed using Kieselgel 60 F_{254} silica gel plates (Merck, Darmstadt, Germany). A Buchi pump controller C-610 and a Buchi pump module C-601 were employed for flash chromatography. Elemental analyses were carried out with an Elementar Vario EL III element analyser.

IR equipment

The equipment used for irradiation with IR energy was created by employing an empty cylindrical metal vessel in which an Osram lamp (bulb model Thera-Therm, 250 W, 125 V) was inserted. This lamp is special short-wave IR lamp (IR-A) for use in body care and wellness applications, with a maximum radiation at a wavelength of about 1100 nm. The lamp instantly emits a full thermal output as soon as it is switched on. For controlling the temperature, a Digi-Sense variable-time power controller was used. This time controller turned the output load on and off and then repeated the cycle.

Typical procedure for the Willgerodt–Kindler reaction employing IR energy

For the synthesis of **3a**, the following were placed in a tube: acetophenone **1a** (100 mg, 0.83 mmol), elemental sulfur (27 mg, 0.83 mmol), and amine **2a** (73 mg, 0.83 mmol). This tube was then sealed and placed inside of the IR equipment at 3–5 cm above the IR lamp. The reaction mixture was irradiated at a wavelength of 1100 nm with IR energy at 100 °C for the appropriate time (30–150 min according to Table 1) and monitored using TLC. The products obtained as brown dark oils were purified using preparative plates or flash chromatography with silica gel as a stationary phase and a mixture of hexane – ethyl acetate as a mobile phase;

Table 2. Conversion percentages using acetophenones, elemental sulfur, and heterocyclic amines at room temperature.

Entry	Compound	Conversion (%)[a]	Compound	Conversion (%)[a]	Acetophenone (%)[b]
1	**3a**	19	**4a**	32	39
2	**3b**	12	**4b**	14	33
3	**3c**	10	**4c**	3	18
4	**3d**	43	**4d**	4	14
5	**3e**	36	**4e**	13	18
6	**3f**	30	**4f**	Not formed	37
7	**3g**	9	**4g**	12	56
8	**3h**	9	**4h**	10	55

[a]Percentage of conversion was measured by GC–MS.
[b]Unreacted raw material.

recrystallization processes were not necessary and pure products were characterized by ^{1}H and ^{13}C NMR and mass spectrometry. Syntheses of **3b**–**3h** were carried out with the same procedure. Products **4a**–**4h** were isolated and characterized from the mixture of the reactions for the synthesis of **3a**–**3h**.

Typical procedure for the Willgerodt–Kindler reaction at room temperature

For the formation of **3a**, elemental sulfur (184 mg, 5.7 mmol) was added to 500 mg (5.7 mmol) of amine **2a**, the reaction mixture was stirred for 2 h until the sulfur was completely dissolved in the amine, and then acetophenone **1a** (690 mg, 5.7 mmol) was added to the amine–sulfur mixture and stirred at room temperature for 48 h. The reaction was monitored by TLC and the conversion rates were determined by GC–MS. Compounds **3b**–**3h** were obtained, replacing the corresponding acetophenones **1a**–**1c** and amines **2a**–**2e** following the typical procedure for **3a**.

2-Morpholino-1-phenyl-2-thioxoethanone (3a)[13,14,16]

Yield: 109 mg (56%); pale yellow solid, mp 107–109 °C. R_f (70% Hex/AcOEt): 0.42. ^{1}H NMR (200 MHz, $CDCl_3$, Me_4Si) δ_H: 8.01–7.97 (2H, m), 7.34–7.31 (3H, m), 4.37–4.33 (1H, t, J = 9.8 Hz), 3.76–3.71 (1H, t, J = 9.8 Hz), 3.65–3.60 (1H, t, J = 9.6 Hz), 3.40–3.35 (1H, t, J = 9.6 Hz). ^{13}C NMR (50 MHz, $CDCl_3$) δ_C: 199.9 (C=S), 187.8 (C=O), 135.7, 128.9, 127.7, 127.1, 66.3, 50.7, 50.5, 50.1. MS (EI) m/z: 235 ($M^{+\bullet}$, 15%), 221 (100), 130 (35), 105 (5). HRMS-EI calcd for $C_{12}H_{13}O_2NS$: 235.0667; found: 235.0655.

1-Phenyl-2-(piperidin-1-yl)-2-thioxoethanone (3b)[14,19]

Yield: 97 mg (50%); pale yellow solid, mp 53–55 °C. R_f (90% Hex/AcOEt, eluted twice): 0.48. IR (KBr, cm^{-1}): 2944, 2862, 1666, 1590. ^{1}H NMR (300 MHz, $CDCl_3$, Me_4Si) δ_H: 7.99–7.96 (1H, m), 7.62–7.56 (2H, m), 7.50–7.44 (2H, m), 4.25–4.22 (2H, m), 3.54–3.50 (2H, m), 2.16 (2H, s), 1.82–1.73 (2H, br), 1.62–1.60 (2H, br). ^{13}C NMR (75 MHz, $CDCl_3$) δ_C: 194.2 (C=S), 187.9 (C=O), 134.1, 133.2, 129.6, 128.7, 52.9, 48.0, 26.3, 25.2, 23.9. MS (EI) m/z: 233 ($M^{+\bullet}$, 78.1%), 128 (100), 84 (53.1). HRMS-EI calcd for $C_{17}H_{22}O_2N_2S$: 233.0874; found: 233.0873.

2-(2-Methylpiperidin-1-yl)-1-phenyl-2-thioxoethanone (3c)[19]

Yield: 42 mg (20%); yellow solid,. mp 65–68 °C. R_f (90% Hex/AcOEt, eluted twice): 0.22. IR (KBr, cm^{-1}): 2928, 2860, 1737, 1667. ^{1}H NMR (300 MHz, $CDCl_3$, Me_4Si) δ_H: 8.01–7.94 (1H, m), 7.60–7.57 (2H, m), 7.51–7.46 (2H, m), 5.43–5.39 (1H, m), 4.09 (2H, m), 3.64–3.57 (2H, m), 1.99 (2H, m), 1.75 (2H, br), 1.25 (3H, s). ^{13}C NMR (75 MHz, $CDCl_3$) δ_C: 194.3 (C=S), 187.5 (C=O), 134.0, 133.4, 129.6, 128.7, 56.3, 49.7, 47.5, 41.9, 30.6, 29.6, 25.9, 25.3, 18.5, 18.3, 16.4, 14.7. MS (EI) m/z: 247 ($M^{+\bullet}$, 64.37%), 142 (75), 98 (62.5), 18 (100). HRMS-EI calcd for $C_{14}H_{17}ONS$: 247.1031; found: 247.1033.

2-(3-Methylpiperidin-1-yl)-1-phenyl-2-thioxoethanone (3d)

Yield: 138 mg (67%); yellow solid, mp 45 °C. R_f (90% Hex/AcOEt, eluted twice): 0.22. ^{1}H NMR (300 MHz, $CDCl_3$, Me_4Si) δ_H: 7.99–7.96 (1H, m), 7.62–7.57 (2H, m), 7.50–7.45 (2H, m), 5.33–5.21 (1H, m), 3.75–3.63 (2H, m), 3.28–3.07 (2H, m), 1.94–1.90 (2H, br), 1.82–1.68 (2H, br), 0.82–0.79 (3H, m). ^{13}C NMR (75 MHz, $CDCl_3$) δ_C: 194.4 (C=S), 187.8 (C=O), 134.0, 133.3, 129.7, 128.7, 58.9, 53.9, 52.4, 47.5, 32.5, 32.1, 31.2, 25.6, 24.4, 18.9, 18.5. HRMS-EI calcd for $C_{14}H_{17}ONS$: 247.1031; found: 247.1030.

2-(4-Methylpiperidin-1-yl)-1-phenyl-2-thioxoethanone (3e)

Yield: 99 mg (48%); yellow solid, mp 53–55 °C. R_f (90% Hex/AcOEt, eluted twice): 0.22. IR (KBr, cm^{-1}): 2928, 2860, 1737, 1667. ^{1}H NMR (300 MHz, $CDCl_3$, Me_4Si) δ_H: 7.98–7.94 (1H, m), 7.60–7.54 (2H, m), 7.49–7.43 (2H, m), 5.41–5.33 (1H, m), 3.78–3.70 (2H, m), 3.31–3.22 (2H, m), 1.96 (2H, m), 1.92–1.61 (2H, br), 1.22 (3H, s). ^{13}C NMR (75 MHz, $CDCl_3$) δ_C: 194.4 (C=S), 187.9 (C=O), 134.0, 133.3, 129.7, 128.7, 52.0, 47.3, 34.2, 33.2, 30.7, 21.1. MS (EI) m/z: 247 ($M^{+\bullet}$, 64.37%), 142 (75), 98 (62.5), 18 (100). HRMS-EI calcd for $C_{14}H_{17}ONS$: 247.1031; found: 247.1032.

1-(4-Nitrophenyl)-2-(piperidin-1-yl)-2-thioxoethanone (3f)

Yield: 91 mg (54%); yellow solid, mp 123–125 °C. R_f (66% Hex/acetone): 0.46. ^{1}H NMR (300 MHz, $CDCl_3$, Me_4Si) δ_H: 7.77–7.74 (2H, m), 6.62–6.59 (2H, m), 4.43 (2H, m), 4.23 (2H, m), 3.53 (2H, m), 1.77 (2H, br), 1.74 (2H, br). ^{13}C NMR (75 MHz, $CDCl_3$) δ_C: 195.5 (C=S), 187.7 (C=O), 152.6, 132.5, 122.8, 113.9, 53.0, 48.2, 26.5, 25.4, 24.1. MS (EI) m/z: 278 ($M^{+\bullet}$, 48%), 150 (6), 128 (100), 84 (96). Anal. calcd for $C_{13}H_{14}N_2O_3S$ (278.3): C 56.10, H 5.07, N 10.06; found: C 60.49, H 6.19, N 10.23.

1-(4-Chlorophenyl)-2-morpholino-2-thioxoethanone (3g)[16]

Yield: 33 mg (19%); yellow solid, mp 150–152 °C. R_f (73% Hex/AcOEt): 0.25. ^{1}H NMR (300 MHz, $CDCl_3$, Me_4Si) δ_H: 7.94–7.91 (2H, d, J = 8.7 Hz), 7.48–7.45 (2H, d, J = 9 Hz), 4.33–4.30 (1H, t, J = 9.9 Hz), 3.91–3.88 (1H, t, J = 9.9 Hz), 3.71–3.68 (1H, t, J = 9 Hz), 3.60–3.57 (1H, t, J = 9.3 Hz). ^{13}C NMR (50 MHz, $CDCl_3$) δ_C: 194.8 (C=S), 186.3 (C=O), 140.9, 131.1, 129.2, 125.7, 66.4, 66.3, 51.9, 47.1. MS (EI) *m/z*: 269 ($M^{+\bullet}$, 12%), 139 (33), 130 (100), 86 (76). Anal. calcd for $C_{12}H_{12}ClNO_2S$ (269.7): C 53.43, H 4.48, N 5.19; found: C 53.33, H 5.47, N 4.35.

1-(4-Chlorophenyl)-2-(piperidin-1-yl)-2-thioxoethanone (3h)[19]

Yield: 21 mg (12%); yellow solid, 120–122 °C. R_f (70% Hex/AcOEt): 0.18. IR (KBr, cm^{-1}): 2949, 2858, 1665, 1586. ^{1}H NMR (300 MHz, acetone-d_6, Me_4Si) δ_H: 8.00–7.97 (2H, d, J = 9 Hz), 7.61–7.58 (2H, d, J = 8.7 Hz), 4.26 (2H, m), 3.63–3.59 (2H, t, J = 11.4 Hz), 2 (2H, m) 1.81–1.77 (2H, m) 1.62 (2H, m). ^{13}C NMR (75 MHz, acetone-d_6) δ_C: 194.0 (C=S), 186.9 (C=O), 140.5, 133.3, 132.0, 129.9, 53.5, 48.4, 27.2, 25.9, 24.5. MS (EI) *m/z*: 267 ($M^{+\bullet}$, 30%), 138 (17), 128 (36), 84 (100). Anal. calcd for $C_{13}H_{14}ClNO_2S$ (267.7): C 58.31, H 5.27, N 5.23; found: C 58.20, H 7.26, N 2.91.

2-Phenyl-1-(piperidin-1-yl)ethanethione (4b)

Yield: 72 mg (39%); pale yellow solid, mp 55–57 °C. R_f (90% Hex/AcOEt, eluted twice): 0.51. ^{1}H NMR (300 MHz, $CDCl_3$, Me_4Si) δ_H: 7.33–7.18 (5H, m), 4.32 (2H, s), 4.26–4.23 (2H, m, J = 10.5 Hz), 3.57–3.53 (2H, m, J = 11.1 Hz), 2.02–1.97 (2H, bs), 1.64–1.61 (2H, m), 1.30–1.26 (2H, m). ^{13}C NMR (75 MHz, $CDCl_3$) δ_C: 198.1, 136.0, 128.7, 127.7, 126.7, 51.5, 50.9, 26.1, 25.1, 23.7. MS (EI) *m/z*: 219 ($M^{+\bullet}$, 100%), 128 (75), 91 (80). Anal. calcd for $C_{13}H_{17}NS$ (219.3): C 71.18, H 7.81, N 6.39; found: C 64.47, H 7.01, N 6.34.

2-(4-Chlorophenyl)-1-morpholinoethanethione (4g)

Yield: 69 mg (42%); yellow solid, mp 125–127 °C. R_f (73% Hex/AcOEt): 0.31. ^{1}H NMR (300 MHz, $CDCl_3$, Me_4Si) δ_H: 7.30–7.23 (5H, m), 4.34–4.31 (1H, t, J = 9.9 Hz), 4.28 (2H, s), 3.74–3.71 (1H, t, J = 9.9 Hz), 3.61–3.58 (1H, t, J = 9.6 Hz), 3.43–3.40 (1H, t, J = 9.9 Hz). ^{13}C NMR (50 MHz, $CDCl_3$) δ_C: 199.2, 134.1, 132.8, 129.1, 129.0, 66.2, 66.0, 50.6, 50.0, 49.6. MS (EI) *m/z*: 255 ($M^{+\bullet}$, 100%), 130 (55), 125 (35). Anal. calcd for $C_{12}H_{14}ClNOS$ (255.7): C 56.35, H 5.52, N 5.48; found: C 57.07, H 6.33, N 4.75.

Supplementary data

Supplementary data are available with the article through the journal Web site http://nrcresearchpress.com/doi/suppl/10.1139/v2012-030. CCDC 819515 contains the X-ray data in CIF format for this manuscript. These data can be obtained, free of charge, via http://www.ccdc.cam.ac.uk/products/csd/request (Or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: 44 1223 336033; or e-mail: deposit@ccdc.cam.ac.uk.

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