A novel method for heterocyclic amide–thioamide transformations

Walid Fathalla*1, Ibrahim A. I. Ali2 and Pavel Pazdera3

Abstract
In this paper, we introduce a novel and convenient method for the transformation of heterocyclic amides into heterocyclic thioamides. A two-step approach was applied for this transformation: Firstly, we applied a chlorination of the heterocyclic amides to afford the corresponding chloroheterocycles. Secondly, the chloroheterocycles and N-cyclohexyl dithiocarbamate cyclohexylammonium salt were heated in chloroform for 12 h at 61 °C to afford heterocyclic thioamides in excellent yields.

Introduction
Transforming heterocyclic amides into thioamides is an important task in organic synthesis. Earlier reports for this type of O/S conversions were achieved by several thiating reagents; for instance, Lawesson's reagent (2,4-bis(4-methoxyphenyl)-1,3-dithia-2,4-diphosphetane 2,4-disulfide) [1-3], Berzelius reagent (4-6) (P4S10), and phosphorus pentasulfide [7] in dry toluene, xylene or pyridine under reflux conditions. A two-step approach for the purpose of thiation of heterocyclic amides attracted our attention: as a first step, we applied a chlorination of heterocyclic amides, followed by thiation via reaction with thiourea on the basis of reagent-promoted desulfurylation of iso-thiourea under strong basic conditions [8,9]. Aiming to continue our research work on the structure modification of functionalized heterocyclic amides and thioamides [10-17], we found it interesting to design a new convenient and simple method for the thiation of heterocyclic amides.

Results and Discussion
Many synthetic methods related to thiation of heterocyclic amides have been reported to date. Most methods suffer from
the employment of expensive specific reagents, high temperature, use of strong basic conditions, ultra-dry solvents, bad smell, low yield, difficulties in work-up procedures or from a narrow substrate scope. Therefore, the development of a more efficient method for the transformation of heterocyclic amides to heterocyclic thioamides gained great attention.

The reaction of three molar equivalents of cyclohexylamine (1) with one molar equivalent of carbon disulfide in water typically afforded \(N\)-cyclohexyl dithiocarbamate cyclohexylammonium salt (2) as an excellent new thiating reagent in high yield, Scheme 1.

![Scheme 1: Synthesis of \(N\)-cyclohexyl dithiocarbamate cyclohexylammonium salt (2).](image)

The structure assignment of the prepared \(N\)-cyclohexyl dithiocarbamate cyclohexylammonium salt (2) is based on \(^1\)H and \(^{13}\)C NMR spectral and physicochemical analysis. The \(^1\)H NMR spectrum displays a broad singlet signal at 8.01 ppm associated with three NH protons. The \(^1\)H NMR spectrum also shows three multiplet signals at 4.15–3.95 and 3.05–2.96 and 1.98–0.96 ppm corresponding to two CH and 10 CH\(_2\) groups, respectively. The \(^{13}\)C NMR spectrum of 2 displays signals at \(\delta\) 212.4, 55.3 and 50.0 ppm associated with (C=S) and two CH groups, respectively. The \(^{13}\)C NMR spectrum of 2 also shows signals at 32.3, 30.9, 25.8, 25.5, 25.1, and 24.3 ppm due to cyclohexyl CH\(_2\) groups.

Heterocyclic amides A1–13 used in this context were prepared as described in literature expanding simple one-step procedures to multi-step sequential reactions. Quinazoline-4-one (A1) [18] was prepared by Niementowski reaction by fusion of anthranilic acid with formamide at 120 °C for 5 h. A number of quinazoline derivatives A2–A6 [19-21] were prepared via sequential steps starting from easily available carboxylic acid chlorides. The acid chlorides reacted with anthranilic acid to afford benzoxazines, followed by sequential reaction with ammonia to afford the benzamidine derivatives and finally, benzamidines were cyclized by heating in sodium hydrosulfide solution and gave quinazolines A2–A6. Methyl 1,2-dihydro-2-oxoquinoline-4-carboxylate (A9) [22,23] was prepared by heating isatine with malonic acid followed by esterification of the produced quinoline carboxylic acid with methanol in the presence of sulfuric acid at 80 °C for 6 h. 4-Arylphthalazin-1(2\(H\))-ones A7 and A8 [24,25] were prepared by Friedel–Crafts acylation reaction of N-aminophthalimide with either benzene or toluene in the presence of AlCl\(_3\), respectively. A number of quinoxalin-2-one derivatives A10–13 [26-29] were prepared by the reaction of \(o\)-phenylenediamine with oxoacids or oxoesters either in HCl solution or in ethanol.

Heterocyclic amides A1–9 were heated with POCl\(_3\) for 2–5 h as reported in literature to afford the respective chloroheterocycles [30-37] B1–9 and 13 and were purified using flash column chromatography; petroleum ether (60–80)/ethyl acetate (9:1) as an eluent. Best results for the preparation of chloroquinoxalines B11 and B12 [38,39] were achieved by dropwise addition of \(N,N\)-dimethylamine to a stirred cold solution of quinoxalines A11 and A12 and POCl\(_3\), the reaction mixture was refluxed for 15 minutes.

Thus, \(N\)-cyclohexyl dithiocarbamate cyclohexylammonium salt (2) was added to 4-chloro-2-phenylquinazoline (B2) solution in CHCl\(_3\), the reaction mixture was heated at 61 °C for 12 h. The reaction mixture was evaporated and poured in ethanol to give bright yellow crystals as only isolated product, identified as 2-phenylquinazoline-4(3\(H\))-thione (C2). The filtrate was once again evaporated and crystalized from ethanol/water to give dicyclohexylthiourea (3, Scheme 2). We have extended the scope of this process to involve the transformation of a number of heterocyclic amides; quinazolin-4(3\(H\))-one (A1), 2-substituted quinazolin-4(3\(H\))-one A3–A6 and 4-substituted phthalazin-1(2\(H\))-ones A7 and A8 into the corresponding heterocyclic thioamides C1 and C3–C8, respectively (Scheme 2, Table 1 and Table 2).

![Scheme 2: The two-step thiation of quinazolin-4-one A1–6 and phthalazin-1-ones A7 and A8.](image)
Table 1: Synthesis of quinazolin-4-thiones.

| No. | heterocyclic amide A | chloro-heterocycles B | heterocyclic thioamide C | Yield\(b\) % |
|-----|---------------------|-----------------------|--------------------------|--------------|
| 1   | ![A1](image1)       | ![B1](image2)        | ![C1](image3)           | 76%          |
| 2   | ![A2](image4)       | ![B2](image5)        | ![C2](image6)           | 92%          |
| 3   | ![A3](image7)       | ![B3](image8)        | ![C3](image9)           | 84%          |
| 4   | ![A4](image10)      | ![B4](image11)       | ![C4](image12)          | 89%          |
| 5   | ![A5](image13)      | ![B5](image14)       | ![C5](image15)          | 95%          |
| 6   | ![A6](image16)      | ![B6](image17)       | ![C6](image18)          | 81%          |

\(a\) Reaction conditions: chloroheterocycles (20 mmol) and \(N\)-cyclohexyl dithiocarbamate cyclohexylammonium salt \((2, 20 \text{ mmol})\) were heated in \(\text{CHCl}_3\) (25 mL) at 61 °C for 12 h. \(b\) Yields refer to isolated pure product of the reaction from B to C.

The \(N\)-cyclohexyl dithiocarbamate cyclohexylammonium salt \((2)\) has been found to be an excellent reagent for thiation of heterocyclic amides into thioamides at position 4, Scheme 2, Table 1 and Table 2. We have extended the scope of this thiation process to involve heterocyclic amides at positions 2 and 3. Thus, methyl 1,2-dihydro-2-oxoquinoline-4-carboxylate (A9) and 3-substituted quinoxalin-2(1H)-ones A10–13 reacted similarly with phosphorous oxychloride to afford the chloro derivatives B9–13 which were subsequently converted into the corresponding thioamides C9–13 by the reaction with \(N\)-cyclohexyl dithiocarbamate cyclohexylammonium salt \((2)\) in CHCl3 under reflux conditions for 12 h (Scheme 3, Table 3).

The synthetic procedure for the formation of C1–13 reported herein have the advantage of operational simplicity and availability of both the substrate and the reagents giving a series of
Table 2: Synthesis of phthalizin-1-thiones C7 and C8.a.

| No. | heterocyclic amide A | chloro-heterocycles B | heterocyclic thioamide C | Yieldb % |
|-----|----------------------|-----------------------|--------------------------|----------|
| 7   | ![A7](image)         | ![B7](image)         | ![C7](image)             | 91%      |
| 8   | ![A8](image)         | ![B8](image)         | ![C8](image)             | 78%      |

*aReaction conditions as described before. bYields refer to isolated pure product of the reaction from B to C.

Scheme 3: Thiation of quinoline A9 and quinoxalinone A10–13.

Table 3: Synthesis of quinolin-2-thiones C9 and quinoxalin-2-thiones C10–C13.a.

| No. | heterocyclic amide A | chloro-heterocycles B | heterocyclic thioamide C | Yieldb % |
|-----|----------------------|-----------------------|--------------------------|----------|
| 9   | ![A9](image)         | ![B9](image)         | ![C9](image)             | 76%      |
| 10  | ![A10](image)        | ![B10](image)        | ![C10](image)            | 69%      |
| 11  | ![A11](image)        | ![B11](image)        | ![C11](image)            | 83%      |
very interesting compounds. This method also was adjusted to involve a one-pot strategy starting from heterocyclic amides A1–13 to directly afford the heterocyclic thioamides C1–13. Thus, 2-phenylquinazolin-4(3H)-one (A2) was heated with phosphorous oxychloride for 2 h. The reaction mixture was evaporated and poured in ice-cold ammonia solution, then extracted with chloroform and dried over sodium sulfate. N-cyclohexyl dithiocarbamate cyclohexylammonium salt (2) was added to the chloroform solution of chloroquinazoline B2 and heated at 61 °C for 12 h. The reaction mixture was evaporated and ethanol was added successively to give the desired product C2.

The structure assignment of the prepared heterocyclic thioamides C1–13 is based on 1H and 13C NMR spectral and physicochemical analyses. The 1H NMR spectrum of 2-(4-methoxyphenyl)quinazoline-4(3H)-thione (C5) gave a broad singlet and a singlet signal at δ 13.71 and 3.87 ppm, associated with NH and OCH3 groups, respectively. The significant downfield shift of the NH proton is probably due to intermolecular hydrogen bond interactions of the type NH⋯S=C. All the isolated thioureas C1–13 exhibited similar 1H NMR spectral patterns with the NH protons at similar chemical shifts and they adopt paired thioamide structures (vide infra). The 1H NMR spectrum also shows four doublet and two triplet signals at δ 8.60, 8.19, 7.75, 7.11, 7.88, 7.56, respectively due to eight aromatic protons. The 13C NMR spectrum of C5 displays signals at δ 187.9 and 56.0 ppm due to C=S and OCH3, respectively.

A mechanistic rationalization for this interesting rearrangement is given in Scheme 4. The reaction of 4-chloro-2-phenylquinazoline (B2) with N-cyclohexyl dithiocarbamate cyclohexylammonium salt (2) in CHCl3 at 61 °C for 12 h was principally expected to give 2-phenylquinazolin-4-yl cyclohexylcarbamodithioate (I) and cyclohexylamine hydrochloride. Cyclohexylamine hydrochloride under heating conditions will eliminate an HCl molecule forming the free cyclohexylamine base.

Cyclohexylamine will further abstract a proton from I followed by electron delocalization and the overall formation of cyclohexyl isothiocyanate (4) via C=S bond cleavage and the formation of quinazoline thiol anion II having a negative charge centered on the nitrogen atom. The protonated cyclohexylamine in the previous step will transfer this extra proton to II to afford the quinazoline thione C2. On the other hand the free cyclohexylamine will add to cyclohexyl isothiocyanate (4) to form the thiourea 3. Similar results were obtained by Furumoto [40], and Sun [41] reported the application of cyanuric chloride (2,4,6-trichloro-1,3,5-triazine, TCT) as a desulfurylation reagent in the synthesis of carbodiimides or alkyl isothiocyanates from thioureas under mild conditions.

**Conclusion**

Several synthetic procedures related to thiation of heterocyclic amides have been reported to date. The drawback of the existing methods is the use of expensive specific reagents, high temperature, use of strong basic conditions, ultra-dry solvents, bad smell, low yield, difficulties in work-up procedures or from a narrow substrate scope. In this work, we successfully developed a facile and convenient general method for the transformation of heterocyclic amides into heterocyclic thioamides. Generally, in the proposed technique we transformed heterocyclic amides to chloroheterocyclic compounds by the action of phosphorous oxychloride. Subsequently, chloroheterocyclic derivatives reacted with N-cyclohexyl dithiocarbamate cyclohexylammonium salt in chloroform at 61 °C for 12 h to finally afford the heterocyclic thiocyanates in excellent yields. Furthermore, this method is advantageous over existing methods in the matter of simplicity of the work-up procedure, higher yield, odorless, lower reaction temperature and finally the availability of both precursors and reagent.
Scheme 4: Rational mechanism of the reaction of 4-chloro-2-phenylquinazoline (B2) to 2-phenylquinazolin-4(3H)-thione.

**Experimental**

**General procedures**

Solvents were purified and dried by standard procedures. The boiling range of the petroleum ether used was 40–60 °C. Thin-layer chromatography (TLC): silica gel 60 F254 plastic plates (E. Merck, layer thickness 0.2 mm) detected by UV absorption. Elemental analyses were performed on a Flash EA-1112 instrument at the Microanalytical laboratory, Faculty of Science, Suez Canal University, Ismailia, Egypt. Melting points were determined on a Büchi 510 melting-point apparatus and the values are uncorrected. 1H and 13C NMR spectra were recorded at 300 MHz and 75.5 MHz, respectively (Bruker AC 300) in CDCl3 and DMSO solution with tetramethylsilane as an internal standard. The NMR analyses were performed at the Organic Chemistry Department Masaryk University, Brno, Czech Republic. Compounds A1–13 and B1–13 were obtained by published methods [18-39], and their melting points and 1H and 13C NMR spectra corresponded to those given in the literature.

**General method for the preparation of thiating reagent N-cyclohexyl dithiocarbamate cyclohexylammonium salt (2).** To a mixture of freshly distilled cyclohexylamine (60 mmol) and water (50 mL) was added carbon disulfide (21 mmol) dropwise. The reaction mixture was stirred at room temperature for 2 h. The white solid obtained was filtered, washed with water, dried and crystalized from ethanol to provide the pure product. Yield 98% (ethanol 95%) white crystals, mp 188–189 °C; 1H NMR (300 MHz, DMSO-d6) δ 8.01 (bs, 3H, 3NH), 4.15–3.95 (m, 1H, CH), 3.05–2.96 (m, 1H, CH), 1.98–0.96 (20H, m, 10CH 2); 13C NMR (75.0 MHz, DMSO-d6) δ 212.4 (C=S), 55.3 (CH), 50.0 (CH), 32.3 (2CH 2), 30.9 (2CH 2), 25.8 (CH 2), 25.5 (2CH 2), 25.1 (CH 2), 24.3 (2CH 2); anal. calcd for C13H26N2S2 (274.2): C, 56.56; H, 9.43; N, 10.09; found: C, 56.88; H, 9.55; N, 10.21.

**General method for the preparation of heterocyclic thioamides**

**Method A.** To a solution of chloroheterocycles (2.5 mmol) in CHCl3 (25 mL) was added (0.69 g, 2.5 mmol) of N-cyclohexyl dithiocarbamate cyclohexylammonium salt. The reaction mixture was refluxed at 61 °C for 12 h. The reaction mixture was evaporated under reduced pressure and 25 mL of ethanol was added to the solid residue. The yellowish–orange precipitate was filtered to give the desired product. The crude compounds
were pure enough for analytical purposes. Purification of products for analysis was achieved by crystallization from the appropriate solvent; chromatographed with the appropriate eluent or by repeated dissolution in KOH and reprecipitation by acetic acid. The filtrate was evaporated once again and the solid obtained was crystallized from ethanol water to give symmetrical dicyclohexylthiourea (3).

**Method B.** To a cold solution of heterocyclic amide (2.5 mmol) in POCl₃ (25 mL) was added dimethylaniline (2.5 mmol). The reaction mixture was stirred under reflux (100–105 °C) for 1.5–2 h. The excess POCl₃ was removed under reduced pressure. The residue was poured into a mixture of chloroform (50 mL), ice water (80 mL) and ammonia (5 mL). The chloroform layer was separated, dried over Na₂SO₄ and filtered. To this chloroform solution of the in situ generated chloroheterocycles were added (0.69 g, 2.5 mmol) of N-cyclohexyl dithiocarbamate cyclohexylammonium salt. The reaction mixture was refluxed at 61 °C for 12 h. The reaction mixture was evaporated under reduced pressure and 25 mL of ethanol was added to the solid residue. The yellowish–orange precipitate was filtered to give the desired product. The crude compounds were pure enough for analytical purposes. Purification of products for analysis was achieved by crystallization from the appropriate solvent; chromatographed with the appropriate eluent or by repeated dissolution in KOH and reprecipitation by acetic acid.

**Dicyclohexylthiourea (3)** [42]: Yield 65% (ethanol 95%–H₂O) white crystals, mp 180–181 °C; ¹H NMR (300 MHz, DMSO-d₆) δ 7.05 (bs, 2H, NH), 4.05–3.89 (m, 2H, 2CH₂), 1.87–1.52 (m, 10H, 5CH₂); ¹³C NMR (75.0 MHz, DMSO-d₆) δ 187.7 (C=S), 155.5 (C Ar), 144.7 (C Ar), 136.8 (C Ar), 135.8 (CHAr), 134.0 (CHAr), 130.9 (C Ar), 130.6 (CHAr), 129.7 (CHAr), 128.6 (CHAr), 128.0 (CHAr), 126.1 (C Ar), 19.9 (CH₃); anal. calcld for C₁₃H₁₂N₂S (252.1): C, 71.40; H, 4.79; N, 11.65; found: C, 71.28; H, 4.61; N, 11.84.

**Quinazoline-4(3H)-thione (C1)** [43]: Yield 76% (H₂O) yellow crystals, mp 320–321 °C; ¹H NMR (300 MHz, DMSO-d₆) δ 13.83 (bs, 1H, NH), 8.55–7.28 (m, 5H, ArH); ¹³C NMR (75.0 MHz, DMSO-d₆) δ 186.2 (C=S), 144.8 (C Ar), 144.2 (CHAr), 135.7 (CHAr), 129.7 (CHAr), 129.4 (C Ar), 128.7 (CHAr), 128.5 (CHAr); anal. calcld for C₉H₆N₂S (162.0): C, 59.23; H, 3.73; N, 17.27; found: C, 59.17; H, 3.69; N, 17.15.

**2-Phenylquinazoline-4(3H)-thione (C2)** [44]: Yield 92% (ethanol 95%–DMF) yellow crystals, mp 222–223 °C; ¹H NMR (300 MHz, DMSO-d₆) δ 13.75 (bs, 1H, NH), 8.63 (d, J = 8.0 Hz, 1H, ArH), 8.17 (d, J = 8.0 Hz, 2H, ArH), 7.93–7.89 (m, 3H, ArH), 7.82–7.57 (m, 3H, ArH); ¹³C NMR (75.0 MHz, DMSO-d₆) δ 188.5 (C=S), 152.1 (C Ar), 144.8 (C Ar), 135.8 (CHAr), 132.8 (C Ar), 131.9 (CHAr), 129.8 (CHAr), 128.9 (CHAr), 128.6 (CHAr), 128.4 (CHAr), 128.1 (C Ar); anal. calcld for C₁₄H₁₀N₂S (238.1): C, 70.56; H, 4.23; N, 11.76; found: C, 70.48; H, 4.16; N, 11.49.

**2-o-Tolyquinazoline-4(3H)-thione (C3)** [45]: Yield 84% (ethanol 95%–DMF) yellow crystals, mp 183–184 °C; ¹H NMR (300 MHz, DMSO-d₆) δ 13.97 (bs, 1H, NH), 8.65 (d, J = 8.0 Hz, 1H, ArH), 7.96 (t, J = 8.0 Hz, 1H, ArH), 7.75 (d, J = 8.0 Hz, 1H, ArH), 7.66–7.35 (m, 5H, ArH), 2.39 (s, 3H, CH₃); ¹³C NMR (75.0 MHz, DMSO-d₆) δ 187.7 (C=S), 155.5 (C Ar), 144.7 (C Ar), 136.8 (C Ar), 135.8 (CHAr), 134.0 (CHAr), 130.9 (C Ar), 130.6 (CHAr), 129.7 (CHAr), 128.6 (CHAr), 128.0 (CHAr), 126.1 (C Ar), 19.9 (CH₃); anal. calcld for C₁₃H₁₂N₂S (252.1): C, 71.40; H, 4.79; N, 11.10; found: C, 71.21; H, 4.65; N, 10.94.

**2-p-Tolyquinazoline-4(3H)-thione (C4)** [46]: Yield 89% (ethanol 95%–DMF) yellow crystals, mp 218–219 °C; ¹H NMR (300 MHz, DMSO-d₆) δ 13.78 (bs, 1H, NH), 8.62 (d, J = 8.0 Hz, 1H, ArH), 8.10 (d, J = 8.0 Hz, 2H, ArH), 7.93–7.76 (m, 2H, ArH), 7.58 (t, J = 8.0 Hz, 1H, ArH), 7.37 (d, J = 8.0 Hz, 2H, ArH), 2.41 (s, 3H, CH₃); ¹³C NMR (75.0 MHz, DMSO-d₆) δ 187.9 (C=S), 151.9 (C Ar), 149.3 (C Ar), 142.1 (C Ar), 135.9 (C Ar), 130.4 (C Ar), 129.8 (CHAr), 129.7 (CHAr), 129.6 (CHAr), 128.8 (CHAr), 128.3 (CHAr), 128.0 (CHAr), 126.4 (CHAr), 21.5 (CH₃); anal. calcld for C₁₅H₁₂N₂S (252.1): C, 71.40; H, 4.79; N, 11.10; found: C, 71.28; H, 4.61; N, 11.84.

The yield, ¹H, ¹³C NMR spectral data and physicochemical analysis of other prepared thioamides (C5–C13) are presented in Supporting Information File 1.

**Supporting Information**

**Supporting Information File 1**
Additional experimental and analytical data. [http://www.beilstein-journals.org/bjoc/content/supplementary/1860-5397-13-20-S1.pdf]

**Acknowledgements**
We would like to thank the Department of Organic Chemistry, Faculty of Science, Masaryk University, Brno, Czech Republic and the Ministry of high education Egypt for funding this research proposal. We would like to thank Dr. Hewaya El-Ghawalby for technical support.

**References**
1. Ozturk, T.; Ertas, E.; Mert, O. Chem. Rev. 2007, 107, 5210. doi:10.1021/cr900243d
2. Ozturk, T.; Ertas, E.; Mert, O. Chem. Rev. 2010, 110, 3419. doi:10.1021/cr900243d
3. Curphey, T. J. J. Org. Chem. 2002, 67, 6461. doi:10.1021/jo0256742
4. Libermann, R. Bull. Soc. Chim. Fr. 1959, 1793.
5. Leonard, N. J.; Curtin, D. Y. J. Org. Chem. 1946, 11, 349. doi:10.1021/jo01174a007
6. Armstrong, R. T. Vulcanization accelerators. U.S. Patent US2382769, Aug 14, 1945.
7. Morrison, D. C.; Furst, A. J. Org. Chem. 1956, 21, 470. doi:10.1021/jo01110a026
8. Asano, K. Yakugaku Zasshi 1958, 78, 729.
9. El-Hawash, S. A. M.; Abdel Wahab, A. E. Arch. Pharm. 2006, 339, 437. doi:10.1002/ardp.200600012
10. Fathalla, W.; Cajan, M.; Pazdera, P. Molecules 2000, 5, 1210. doi:10.3390/1021210
11. Fathalla, W.; Cajan, M.; Pazdera, P. Molecules 2001, 6, 557. doi:10.3390/86060557
12. Fathalla, W.; Pazdera, P.; Marek, J. J. Heterocycl. Chem. 2002, 39, 1139. doi:10.1002/jhet.5570390605
13. Fathalla, W.; Marek, J.; Pazdera, P. J. Sulfur Chem. 2008, 29, 31. doi:10.1016/j.17415990701759685
14. Fathalla, W. ARKIVOC 2008, xii, 245.
15. Ali, I. A. I.; Fathalla, W. Heterotet. Chem. 2006, 17, 280. doi:10.1002/hc.20203
16. Fathalla, W.; El Rayes, S.; Ali, I. A. I. ARKIVOC 2008, xiii, 179.
17. Fathalla, W. Heterocycl. Chem. Compd. 2015, 51, 67. doi:10.1007/s10593-015-1661-1
18. Yamamoto, Y. Methods of molecular hetarenes and related ring systems; Science of Synthesis: Houben-Weyl, Vol. 16; 2003; pp 726 ff.
19. Sundaram, R.; Yuvaraj, E.; Babu, G. Indian J. Chem., Sect. B: Org. Chem. Incl. Med. Chem. 1999, 38, 905.
20. Lee, E. S.; Son, J. K.; Na, Y. H.; Jahng, Y. Heterocycl. Commun. 2004, 10, 325. doi:10.1515/HCC.2004.10.4-5.325
21. Okada, K.; Sakuma, H.; Inoue, S. Chem. Lett. 1979, 8, 131. doi:10.1246/cl.1979.131
22. Chawla, H. M.; Gupta, T. J. Inclusion Phenom. Macrocyclic Chem. 2015, 81, 49. doi:10.1007/s10847-014-0432-4
23. Debhala, H. A. Y. Indian J. Chem., Sect. B: Org. Chem. Incl. Med. Chem. 1994, 33, 779.
24. Ismail, M. F.; Kandall, N. G. Acta Chim. Hung. 1991, 128, 251.
25. Ajarri, O. O.; Obafiemi, C. A.; Ikor, C. O.; Oggunniran, K. O.; Nwinyi, O. C. Heterocycl. Chem. Compd. 2009, 45, 1370. doi:10.1007/s10593-010-0435-z
26. Noorvi, M. N.; Patel, H. M.; Bhardwaj, V.; Chauhan, A. Eur. J. Med. Chem. 2011, 46, 2327. doi:10.1016/j.ejmech.2011.03.015
27. Mahesh, R.; Dhar, A. K.; Sasank, T. V. N. V. T.; Thirunavukkarasu, S.; Devadoss, T. Chin. Chem. Lett. 2011, 22, 389. doi:10.1016/j.ccl.2010.11.002
28. Elhelbity, A. A.; Ayyad, R. R.; Zayed, M. F. Arzneim. Forsch. 2011, 61, 379. doi:10.1556/0013-1298214
29. Shi, L.; Wu, T.-T.; Wang, Z.; Xu, J.-Y.; Xu, Y.-G. Bioorg. Med. Chem. 2011, 22, 4735. doi:10.1016/j.bmc.2014.07.008
30. Marvania, B.; Lee, P.-C.; Chaniyara, R.; Dong, H.; Suman, S.; Kakadiya, R.; Chou, T.-C.; Lee, T.-C.; Shah, A.; Su, T.-L. Bioorg. Med. Chem. 2011, 19, 1987. doi:10.1016/j.bmc.2011.01.055
31. Ali, A. A. J. Chin. Chem. Soc. 2007, 54, 437. doi:10.1002/pocs.200700061
32. Browner, M.; Clark, D.; Cushing, T.; Hao, X.; Hawley, R.; He, X.; Jaen, J.; Lebadie, S.; Smith, M.-L.; Talmas, F.; Walker, N.; Labelle, M. Antinflammation agents. U.S. Pat. Appl. US20020161004 A1, Oct 31, 2002.