# Synthesis and structure analysis of 2-(2'-propanonylthio)-3-(*o*-methyl phenyl) quinazol-4(3H)-one

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The three-dimensional molecular and crystal structure of 2-(2'-propanonylthio)3-(*o*-methyl phenyl)quinazol-4(3H)-one has been determined by X-ray crystallographic methods. This compound crystallizes in the orthorhombic space group  $P_{bca}$  with unit cell parameters: a = 9.649(5), b = 30.102(10), c = 11.403(9) Å. It has been solved by direct methods and refined to a residual index of 0.054. The magnitude of torsion along C16–C11–N3–C4 bond is 93.5(4)°. The dihedral angle between the plane comprising all the ring atoms of quinazoline moiety and the atoms of the methyl substituted phenyl ring is 94.12(1)°. The crystal structure is stabilized by one intramolecular C–H···O interaction and three intermolecular C–H···N contacts.

KEY WORDS: Crystal structure; molecular interactions; X-ray diffraction; side chain descriptors.

## Introduction

Alkaloids containing a quinazoline moiety are known for their biological properties.<sup>1–4</sup> Recent studies have shown some remarkable properties exhibited by a variety of quinazoline derivatives and most notable among these have found place in analgesic, antiallergic, antiinflammatory, secretion inhibition, anticoagulant, etc.<sup>5</sup> The study being reported in this paper is a part of our ongoing work on the synthesis and structure analysis of a variety of quinazoline molecules.<sup>6–9</sup>

# Experimental

Step I: Synthesis of 3-(o-methyl phenyl)2thioquinazolin-4(3H)-one



Thiocarbonate salt of o-toludine was heated with anthranilic acid in ethanol on a steam bath for 6 h, cooled, and the excess of solvent removed under reduced pressure. The semisolid mass was dissolved in NaOH (10%) and filtered. The filtrate on neutralization with HCl (1:1) yielded a solid which was recrystallized from ethanol to get I, (90%), mp 542 K.

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Step II: Synthesis of 2-(2'-propanonylthio)-3-(omethylphenyl)quinazol- 4(3H)-one



A mixture of I (0.02 mole) and chloroacetone (0.02 mole) in acetone (10 mL), to which anhydrous  $K_2CO_3$  (0.5 g) was added and the reaction mixture was refluxed for 18 h, cooled, and the solvent removed under reduced pressure to get a solid which was recrystallized from ethanol, vield (80%), mp 373 K. The chemical structure as shown above has been assigned on the basis of IR, UV, NMR, and mass spectral data (M.B. Deshmukh, Private communication, 2002, Shivaji University, Kolhapur, India).

Three-dimensional intensity data of transparent rectangular plate single crystal of 2-(2'-propanonylthio)-3-(o-methylphenyl)quinazol -4(3H)-one were collected on an Enraf-Nonius CAD-4 diffractometer using MoK $\alpha$  radiation  $(\lambda = 0.71073$  Å. The  $\omega/2\theta$  scan mode was



employed for data collection. The  $\theta$ -range for the entire data collection is 2.24-24.98°. A total of 2861 reflections were found unique (0 < h < 11),  $0 \le k \le 35$ ,  $0 \le l \le 13$ ). Two standard reflections  $(\bar{2}\bar{4}\bar{9})$  (0 2 16) measured every 100 reflections showed no significant variation in the intensity data. The reflection data were corrected for Lorentz and polarization effects. Absorption and extinction corrections were not applied.

The structure has been elucidated by direct methods using SHELXS program.<sup>10</sup> All nonhydrogen atoms of the molecule were located from

Table 2. Atomic Coordinates and Equivalent Isotropic Displacement Parameters (Å<sup>2</sup>) with esd's in Parentheses, for the Non-Hydrogen Atoms

Y

Ζ

 $U_{eq.}^{a}$ 

Χ

| Table 1. Crystal Data and Structure Refinement Details |  | S1  | 0.0266(1)  | 0.4394(0) | 0.5275(1) | 0.0582(3)  |
|--|--|-----|------------|-----------|-----------|------------|
|  |  | 01  | -0.3041(2) | 0.3164(1) | 0.4778(2) | 0.0653(8)  |
| CCDC   | 203248   | 02  | -0.0613(2) | 0.4886(1) | 0.7502(2) | 0.0731(8)  |
| Crystal description                                    | Rectangular plates   | N1  | -0.0463(3) | 0.3842(1) | 0.6972(2) | 0.0496(8)  |
| Empirical formula                                      | $C_{18} H_{16} N_2 O_2 S$  | N3  | -0.1439(2) | 0.3705(1) | 0.5099(2) | 0.0442(8)  |
| Formula weight   | 324.39   | C2  | -0.0600(3) | 0.3934(1) | 0.5886(3) | 0.0452(9)  |
| Temperature  | 293(2)K  | C4  | -0.2279(3) | 0.3351(1) | 0.5476(3) | 0.0495(1)  |
| Crystal system, space group                            | Orthorhombic, $P_{hca}$  | C5  | -0.2875(4) | 0.2885(1) | 0.7187(3) | 0.0710(14) |
| Radiation. Wavelength $(\lambda)$                      | MoKα, 0.71073 Å  | C6  | -0.2719(4) | 0.2776(1) | 0.8334(4) | 0.0809(17) |
| Unit cell dimensions                                   | a = 9.649(5), b = 30.102(10),  | C7  | -0.1822(4) | 0.3015(1) | 0.9038(3) | 0.0768(16) |
|  | c = 11.403(9)  Å   | C8  | -0.1077(3) | 0.3365(1) | 0.8583(3) | 0.0614(12) |
|  | 8 3312(3) $Å^3$ 1 301 Mg/m <sup>3</sup>  | C9  | -0.1218(3) | 0.3484(1) | 0.7412(3) | 0.0498(10) |
| E(000)   | 1360   | C10 | -0.2125(1) | 0.3237(1) | 0.6697(3) | 0.0505(11) |
| Crystal size   | $0.3 \times 0.3 \times 0.2 \text{ mm}$   | C11 | -0.1432(3) | 0.3816(1) | 0.3860(3) | 0.0448(9)  |
| $\theta$ range for data collection                     | 2 24_24 98°  | C12 | -0.0580(3) | 0.3579(1) | 0.3115(3) | 0.0514(10) |
| Index ranges   | $0 \le h \le 11, 0 \le k \le 35$   | C13 | -0.0611(3) | 0.3687(1) | 0.1936(3) | 0.0609(12) |
| index ranges   | $0 \le n \le 11, 0 \le k \le 55,$<br>0 < l < 13  | C14 | -0.1491(4) | 0.4012(1) | 0.1525(3) | 0.0644(13) |
| No of reflections collected/unique                     | 2861/2861  | C15 | -0.2342(3) | 0.4238(1) | 0.2275(3) | 0.0596(11) |
| Largest diff. Peak and hole                            | $0.28 \le 0.22 \Rightarrow 0.20 \Rightarrow 0.30 = $ | C16 | -0.2318(3) | 0.4138(1) | 0.3448(3) | 0.0527(11) |
| Pafinement method                                      | $0.28 < \Delta \rho < -0.29 \text{ c A}$<br>Full matrix least square on $E^2$  | C17 | -0.0391(4) | 0.3225(1) | 0.3560(3) | 0.0777(15) |
| Data/restraints/parameters                             | 2857/0/208   | C18 | -0.1288(3) | 0.4541(1) | 0.6533(3) | 0.0565(10) |
| Final R indices $[F_0 > A(\sigma F_0)]$                | $P_{1}(0,054) = P_{2}(0,1325)$   | C19 | -0.0486(3) | 0.4700(1) | 0.7583(3) | 0.0544(11) |
| R indices (all data)                                   | $R_1 = 0.0834, wR_2 = 0.1499$  | C20 | -0.1171(4) | 0.4617(2) | 0.8739(3) | 0.0774(15) |
| Goodness of Fit  | 1.093  |     |            | ale ale a |           |            |

Atom

 ${}^{a}U_{eq}^{*} = (1/3)\sum_{i}\sum_{j}U_{ij}a_{i}^{*}a_{j}^{*}(a_{i}\cdot a_{j}).$ 

the E-map. Full-matrix least-squares refinement of the structure has been carried out by using SHELXL program.<sup>11</sup> The positional and thermal parameters of non-hydrogen atoms were refined isotropically. All hydrogen atoms were fixed stereochemically. Further refinement with anisotropic thermal parameters resulted into a final value of the reliability index, R(0.054). The maximum and minimum values for the residual electron density are 0.28 and -0.29 eÅ<sup>-3</sup>, respectively. Atomic scattering factors were obtained from International Tables for Crystallography (1992, Vol. C, Tables 4.2.6.8 and 6.1.1.4). The crystallographic data are listed in Table 1.

"CCDC 203248 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac. uk/uk/conts/retrieving.html [or from the Cam-

 Table 3. Bond Distances (Å) and Bond Angles (°) for Non
 -Hydrogen Atoms (esd's Are Given in Parentheses)

| S1-C2     | 1.761(3) | C6—C7       | 1.382(5) |
|-----------|----------|-------------|----------|
| S1-C18    | 1.796(4) | C7–C8       | 1.376(5) |
| 01-C4     | 1.221(4) | C8-C9       | 1.389(5) |
| O2-C19    | 1.202(4) | C9-C10      | 1.408(4) |
| N1-C2     | 1.276(4) | C11-C12     | 1.387(5) |
| N1-C9     | 1.394(4) | C11-C16     | 1.375(4) |
| N3-C11    | 1.451(4) | C12-C13     | 1.383(5) |
| N3-C2     | 1.391(5) | C12-C17     | 1.499(5) |
| C13-C14   | 1.377(5) | C4-C10      | 1.441(5) |
| C14-C15   | 1.366(5) | C5-C6       | 1.356(6) |
| C15-C16   | 1.371(5) | C5-C10      | 1.399(4) |
| C18-C19   | 1.503(5) | C19-C20     | 1.495(5) |
| C2-S1-C18 | 97.9(1)  | C4-C10-C9   | 119.8(3) |
| C2-N1-C9  | 117.6(3) | C4-C10-C5   | 120.8(3) |
| C4-N3-C11 | 118.3(3) | N3-C11-C16  | 119.5(3) |
| C2-N3-C11 | 120.7(3) | N3-C11-C12  | 118.7(3) |
| C2-N3-C4  | 120.9(2) | C12-C11-C16 | 121.8(3) |
| N1-C2-N3  | 125.4(3) | C11-C12-C13 | 119.5(1) |
| S1-C2-N3  | 114.2(2) | C13-C12-C17 | 120.9(3) |
| S1-C2-N1  | 120.4(3) | C12-C13-C14 | 121.1(3) |
| O1-C4-N3  | 119.8(3) | C13-C14-C15 | 120.7(3) |
| N3-C4-C10 | 114.6(3) | C14-C15-C16 | 119.4(3) |
| O1-C4-C10 | 125.6(3) | C11-C16-C15 | 119.9(3) |
| C5-C6-C7  | 120.2(4) | S1-C18-C19  | 115.6(2) |
| C6-C5-C10 | 120.7(3) | O2-C19-C18  | 122.7(3) |
| C5-C6-C7  | 120.2(4) | C18-C19-C20 | 114.9(3) |
| C6-C7-C8  | 120.4(3) | C7-C8-C9    | 120.6(3) |
| N1-C9-C10 | 119.6(3) | O2-C19-C20  | 122.4(3) |
| C5-C10-C9 | 119.3(3) | C4-C10-C9   | 119.8(3) |
| N1-C9-C8  | 119.6(3) | C11-C12-C17 | 121.9(3) |
| C8-C9-C10 | 118.8(3) |             |          |
|           |          |             |          |



Fig. 1. The chemical structure with atom numbering scheme.

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# **Results and discussion**

The final atomic positions and equivalent isotropic displacement parameters for all the non-hydrogen atoms are listed in Table 2. Bond lengths and bond angles for non-hydrogen atoms are given in Table 3. A general view of the molecule indicating atom numbering scheme (thermal ellipsoid drawn at 50% probability) is shown in Fig. 2.<sup>12</sup> The geometrical calculations were performed using PARST program.<sup>13</sup>

The bond lengths and bond angles of pyridine ring and phenyl ring are quite close to the values as obtained in case of some analogous structures.<sup>14–17</sup> The length of S1–C18 bond is significantly long (1.796 Å) than the standard



Fig. 2. A general view of the molecules (thermal ellipsoid drawn at 50% probability).

value  $(1.70 \text{ Å})^{18}$  and variation of this kind in the bond length could be attributed to the hybridization state of C18(sp<sup>3</sup>) and C2(sp<sup>2</sup>) atoms.<sup>19</sup> A comparison of some S—C bond distances obtained in the present case and those which exists in literature clearly indicates that the S1—C18 and S1—C2 bond lengths are significantly large.<sup>20–24</sup> The bond angle between S1—C2 and S1—C18 is well within the expected value.<sup>19</sup> Both the phenyl rings i.e. B & C have normal bond distances and angles.

All the three rings are planar as depicted by the magnitude of the torsion angles present in these rings. The oxygen atom O1 is deviated below the plane of the ring A [deviation being (-0.041(2) Å]. The magnitude of torsion present in the bond C16–C11–N3–C4 [93.5(4)°] is indicative of the dihedral angle [94.1(1)°] between the quinazoline moiety and the methyl substituted phenyl ring. The crystal structure is stabilized by the following interactions:

| D-H···A                       | $H{\cdots}A(\mathring{A})$ | $D{\cdots}A(\mathring{A})$ | $D\text{-}H{\cdot}\cdot{\cdot}A(^\circ)$ |
|-------------------------------|----------------------------|----------------------------|--|
| C17—H17A…N3                   | 2.40(4)                    | 2.87(4)                    | 110.5(3)                                 |
| C6-H6···O1 <sup>(i)</sup>     | 2.49(5)                    | 3.29(5)                    | 144.5(3)                                 |
| C15—H15···O2 <sup>(iii)</sup> | 2.50(4)                    | 3.30(4)                    | 145.8(3)                                 |
| C13—H13····O1 <sup>(ii)</sup> | 2.61(4)                    | 3.53(4)                    | 168.8(3)                                 |

Equivalent position: (i) x, -y + 1/2 + 1, z + 1/2. (ii) x + 1/2, y, -z + 1/2. (iii) x + 1/2, (+y, -z - 1/2).

The conformational side chain designations across the single bonds S1–C18, S1–C2, and C18–C19 are -synclinal, synperiplanar, and synperiplanar, respectively.<sup>25</sup>

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### References

- 1. Asano, K.; Asai, S. Yakugaku Zasshi. 1958, 78, 450.
- Baker, B.R.; Koehler, R.; Goodman, L.; De Graw, J. Org. Chem. 1961, 26, 1156.
- Desai, N.C.; Undavia, N.K.; Trivedi, P.B.; Dipika, D.; Vyas, G.D. Indian J. Exp. Biol. 1998, 36, 1280.
- Siegfield, L.; Karl, D.; Guenther, W.; Herwart, A.; Dieter, I. C.A. 1992, 116, 34567.
- 5. Babita, M. *PhD Thesis*; Regional Research Laboratory: Jammu Tawi, India, 1994.
- Thappa, R.K.; Agarwal, S.G.; Dhar, K.L.; Gupta, V.K.; Goswami, K.N. Phytochemistry 1996, 42, 1485.
- Magotra, D.K.; Gupta, V.K.; Rajnikant; Goswami, K.N.; Thappa, R.K.; Aggarwal, S.G. Acta Crystallogr. 1996, C52, 521.
- Rajnikant; Gupta, V.K.; Singh, A. Crystallogr. Rep. 2000, 45, 611.
- Rajnikant; Gupta, V.K.; Deshmukh, M.B.; Varghese, B.; Dinesh. Cryst. Res. Technol. 2001, 36, 1456.
- Sheldrick, G.M. SHELXS86, Program for the Solution of Crystal Structures; University of Gottingen: Germany, 1986.
- Sheldrick, G.M. SHELXS93, Program for the Refinement of Crystal Structures; University of Gottingen: Germany, 1993.
- 12. Farrugia, L.J. Molecular Graphics—ORTEP-3 for Windows. J. Appl. Cryst. 1997, 30, 565.
- 13. Nardelli, M. Comput. Chem. 1983, 7, 95.
- 14. Freer, A.A.; Robins, D.J.; Sheldrake, G.N. Acta Crystallogr. 1987, C43, 1119.
- 15. Johnson, A.T.; Kelszler, D.A.; Sakuma, K.; White, J.D. Acta Crystallogr. 1989, C45, 1114.
- Djinovic, K.; Golic, L.; Leban, I. Acta Crystallogr. 1990, C46, 281.
- 17. Pecorari, P.; Renaldi, M.; Antolini, L. Acta Crystallogr. 1992, C48, 2027.
- Sutton, L.E. Tables of Interatomic Distances and Configuration in Molecules and Ions, Chemical Society Special Publication No. 18; Chemical Society: London, 1965.
- 19. Form, G.R.; Raper, E.S. Acta Crystallogr. 1974, B30, 342.
- 20. Fehlmann, M. Acta Crystallogr. 1970, B26, 1736.
- 21. Stenson, P.E. Acta Chem. Scand. 1970, 24, 3729.
- 22. Kruger, G.J.; Gafner, G. Acta Crystallogr. 1971, B27, 326.
- Amirthalingham, V.; Mauralidharan, K.V. Acta Crystallogr. 1972a, B28, 2417.
- Amirthalingham, V.; Mauralidharan, K.V. Acta Crystallogr. 1972b, B28, 2421.
- 25. Klyne, W.; Prelong, V. Experientia 1960, 16, 521.