

# Synthesis of N-tetra-O-acetyl- $\beta$ -d-glucopyranosyl-N'-(4',6'-diarylpyrimidin-2'-yl)thioureas

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**Abstract:** Some 2-amino-4,6-diarylpyrimidines 2 have been prepared from substituted benzylideneacetophenones and guanidine hydrochloride in the presence of alkali by conventional heating in alcoholic medium and microwave heating in solvent-free conditions. N-(2,3,4,6-Tetra-O-acetyl- $\beta$ -d-glucopyranosyl)-N'-(4',6'-diarylpyrimidin-2'-yl)thioureas 4 have been synthesized by reaction of per-O-acetylated glucopyranosyl isothiocyanate 1 and substituted 2-amino-4,6-diarylpyrimidines 2. Two different methods have been used, namely, refluxing in anhydrous dioxane and solvent-free microwave-assisted coupling. The second procedure afforded higher yields in much shorter reaction times. The compounds 2 and 4 were tested for their antibacterial and antifungal activities in vitro against *Staphylococcus epidermidis*, *Enterobacter aerogenes* and *Candida albicans* by disc diffusion method. © 2009 Elsevier Ltd. All rights reserved.

**Author Keywords:** Glucopyranosyl isothiocyanate; Glucopyranosyl thiourea; Microwave-assisted method; Pyrimidine

**Index Keywords:** Antibacterial and antifungal activity; *Candida albicans*; Conventional heating; Diffusion method; *Enterobacter aerogenes*; Glucopyranosyl isothiocyanate; Glucopyranosyl thiourea; Guanidine hydrochloride; Higher yield; In-vitro; Isothiocyanates; Microwave-assisted; Microwave-assisted method; Pyrimidine; Reaction time; Refluxing; Second procedures; Solvent free; Solvent free conditions; *Staphylococcus epidermidis*; Amination; Amines; Ethers; Heating; Microwaves; Synthesis (chemical); Urea; Thioureas; 2 amino 4 (2 hydroxyphenyl) 6 phenylpyrimidine; 2 amino 4 (3 chlorophenyl) 6 phenylpyrimidine; 2 amino 4 (3 methoxyphenyl) 6 phenylpyrimidine; 2 amino 4 (4 bromophenyl) 6 phenylpyrimidine; 2 amino 4 (4 chlorophenyl) 6 phenylpyrimidine; 2 amino 4 (4 fluorophenyl) 6 phenylpyrimidine; 2 amino 4 (4 isopropenyl) 6 phenylpyrimidine; 2 amino 4 (4 methoxyphenyl) 6 phenylpyrimidine; 2 amino 4 (4 methylphenyl) 6 phenylpyrimidine; 2 amino 4,6 diphenylpyrimidine; alkali; antifungal agent; antiinfective agent; chalcone derivative; guanidine; n (2,3,4,6 tetra O acetyl beta dexro glucopyranosyl) n' (4',6' diphenylpyrimidin 2' yl)thiourea; n (2,3,4,6 tetra O acetyl beta dexro glucopyranosyl) n' [4' (2 hydroxyphenyl) 6' phenyl pyrimidin 2' yl]thiourea; n (2,3,4,6 tetra O acetyl beta dexro glucopyranosyl) n' [4' (3 chlorophenyl) 6' phenyl pyrimidin 2' yl]thiourea; n (2,3,4,6 tetra O acetyl beta dexro glucopyranosyl) n' [4' (3 methoxyphenyl) 6' phenyl pyrimidin 2' yl]thiourea; n (2,3,4,6 tetra O acetyl beta dexro glucopyranosyl) n' [4' (4 bromophenyl) 6' phenyl pyrimidin 2' yl]thiourea; n (2,3,4,6 tetra O acetyl beta dexro glucopyranosyl) n' [4' (4 chlorophenyl) 6' phenyl pyrimidin 2' yl]thiourea; n (2,3,4,6 tetra O acetyl beta dexro glucopyranosyl) n' [4' (4 fluorophenyl) 6' phenyl pyrimidin 2' yl]thiourea; n (2,3,4,6 tetra O acetyl beta dexro glucopyranosyl) n' [4' (4 isopropylphenyl) 6' phenyl pyrimidin 2' yl]thiourea; n (2,3,4,6 tetra O acetyl beta dexro glucopyranosyl) n' [4' (4 methoxyphenyl) 6' phenyl pyrimidin 2' yl]thiourea; n (2,3,4,6 tetra O acetyl beta dexro glucopyranosyl) n' [4' (4 methylphenyl) 6' phenyl pyrimidin 2' yl]thiourea; n tetra O

acetyl beta dextro glucopyranosyl '(4',6' diarylpyrimidin 2' yl)thiourea derivative; pyrimidine derivative; thiourea derivative; unclassified drug; acetylation; antibacterial activity; antifungal activity; article; Candida albicans; chemical procedures; chemical reaction; disk diffusion; drug activity; drug structure; drug synthesis; Enterobacter aerogenes; in vitro study; microwave cooking; nonhuman; priority journal; reaction time; Staphylococcus epidermidis; Acetylglucosamine; Anti-Bacterial Agents; Antifungal Agents; Candida albicans; Enterobacter aerogenes; Microbial Sensitivity Tests; Pyrimidines; Staphylococcus epidermidis; Thiourea; Candida albicans; Enterobacter aerogenes; Staphylococcus epidermidis; Tetra

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References:

- Sayle, K.L., Bentley, J., Boyle, F.T., Calvert, A.H., Cheng, Y., Curtin, N.J., Endicott, J.A., Griffin, R.J., (2003) Bioorg. Med. Chem. Lett., 13, pp. 3079-3082
- Balasankar, T., Nagarajan, S., (2004) Heterocycl. Commun., 10, pp. 465-468
- Chandrasekaran, S., Nagarajan, S., (2005) Il Farmaco, 60, pp. 279-282
- Cocco, M.T., Congiu, C., Liliu, V., Onnis, V., (2006) Bioorg. Med. Chem., 14, pp. 366-372
- Gadhachanda, V.R., Wu, B., Wang, Z., Kuhen, K.L., Caldwell, J., Zondler, H., Walter, H., He, Y., (2007) Bioorg. Med. Chem. Lett., 17, pp. 260-265
- El-Hashash, M.A., Mahmmoud, M.R., Madboli, S.A., (1993) Indian J. Chem., 32 B, pp. 449-453
- Wustrow, D., Akunne, H., Belliotti, T., Davis, M.D., Heffner, T., Kesten, S., Meltzer, L., Wise, L., (1996) Eur. Neuropsychopharmacol., 6, pp. S4

- Rashinkar, G.S., Pore, S.B., Mote, K.B., Salunkhe, R.S., (2009) Indian J. Chem., 48 B, pp. 606-610
- Witczak, Z. J. In Adv. Carbohydr. Chem. Biochem., Tipson, S., Ed.
- Academic Press: New York, 1986
- 44, pp 91-145 Lindhorst, T.K., Kieburg, C., (1995) Synthesis, pp. 1228-1230
- Jiménez Blanco, J.L., Sylla, B., Ortiz-Mellet, C., García Fernández, J.M., (2007) J. Org. Chem., 72, pp. 4547-4550
- Kühne, M., Györgydeák, Z., Lindhorst, T.K., (2006) Synthesis, pp. 949-951
- García-Fernández, J.M., Ortiz-Mellet, C., (1996) Sulfur Rep., 19, pp. 61-159
- García-Fernández, J.M., Ortiz-Mellet, C., (2000) Adv. Carbohydr. Chem. Biochem., 55, pp. 36-135. , Horton D. (Ed), Academic Press, New York
- Naito, T., Sano, M., (1961) Chem. Pharm. Bull., 9, pp. 709-714
- Ukita, T., Hamada, A., Yoshida, M., (1964) Chem. Pharm. Bull., 12, pp. 454-459
- Ogura, H., Takahashi, H., (1977) Heterocycles, 8, pp. 125-146
- Camarasa, M.J., Fernandez-Resa, P., Garcia-Lopez, M.T., de las Heras, F.G., Mendez-Castrillon, P.P., San Felix, A., (1984) Synthesis, pp. 509-510
- Prata, C., Mora, N., Lacombe, J.-M., Maurizis, J.-C., Pucci, B., (1999) Carbohydr. Res., 321, pp. 4-14
- Abramovitch, R.A., (1991) Org. Prep. Proc. Int., 23, pp. 683-712
- Larhed, M., Moberg, C., Hallberg, A., (2002) Acc. Chem. Res., 35, p. 717
- Lidström, P., Tierney, J., Wathey, B., Westman, J., (2001) Tetrahedron, 57, pp. 9225-9283
- Loupy, A., (2006) Microwaves in Organic Synthesis. 2nd ed., , Wiley and Sons, Weinheim
- (1997) Microwave-Enhanced Chemistry: Fundamental, Sample Preparation, and Applications, , Kingston H.M., and Haswell S.J. (Eds), American Chemical Society, New York
- Gedye, R., Smith, F., Westaway, K., Ali, H., Baldisera, L., Laberge, L., Roussel, J., (1986) Tetrahedron Lett., 27, p. 279
- Caddick, S., (1995) Tetrahedron, 51, pp. 10403-10432
- Gabriel, C., Gabriel, S., Grant, E., Halstead, B.S.J., Mingos, D., (1997) Chem. Soc. Rev., 27, pp. 213-224
- Chen, S.-T., Sookkheo, B., Phutrahul, S., Wang, K.-T., (2001) Methods Biotechnol., 15, p. 373
- Soderberg, E., Westman, J., Oscarson, S., (2001) J. Carbohydr. Chem., 20, p. 397
- Lidstrom, P., Tierney, J., Wathey, B., Westman, J., (2001) Tetrahedron, 57, pp. 9225-9283
- Walpole, C., Ko, S.Y., Brown, M., Beattie, D., Campbell, E., Dickenson, F., Ewan, S., Urban, L., (1998) J. Med. Chem., 41, pp. 3159-3173
- Chalina, E.G., Chakarova, L., (1998) Eur. J. Med. Chem., 33, pp. 975-983
- Stark, H., Purand, K., Ligneau, X., Rouleau, A., Arrang, J.-M., Garbarg, M., Schwartz, J.-C., Schunack, W., (1996) J. Med. Chem., 39, pp. 1157-1163
- Wang, J., Li, H., Yu, X., Zu, L., Wang, W., (2005) Org. Lett., 7, pp. 4293-4296
- Seayad, J., List, B., (2005) Org. Biomol. Chem., 3, pp. 719-724
- Pihko, P.M., (2004) Angew. Chem., Int. Ed., 43, pp. 2062-2064
- Staab, H.A., (1962) Angew. Chem., Int. Ed. Engl., 1, pp. 351-367
- Staab, H.A., Walther, G., (1962) Leibigs Ann. Chem., 657, pp. 98-103
- Yoon, T.P., Jacobsen, E.N., (2005) Angew. Chem., Int. Ed., 44, pp. 466-468
- Mohanta, P.K., Dhar, S., Samal, S.K., Ila, H., Junjappa, H., (2000) Tetrahedron, 56, pp. 629-637
- Aoyama, T., Murata, S., Nagata, Y., Takido, T., Kodamari, M., (2005) Tetrahedron Lett., 46, pp. 4875-4878
- Rodríguez-Lucena, D., Benito, J.M., Ortiz-Mellet, C., García Fernández, J.M., (2007) Chem. Commun., pp. 831-833

- Jiménez Blanco, J.L., Bootello, P., Gutiérrez Gallego, R., Ortiz-Mellet, C., García Fernández, J.M., (2007) *Synthesis*, pp. 2545-2558
- Sharma, S., (1978) *Synthesis*, pp. 803-820
- Bhandari, K., Srivatsava, S., Shankar, G., (2004) *Bioorg. Med. Chem.*, 12, pp. 4189-4196
- Kodomari, M., Suzuki, M., Tanigawa, K., Aoyama, T., (2005) *Tetrahedron Lett.*, 46, pp. 5841-5843
- Schroeder, D.C., (1955) *Chem. Rev.*, 55, pp. 181-228
- Sridevi, G., Rao, J., Reddy, K.K., (1989) *Synth. Commun.*, 19, pp. 965-972
- Yavari, I., Sayyed-Alangi, S.Z., Sabbaghan, M., Hajinasiri, R., Iravani, N., (2008) *Monatsh. Chem.*, 139, pp. 1025-1028
- Bama, K.B., Rajani, K.G., (1988) *Indian J. Chem.*, 27 B, pp. 1157-1158
- Liu, Y.-H., Cao, L.-H., (2008) *Carbohydr. Res.*, 343, pp. 615-625
- Furniss, B.A., Hannaford, A.J., Smith, P.W., Tatchell, A.R., (1989) *Vogel's Text-Book of Practical Organic Chemistry*. 5th ed., , Longman Scientific & Technical, Harlow
- Oyedapo, A.O., Makanju, V.O., Adewunmi, C.O., Iwalewa, E.O., Adenowo, T.K., (2004) *Afr. J. Trad. CAM*, 1, p. 55
- Adewunmi, C.O., Ogungbamila, F.O., Oluwadiya, J.O., (1987) *Planta. Med.*, 53, p. 110
- El-Hashash, M.A., Mahhmoud, M.R., Madboli, S.A., (1993) *Indian J. Chem.*, 32 B, pp. 449-452
- E. Pretsch, P. Buhlmann, C. Affolter, *Structure Determination of Organic Compounds*, 2nd ed., Springer: Berlin, 2000, p 152, 236.
- Lemieux, R.L., (1963) *Methods in Carbohydrate Chemistry*, 2, pp. 221-222. , Whistler R.L., and Wolfrom M.L. (Eds), Academic, New York