

Short Note

(*E*)-Ethyl 3-(Dimethylamino)-2-(7,9-diphenyl-7*H*-pyrazolo[4,3-*e*][1,2,4]triazolo[1,5-*c*]pyrimidin-2-yl)acrylate

Sobhi M. Gomha and Thoraya A. Farghaly *

Department of Chemistry, Faculty of Science, University of Cairo, Giza, 12613, Egypt

* Author to whom correspondence should be addressed; E-Mail: thoraya-f@hotmail.com.

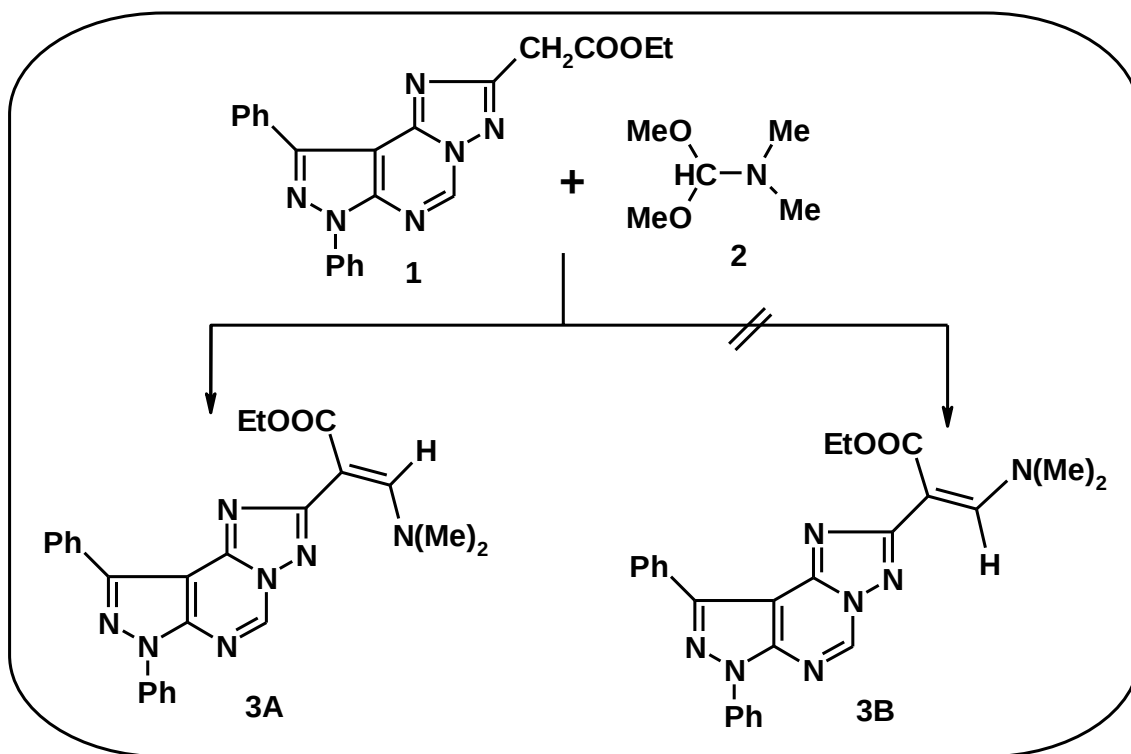
Received: 30 November 2011 / Accepted: 13 December 2011 / Published: 20 December 2011

Abstract: Novel (*E*)-ethyl 3-(dimethylamino)-2-(7,9-diphenyl-7*H*-pyrazolo[4,3-*e*][1,2,4]triazolo[1,5-*c*]pyrimidin-2-yl)acrylate (**3A**), was prepared via condensation of ethyl (1,3-diphenyl-1*H*-pyrazolo[4,3-*e*][1,2,4]triazolo[1,5-*c*]pyrimidin-5-yl)acetate (**1**) and dimethylformamide-dimethylacetal under reflux. The structure of the synthesized compound was assigned on the basis of elemental analysis, IR, ¹H NMR and mass spectral data.

Keywords: pyrazolo-triazolo-pyrimidine; enaminone

Enaminones are poly-dentate reagents that have been utilized extensively in this decade as building blocks in organic synthesis [1-5]. Many reports indicated that the presence of a basic side chain like the *N,N*-dialkylaminoalkyl group enhances the drugs' DNA affinity [6] and their anticancer activity, e.g. against the human breast cancer cell line, MCF-7 [7]. In addition, pyrazolo[4,3-*e*][1,2,4]triazolo[1,5-*c*]pyrimidines have been used as potent and selective adenosine A_{2A} receptor antagonists [8-15]. This finding prompted us to condense ethyl (1,3-diphenyl-1*H*-pyrazolo[4,3-*e*][1,2,4]triazolo[1,5-*c*]pyrimidin-5-yl)acetate (**1**) [16] with dimethylformamide-dimethylacetal (DMF-DMA) to obtain the title compound **3A** (Scheme 1). Elemental analyses and spectral data were in complete accordance with the assigned structure **3**. For example, the ¹H NMR spectrum of compound **3** revealed two singlet signals at δ 3.30 and 7.77 ppm characteristic for *N,N*-dimethylamino and the exocyclic C=CH protons, respectively [1]. The value of the exocyclic C=CH proton signal at δ 7.77 ppm correlated with the *E*-isomer (**3A**), while the *Z*-isomer **3B** of an analogous structure was reported to appear at δ 6.9 ppm [17]. Thus, we have successfully synthesized a new enaminone in good yield which can be used as a building blocks for heterocyclic ring systems in organic synthesis.

Scheme 1. Synthesis of the title compound (3A).



Synthesis of (*E*)-ethyl 3-(dimethylamino)-2-(7,9-diphenyl-7H-pyrazolo[4,3-*e*][1,2,4]triazolo[1,5-*c*]pyrimidin-2-yl)acrylate (3)

A mixture of **1** (4.3 g, 10 mmol) and dimethylformamide-dimethylacetal (10 mL) was refluxed for 20 min. After cooling, the precipitate was collected by filtration, washed with methanol and crystallized from dioxane.

Yield: 92%; pale yellow crystals; m.p. 240 °C.

GC-MS m/z (%): 454 ($M^+ + 1$, 4), 453 (M^+ , 13), 380 (11), 336 (12), 167 (23), 77 (100), 51 (48).

IR (KBr) $\nu_{\max}$ cm^{-1} : 1624 (C=O).

^1H NMR (Bruker, 300 MHz, CDCl_3): δ (ppm) = 1.13 (t, J = 7.0 Hz, 3H, CH_3), 3.30 (s, 6H, 2 CH_3), 4.07 (q, J = 7.0 Hz, 2H, CH_2), 7.47-8.7 (m, 10H, Ar-H), 7.77 (s, 1H, =CH), 9.68 (s, 1H, pyrimidine-H).

Anal. Calcd. for $\text{C}_{25}\text{H}_{23}\text{N}_7\text{O}_2$ (453.19): C, 66.21; H, 5.11; N, 21.62. Found: C, 66.11; H, 5.01; N, 21.39%.

References

1. Farghaly T.A.; Abdel Hafez, N.A.; Ragab, E.A.; Awad, H.M.; Abdalla, M.M. Synthesis, anti-HCV, antioxidant, and peroxynitrite inhibitory activity of fused benzosuberone derivatives. *Eur. J. Med. Chem.* **2010**, *45*, 492-500.

2. Shawali, A.S.; Farghaly, T.A.; Al-Dahshoury, A.R. Synthesis, reactions and antitumor activity of new β -aminovinyl 3- pyrazolyl ketones. *ARKIVOC* **2009**, *xiv*, 88-99.
3. Farghaly, T.A.; Abdalla, M.M. Synthesis, tautomerism, and antimicrobial, anti-HCV, anti-SSPE, antioxidant, and antitumor activities of arylazobenzosuberones. *Bioorg. Med. Chem.* **2009**, *17*, 8012-8019.
4. Farghaly, T.A.; Riyadh, S.M. Microwave assisted synthesis of annelated benzosuberone as new penta-heterocyclic ring systems. *ARKIVOC* **2009**, *x*, 54-63.
5. Riyadh, S.M.; Farghaly, T.A.; Abdallah, M.A.; Abdalla, M.M.; Abd El-Aziz, M.R. New pyrazoles incorporating pyrazolylpyrazole moiety: Synthesis, anti-HCV and antitumor activity. *Eur. J. Med. Chem.* **2010**, *45*, 1042-1050.
6. Ducrocq, C.; Wendling, F.; Tourbez-Perrin, M.; Rivalle, C.; Tambourin, P.; Pochon, F.; Bisagni, E.; Chermann, J.C. Structure-activity relationship in a series of newly synthesized 1-amino-substituted ellipticine derivatives. *J. Med. Chem.* **1980**, *23*, 1212.
7. Ahmed, M.S.M.; Farghaly, T.A. Synthesis and reactions of 3-hydrazino-2,7,8,9-tetrahydro-1*H*-benzo[6',7']cyclohepta[1',2':4,5]pyrido[2,3-*d*]pyrimidin-1-one. *ARKIVOC* **2009**, *xiii*, 31-41.
8. Ongini, E.; Monopoli, A.; Cacciari, B.; Baraldi, P.G. Selective adenosine A_{2A} receptor antagonists. *Il Farmaco* **2001**, *56*, 87-90.
9. Kishore, D.P.; Balakumar, C.; Rao, A.R.; Roy, P.P.; Roy, K. QSAR of adenosine receptor antagonists: Exploring physicochemical requirements for binding of pyrazolo[4,3-*e*]-1,2,4-triazolo[1,5-*c*]pyrimidine derivatives with human adenosine A₃ receptor subtype. *Bioorg. Med. Chem. Lett.* **2011**, *21*, 818-823.
10. Baraldi, P.G.; Manfredini, S.; Simoni, D.; Zappaterra, L.; Zocchi, C.; Dionisotti, S.; Ongini, E. Synthesis of new pyrazolo[4,3-*e*]1,2,4-triazolo[1,5-*c*]pyrimidine and 1,2,3-triazolo[4,5-*e*]1,2,4-triazolo[1,5-*c*]pyrimidine displaying potent and selective activity as A_{2a} adenosine receptor antagonists. *Bioorg. Med. Chem. Lett.* **1994**, *4*, 2539-2544.
11. Kumar, T.S.; Mishra, S.; Deflorian, F.; Yoo, L.S.; Phan, K.; Kecskés, M.; Szabo, A.; Shinkre, B.; Gao, Z-G.; Trenkle, W.; Jacobson, K.A. Molecular probes for the A_{2A} adenosine receptor based on a pyrazolo[4,3-*e*][1,2,4]triazolo[1,5-*c*]pyrimidin-5-amine scaffold. *Bioorg. Med. Chem. Lett.* **2011**, *21*, 2740-2745.
12. Harris, J.M.; Neustadt, B.R.; Zhang, H.; Lachowicz, J.; Cohen-Williams, M.; Varty, G.; Hao, J.; Stamford, A.W. Potent and selective adenosine A_{2A} receptor antagonists: [1,2,4]Triazolo[4,3-*c*]pyrimidin-3-ones. *Bioorg. Med. Chem. Lett.* **2011**, *21*, 2497-2501.
13. Baraldi, P.G.; Bovero, A.; Fruttarolo, F.; Romagnoli, R.; Tabrizi, M.A.; Preti, D.; Varani, K.; Borea, P.A.; Moorman, A.R. New strategies for the synthesis of A₃ adenosine receptor antagonists. *Bioorg. Med. Chem.* **2003**, *11*, 4161-4169.
14. Michielan, L.; Bolcato, C.; Federico, S.; Cacciari, B.; Bacilieri, M.; Klotz, K.-N.; Kachler, S.; Pastorin, G.; Cardin, R.; Sperduti, A.; Spalluto, G.; Moro, S. Combining selectivity and affinity predictions using an integrated Support Vector Machine (SVM) approach: An alternative tool to discriminate between the human adenosine A_{2A} and A₃ receptor pyrazolo-triazolo-pyrimidine antagonists binding sites. *Bioorg. Med. Chem.* **2009**, *17*, 5259-5274.
15. Paeshuyse, J.; Letellier, C.; Froeyen, M.; Dutartre, H.; Vrancken, R.; Canard, B.; De Clercq, E.; Gueiffier, A.; Teulade, J.-C.; Herdewijn, P.; Puerstinger, G.; Koenen, F.; Kerkhofs, P.;

- Baraldi, P.G.; Neyts, J. A pyrazolotriazolopyrimidinamine inhibitor of bovine viral diarrhea virus replication that targets the viral RNA-dependent RNA polymerase. *Antivir. Res.* **2009**, *82*, 141-147.
16. Farghaly, T.A.; Gomha, S.M. Synthesis of ethyl (1,3-diphenyl-1*H*-pyrazolo[4,3-*e*][1,2,4] triazolo-[1,5-*c*]pyrimidin-5-yl)acetate. *Molbank* **2011**, *2011*, M743.
17. Bennett, P.; Donnelly, J.A.; Meaney, D.C.; Boyle, P.O. Stereochemistry of cyclopropyl ketones from the reaction of dimethylsulphoxonium methylide with 3-benzylidenechroman-4-ones. *J. Chem. Soc. Perkin Trans. 1* **1972**, 1554.

© 2011 by the authors; licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution license (<http://creativecommons.org/licenses/by/3.0/>).