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OPPI BRIEF

Synthesis of Thiazoles Catalyzed by Dichlorotriazine Attached to Graphene Oxide

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Among their valuable activities, 1,3-thiazoles show anticancer,[1] antimicrobial,[2] anti-inflammatory,[3] and anti-Candida properties.[4] These properties make 1,3-thiazoles appealing goals in organic synthesis. Past reports on the synthesis of 1,3-thiazole derivatives have mentioned such catalysts as DBU,[5] $HClO_4$-SiO_2,[6] $Bi(SCH_2COOH)_3$,[7] $[Et_3NH][HSO_4]$,[8] and ytterbium(III) triflate.[9] Each of these procedures may have its own advantages but also suffer from such apparent drawbacks as prolonged reaction times, complicated work-up, low yield, or hazardous reaction conditions. Recently, graphene oxide (GO) has attracted significant interest as a catalyst in organic synthesis.[10–11] Graphene and GO have large specific surface areas, chemical stability and high surface-to-volume ratios.[12–13] GO is an efficient platform for functionalized graphene platelets that can potentially confer mechanical, thermal and electronic properties. Both small molecules and polymers have been covalently attached to GO's highly reactive oxygen functionalities, or non-covalently attached on the graphene surfaces, for potential utilization in polymer composites, sensors, paper-like materials, drug-delivery systems and photovoltaic applications.[14–18] We have previously reported the use of crosslinked sulfonated polyacrylamide tethered to nano-Fe_3O_4 as a catalyst for the synthesis of 1,3-thiazoles.[19] As a companion study, we now report an easy method for the synthesis of these compounds through a three-component reaction of carbon disulfide, phenacyl bromide or 4-methoxyphenacyl bromide and a primary amine, using graphene oxide dichlorotriazine (GO-DCT) as an efficient catalyst. The reaction is conducted under reflux in ethanol (Scheme 1).

The process for the preparation of graphene oxide dichlorotriazine (GO-DCT) catalyst is shown in Scheme 2. Graphene oxide nanosheets (GO) were prepared by modified Hummer's method,[17] and subsequently functionalized with dichlorotriazine (see Experimental section).

We used the reaction of carbon disulfide, phenacyl bromide and benzyl amine on 1 mmol scale as a model reaction and carried it out in the presence of CAN, $NaHSO_4$, $NiCl_2$, $ZrOCl_2$, *p*-TSA, CuI and GO-DCT. We found that the reaction gave useful results in the presence of GO-DCT (2 mg) under reflux conditions (Table 1). The best results were exemplified in Entry 12, with 92% yield. Further to this, we also reacted

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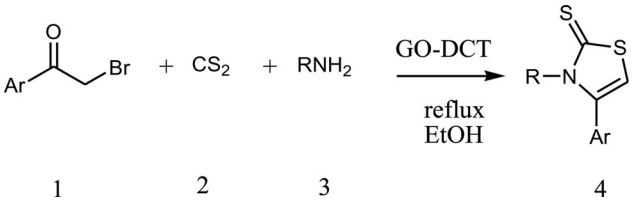
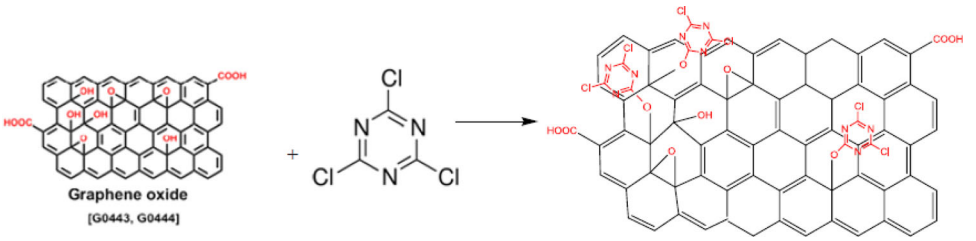


Scheme 1. Synthesis of thiazoles using GO-DCT.



Scheme 2. Preparation route for graphene oxide-dichloro triazine (GO-DCT).

Table 1. Optimization of reaction conditions using different catalysts.[a]

Entry	Solvent (reflux)	Catalyst	Time (min)	Yield (%)[b]
1	EtOH	—	500	39
2	EtOH	CAN (7 mol %)	250	53
3	EtOH	$NaHSO_4$ (5 mol %)	300	45
4	EtOH	$NiCl_2$ (5 mol%)	250	58
5	EtOH	$ZrOCl_2$ (4 mol%)	200	64
6	EtOH	*p*-TSA (4 mol%)	250	62
7	EtOH	CuI (8 mg)	200	70
8	H_2O	GO-DCT (2 mg)	200	73
9	DMF	GO-DCT (2 mg)	200	78
10	CH_3CN	GO-DCT (2 mg)	200	85
11	EtOH	GO-DCT (1 mg)	200	88
12	EtOH	GO-DCT (2 mg)	200	92
13	EtOH	GO-DCT (3 mg)	200	92

[a]Phenacyl bromide (1 mmol), carbon disulfide (1 mmol) and benzyl amine (1 mmol).
[b]Isolated yield.

phenacyl bromide or 4-methoxyphenacyl bromide with carbon disulfide and other primary amines and found uniformly good results (Table 2, mean 83%). The yield did not appear to be particularly sensitive to the substituent groups. The structures of the products were deduced from their ^{1}H NMR, ^{13}C NMR, FT-IR, and elemental analyses. To put the present results into context with our previous report on crosslinked sulfonated polyacrylamide tethered to nano-Fe_3O_4, we found that the GO-DCT catalyst was somewhat easier to prepare once the graphene oxide was on hand. The yields using GO-DCT were only marginally lower and the reaction times were only slightly longer. Either catalyst was thus amply suited to the preparation of the 1,3-thiazoles.

The reusability of GO-DCT was studied for the model reaction, and it was found that product yields lessened only to a very small extent on each reuse (run 1, 92%; run 2, 92%; run 3, 91%; run 4, 91%; run 5, 90%; run 6, 90%). After completion of the

Table 2. Synthesis of thiazoles **4** using GO-DCT.

Product	R	Ar	Time	Yield[a]
4a	$PhCH_2$	Ph	200 min	92%
4b	3,4-Cl_2PhCH_2	Ph	210 min	84%
4c	$PhC_4H_3CH_2$	Ph	220 min	82%
4d	furanyl-CH_2	Ph	200 min	82%
4e	4-$FPhCH_2$	Ph	205 min	86%
4f	2-OMe-$PhCH_2$	Ph	180 min	90%
4g	4-Me-$PhCH_2$	4-OMe-Ph	210 min	86%
4h	$PhCH_2$	4-OMe-Ph	220 min	80%
4i	furanyl-CH_2	4-OMe-Ph	230 min	78%
4j	2-OMe-$PhCH_2$	4-OMe-Ph	200 min	84%

[a]Isolated yield.

reaction (as determined by TLC), $CHCl_3$ was added. The GO-DCT was insoluble in $CHCl_3$ and it could therefore be obtained by simple filtration. The catalyst was washed four times with ethanol and dried at room temperature for 15 h prior to re-use.

In conclusion, our procedure uses GO-DCT under reflux in ethanol for the synthesis of 4-phenyl-1,3-thiazole-thiones. The advantages of this method include its simplicity, the reusability of the catalyst, low catalyst loading, and easy separation of products, with no recrystallization required.

Experimental section

^1H NMR and ^{13}C NMR spectra were recorded on a Bruker Avance-400 MHz spectrometer using $CDCl_3$ as solvent. The progress of the reactions was monitored by thin-layer chromatography (TLC) on Riedel-de Haen plates coated with silica gel 60 F254, using *n*-hexane/ethyl acetate 8:2 as the mobile phase. The elemental analyses (C, H, N) were obtained on a Carlo ERBA Model EA 1108 analyzer. Fourier transform infrared (FT-IR) spectra were recorded on a WQF-510 spectrometer. The mass spectra were recorded on a Joel D-30 instrument at an ionization potential of 70 eV. The energy-dispersive X-ray spectroscopy (EDS) measurements were performed on an SAMX analyzer. Powder X-ray diffraction (XRD) measurements were carried out on a Philips diffractometer of the X'pert Company. The characteristic peaks in the spectrum are in agreement with the standard XRD pattern of functionalized-graphene oxides. SEM images were taken on a MIRA3- TESCAN. Our SEM images of graphene oxide dichlorotriazine nanoplatelets show crumpled thin layers with wrinkles and folds on the surface of GO. The AFM images of GO and graphene oxide dichlorotriazine easily confirm the wrinkled two-dimensional characteristic of the GO nanosheets. Energy Dispersive Spectroscopy (EDS) confirmed the presence of carbon, oxygen, nitrogen and chlorine. XRD, SEM, EDS, FT-IR, and AFM data were submitted for review and are available from the corresponding author upon request.

Preparation of graphene oxide dichlorotriazine (GO-DCT)

GO was prepared from graphite powder according to Hummer's procedure.[17] Graphite powder (500 mg) was dispersed into 200 mL H_2SO_4 (98%); this was sonicated for 2 h at 50° C and stirred for 24 h. Afterward, 10 g $NaNO_3$ was added into the stable dispersion

and the mixture was placed in an ice-water bath under stirring for 1 h. Then 30 g $KMnO_4$ was added slowly and was stirred for 24 h. Next 200 mL H_2O and 60 mL H_2O_2 was added into the mixture. The color of the reaction was light brown. The solid was filtered and washed with water and dried in an oven at 60 °C for 8 hours. The obtained GO (1 g) was dispersed in 10 mL $CHCl_3$, then 500 mg of 2,4,6-trichloro-1,3,5-triazine was added and stirred for 24 h at room temperature. The obtained solid was filtered, rinsed with $CHCl_3$ and dried in an oven at 50 °C for 4 hours.

General procedure for the synthesis of 1,3-thiazoles

A mixture of primary amine (1.0 mmol) and carbon disulfide (1.0 mmol) in ethanol (8 mL) was stirred for 5 min and then phenacyl bromide or 4-methoxyphenacyl bromide (1.0 mmol) and GO-DCT (2 mg) were added, and the mixture was stirred for the appropriate times, as determined by TLC (*n*-hexane/ethyl acetate 8:2). After completion of the reaction, $CHCl_3$ was added. The catalyst was insoluble in $CHCl_3$ and it could therefore be recycled by a simple filtration as described above. The solvent was evaporated and the solid washed with EtOH to get pure product. All of the compounds were known[19] and were identified on the basis of their ^{1}H NMR, ^{13}C NMR, and FT-IR, which were submitted for review.

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References

1. K. M. Dawood and S. M. Gomha, *J. Heterocyclic Chem.*, **52**, 1400 (2015). doi:10.1002/jhet.2250
2. B. F. Abdel-Wahab, H. A. Abdel-Aziz, and E. M. Ahmed, *Monatsh. Chem.*, **140**, 601 (2009). doi:10.1007/s00706-008-0099-x
3. R. N. Sharma, F. P. Xavier, K. K. Vasu, S. C. Chaturvedi, and S. S. Pancholi, *J. Enzyme Inhib. Med. Chem.*, 24, 890 (2009). doi:10.1080/14756360802519558
4. L. T. Maillard, S. Bertout, O. Quinonéro, G. Akalin, G. Turan-Zitouni, P. Fulcrand, F. Demirci, J. Martinez, and N. Masurier, *Bioorganic Med. Chem. Lett.*, **23**, 1803 (2013). doi:10.1016/j.bmcl.2013.01.039
5. T. Masquelin and D. Obrecht, *Tetrahedron*, **57**, 153 (2001). doi:10.1016/S0040-4020(00)01003-6
6. D. Kumar, M. Sonawane, B. Pujala, V. K. Jain, and A. K. Chakraborti, *Green Chem.*, **15**, 2872 (2013). doi:10.1039/c3gc41218k
7. N. Foroughifar and S. Ebrahimi, *Chin. Chem. Lett.*, **24**, 383 (2013).
8. D. D. Subhedar, M. H. Shaikh, M. A. Arkile, A. Yeware, D. Sarkar and B. B. Shingate, *Bioorganic Med. Chem. Lett.*, **26**, 1704 (2016). doi:10.1016/j.bmcl.2016.02.056
9. W. Su, C. Liu, and W. Shan, *Synlett.*, **5**, 725 (2008). doi:10.1055/s-2008-1032100
10. Y. Gao, P. Tang, H. Zhou, W. Zhang, H. Yang, N. Yan, G. Hu, D. Mei, J. Wang, and D. Ma, *Angew. Chem. Int. Ed.*, **55**, 3124 (2016). doi:10.1002/anie.201510081
11. S. Khodabakhshi, F. Marahel, A. Rashidi, and M. K. Abbasabadi, *J. Chin. Chem. Soc.*, **62**, 389 (2015). doi:10.1002/jccs.201400349
12. L. Farzin and M. Amiri. *J. Nanoanalysis*, **5**, 241 (2018).

13. F. Hosseini, H. Shirkhanloo, and N. M. Kazemi, *J. Nanoanalysis*, **4**, 99 (2017).
14. N. Mohanty and V. Berry, *Nano Let.*, **8**, 4469 (2008). doi:10.1021/nl802412n
15. C. H. Lu, H. H. Yang, C. L. Zhu, X. Chen, and G. N. Chen, *Angew. Chem., Int. Ed.*, **48**, 4787 (2009).
16. S. Stankovich, R. Piner, S. T. Nguyen, and R. S. Ruoff, *Carbon*, **44**, 3342 (2006). doi:10.1016/j.carbon.2006.06.004
17. W. S. Hummers and R. E. Offeman, *J. Am. Chem. Soc.*, **80**, 1339 (1958). doi:10.1021/ja01539a017
18. H. N. Tien, V. H. Luan, T. K. Lee, B. S. Kong, J. S. Chung, E. J. Kim, and S. H. Hur, *Chem. Eng. J.*, **211**, 97 (2012). doi:10.1016/j.cej.2012.09.046
19. H. Shahbazi-Alavi, S. Khojasteh-Khosro, J. Safaei-Ghomi and M. Tavazo, *BMC Chemistry*, **13**, 120 (2019).