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N-Iodosaccharin (NISac): a new reusable catalyst for formal [2+4] cycloaddition of imines and enones

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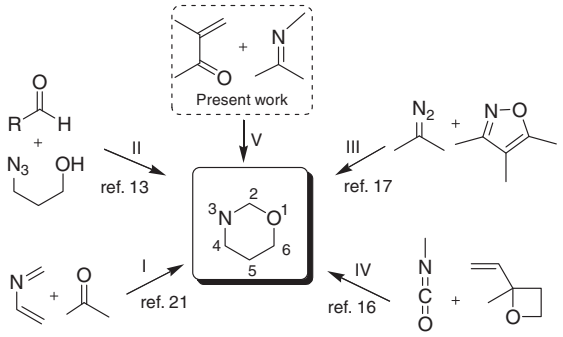
ABSTRACT

The first example of *N*-iodosaccharin (NISac)-catalyzed step, pot and atom economic synthesis of 1,3-oxazines via formal [2+4] cycloaddition of imines and enones has been reported. No by-product formation, operational simplicity, ambient temperature and high yields (85–95%) are the salient features of the present synthetic protocol. After isolation of the product, the catalyst NISac can be easily recovered and reused without any loss of efficiency.

Development of a new catalyst system for the construction of bioactive molecules represents a major challenge for synthetic chemists. Cycloaddition reactions are powerful tools for efficient and stereoselective construction of complex molecules.[1] Especially, [4+2] and [2+4] cycloaddition reactions have been successfully employed for the synthesis of biologically active compounds and natural products under the condition of a well designed combination between diene and dienophile.[2]

1,3-Oxazines constitute an elite class of compounds present in many biologically important natural products[3a] and other bioactive molecules,[3] and have attracted much attention due to their potential as antibiotics,[4a–d] antitumor agents,[4e–g] analgesics,[4h,i] and anticonvulsants.[4] Also, they have generated great interests as anti-psychotic agents and as possible effectors for serotonin and dopamine receptors.[5] Efavirenz (Sustiva), a fused ring 1,3-oxazine derivative, has been approved by the FDA (September 17, 1998) and is currently in clinical use for the treatment of AIDS.[3e] From a chemical viewpoint, 1,3-oxazines are effective as starting materials for the synthesis of different molecules of high biological and medicinal interest, such as 1,3-amino alcohol,[6a] *o*-nitroaniline,[6b] β-lactam,[6c] pyridine,[6d,e] pyrimidine[6f] and quinoline.[6g] Moreover, 1,3-oxazine derivatives have been used as the key intermediates in the synthesis of several natural products, and have also been recognized as chiral auxillaries in asymmetric synthesis.[7]

These unique properties have been the prime driving force for developing new synthetic routes to 1,3-oxazine and its derivatives. Naturally, there has been a continuous effort to develop new, convenient and versatile routes to a variety of substituted 1,3-oxazines which include Vilsmeier cyclisation of amidoalkyl naphthol,[8] cyclisation of α-formylamides,[9] sulfonyl isocyanates,[10] β-amino enones,[11] 2,3-allenamides,[12] 1,3-azidoalcohols,[13] 2-azidoalcohols,[14] intramolecular bis heterocyclization,[15] ring expansion of vinyloxetanes[16] and isoxazoles,[17] one-pot procedure,[18] cycloisomerisation of semicarbazones,[19] and cycloaddition reactions.[13,16,17,20,21] In most of the cases, construction of 1,3-oxazine ring is based on [4+2] cycloaddition involving 2-azadiene partner via 1,2- and 5,6-bond formation (I);[21] [5+1] condensation via 1,2- and 2,3-bond



Scheme 1.

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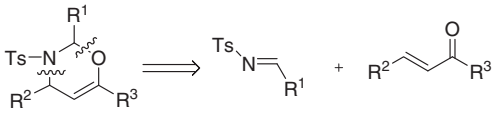
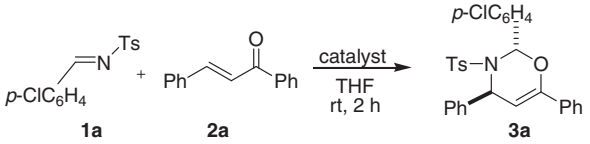


Scheme 2. Disconnection approach to 1,3-oxazines.

formation (II)[13] and via ring opening of isoxazoles (III).[17] The literature records only a few reports on 1,3-oxazine synthesis using C=N moiety in [4+2] cycloaddition via ring opening of 2-vinyloxetane (IV)[16] (Scheme 1). However, to the best of our knowledge, there is no report on [2+4] cycloaddition of imines and enones for the synthesis of 1,3-oxazines. Herein, we report a novel approach via *N*-iodosaccharin (NISac)-catalyzed [2+4] cycloaddition of readily and widely available substrates, that is, imines and enones which may provide an efficient, facile and atom economic alternative to such types of fine chemicals to exploit chemical diversity and generate a drug like library to screen for lead candidates. The reaction involves 1,2- and 3,4-bond forming [4+2] cycloaddition (V, Scheme 1) of enones and imines for 1,3-oxazine synthesis as indicated by disconnection (Scheme 2).

Table 1
Optimization of catalyst for the synthesis of 1,3-oxazine **3a**[a]

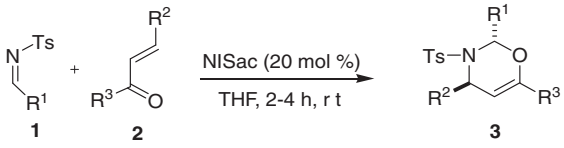


1a **2a** **3a**

Entry	Catalyst	Mol %	Yield[b] (%)
1	*N*-Iodosuccinimide	20	62
2	*N*-Iodophthalimide	20	67
3	*N*-Iodosaccharin	20	90
4	Molecular iodine	20	33
5	*N*-Iodosaccharin	25	90
6	*N*-Iodosaccharin	15	78

[a] For the experimental procedure, see Ref. 24.
[b] Yield of isolated and purified product **3a**.

Table 2
[2+4] Cycloaddition of imines and enones yielding 1,3-oxazines **3**[a]



1 **2** **3**

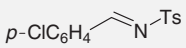
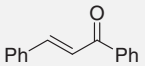
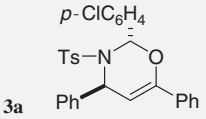
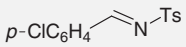
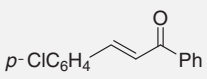
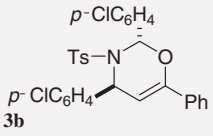
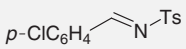
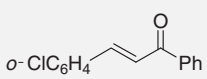
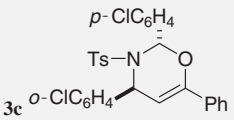
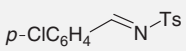
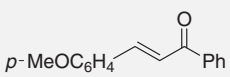
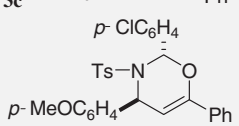
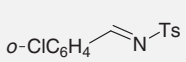
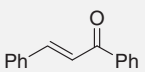
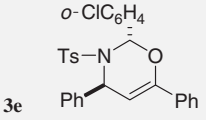
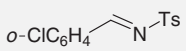
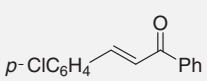
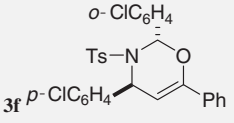
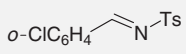
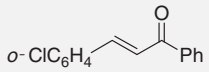
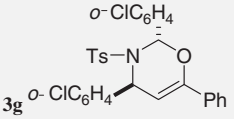
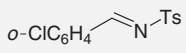
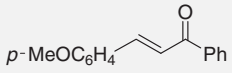
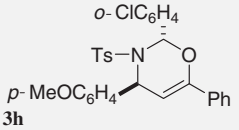
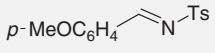
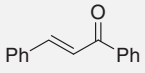
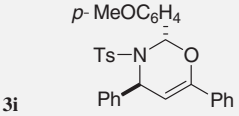
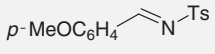
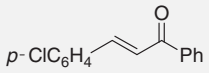
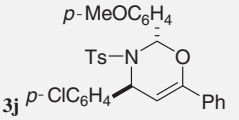
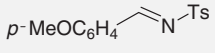
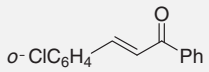
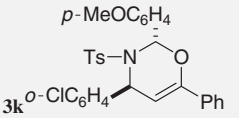
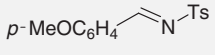
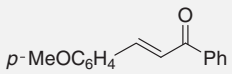
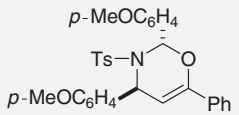
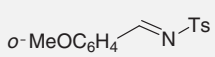
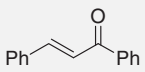
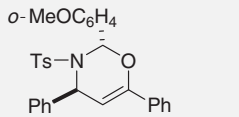
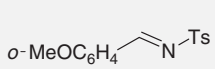
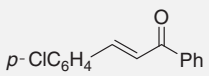
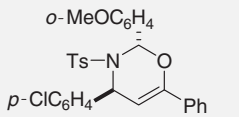
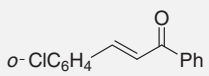
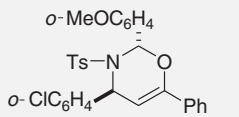
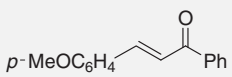
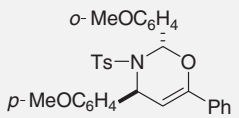
Entry	Imine **1**	Enone **2**	Reaction time[b] (h)	1,3-Oxazine **3**	Yield[c,d] (%)
1			3	 **3a**	90
2			4	 **3b**	95
3			4	 **3c**	91
4			3	 **3d**	89
5			4	 **3e**	85
6			4	 **3f**	92

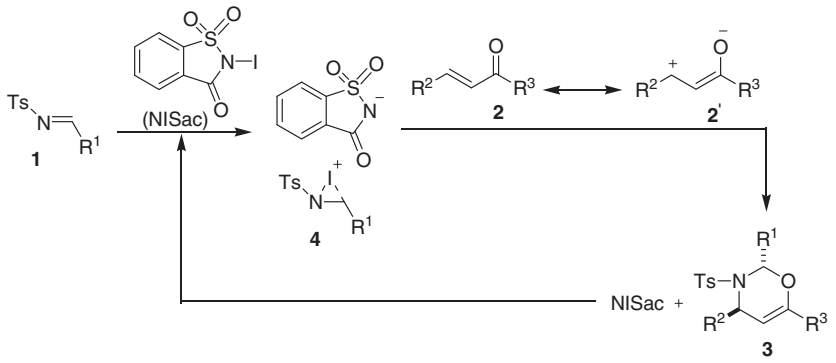
Table 2 (*continued*)

Entry	Imine **1**	Enone **2**	Reaction time[b] (h)	1,3-Oxazine **3**	Yield[c,d] (%)
7			4	 **3g**	91
8			3	 **3h**	92
9			2	 **3i**	87
10			3	 **3j**	94
11			2	 **3k**	90
12			2	 **3l**	92
13			4	 **3m**	88
14			3	 **3n**	93
15			2	 **3o**	91
16			2	 **3p**	95

[a] For the experimental procedure, see Ref. 24.
[b] Time required for completion of the reaction as monitored by TLC.
[c] Yield of isolated and purified products.
[d] All compounds gave C, H and N analyses ±0.38% and satisfactory spectral (IR, ^{1}H NMR, ^{13}C NMR and EIMS) data.

N-Iodosaccharin, bearing relatively a more electropositive iodine atom, is a new and versatile iodinating agent for a variety of substrates.[22] NISac has also found application in the activation of certain reactions, but its excess or stoichiometric quantities have been used.[22] However, the synthetic utility of NISac as a catalyst has not been explored till date, hence it is an interesting target of investigation. The envisaged synthetic protocol is an outcome of our quest for utilizing NISac as a catalyst and pursuing our work on the development of new synthetic methodologies,[23] especially for 1,3-oxazines.[19] This Letter reports the preliminary successful results of NISac-catalyzed one-pot synthesis of 1,3-oxazines from imines and enones, which is 100% atom economic and high yielding.

In our initial attempt, we investigated the optimization of reaction conditions regarding both the catalyst and solvent. Here, imine **1a** and enone **2a** were chosen as representative substrates for the synthesis of 1,3-oxazine **3a**, and the reaction was performed by stirring in THF at room temperature for 2 h (Table 1). It was found that among the catalysts tested, NISac gave the best result (Table 1, entry 3), whereas the other structurally analogous cata-



Scheme 3. Plausible mechanism for the formation of 1,3-oxazines **3** and the recycling of the catalyst NISac.

lysts as well as molecular iodine gave comparatively lower yields (Table 1, entries 1, 2 and 4). It is probably due to the more electrophilic nature of *N*-iodosaccharin than *N*-iodosuccinimide, *N*-phthalimide and molecular iodine. The optimum loading for the catalyst NISac was found to be 20 mol %.When the amount of catalyst was decreased from 20 mol % to 15 mol % relative to substrate **1a**, the yield of the product **3a** reduced (Table 1, entry 6), but the use of 25 mol % of NISac did not affect the yield (Table 1, entries 2 and 5). The reaction did not occur without using the catalyst under the present reaction conditions.

Optimization of solvents for the synthesis of **3a** employing NISac (20 mol %) was also undertaken and it was found that amongst $CHCl_3$, THF, DCM, acetone, CH_3CN and 1,4-dioxane, the best solvent in terms of yield was THF and it was used throughout the present study. It was also noted that a higher reaction temperature, for example, in a refluxing solvent instead of room temperature did not increase the yield. Next, in order to investigate the substrate scope and general validity of the reaction, a variety of imines **1** and enones **2** were used employing the present optimized reaction conditions[24] and the yields were found to be good to excellent (Table 2), the highest yield of **3** being 95% (Table 2, **3b**). The requisite NISac was prepared by reaction of silver salt of saccharin with iodine as described in the literature.[25]

The formation of 1,3-oxazine **3** may be tentatively rationalized by initial reaction of imine **1** and NISac to produce iodonium ion **4**, which delivers the target 1,3-oxazine **3** via [2+4] cycloaddition with 1,4-dipolar species **2′** and regenerates NISac (Scheme 3). The plausible mechanism suggests that NISac is released at the end of the reaction when the 1,3-oxazine ring is formed, this allows the use of NISac in a catalytic amount. The formation of **3** was highly diastereoselective in favour of the thermodynamically more stable *trans* isomer. In all cases only a single stereoisomer (*trans*) of **3** was produced. By analogy the *trans* configuration has been assigned to **3** on the basis of ^{1}H NMR experiments and the literature precedent.[26] The reactions were clean and all the synthesized products were characterized by their elemental analysis and ^{1}H NMR, ^{13}C NMR, IR and mass spectroscopic data.[24]

In summary, we have demonstrated a pot, step and atom economic high yielding synthetic protocol for 1,3-oxazines using a new catalyst NISac via formal [2+4] cycloaddition of imines and enones. In the present protocol there is no by-product formation and also the catalyst NISac used could be easily recycled for further use without any loss of efficiency. Thus, this work opens up a new and efficient route for the synthesis of such kinds of fine chemicals to cater to the needs of academia as well as of industry.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2010.05.113.

References and notes

1. *Cycloaddition Reactions in Organic Synthesis*; Carruthers, W., Ed.; Pergamon: Oxford, 1990; (b) Oppolzer, W. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 10–23.
2. (a) Matsuo, J.-I.; Sasaki, S.; Hoshikawa, T.; Ishibashi, H. *Chem. Commun.* **2010**, *46*, 934–936; (b) González, A. Z.; Toste, F. D. *Org. Lett.* **2010**, *12*, 200–203; (c) Parsons, A. T.; Johnson, J. S. *J. Am. Chem. Soc.* **2009**, *131*, 14202–14203; (d) Kee, I. S., ; Hall, H. K., Jr. *Tetrahedron Lett.* **2009**, *50*, 7116–7117; (e) Bear, B. R.; Sparks, S. M.; Shea, K. J. *Angew. Chem., Int. Ed.* **2001**, *40*, 820–849; (f) Roush, W. R. *Adv. Cycloaddit.* **1990**, *2*, 91–146; (g) Craig, D. *Chem. Soc. Rev.* **1987**, *16*, 187–238; (h) Ciganek, E. *Org. React. (N.Y.)* **1984**, *32*, 1–394; (i) Brieger, G.; Bennett, J. N. *Chem. Rev.* **1980**, *80*, 63–97.
3. (a) Corey, E. J.; Cheng, X.-M. *The Logic of Chemical Synthesis*; John Wiley & Sons: New York, 1989. p. 423; (b) Kobayashi, M.; Kitazawa, M.; Sotio, T.; Yamamoto, R.; Harada, H. *Yakugaku Zasshi* **1984**, *104*, 659–679; *Chem. Abstr.* **1985**, *102*, 6344m.; (c) Testa, E.; Fontanella, L.; Cristiani, G.; Gallo, G. *J. Org. Chem.* **1959**, *24*, 1928–1936; (d) Frauran, C. P.; Douzon, C.; Raynaud, G. M.; Sergant, M. Y. U.S. 3.821.215; *Chem. Abstr.* **1975**, *82*, 49951r.; (e) Vrouenraets, S. M.; Wit, W. F.; van Tongeren, J.; Lange, J. M. *Expert Opin. Pharmacother.* **2007**, *8*, 851–871.
4. (a) Haneishi, T.; Okazaki, T.; Hata, T.; Tamura, C.; Nomura, M.; Naito, A.; Seki, I.; Arai, M. *J. Antibiot.* **1971**, *24*, 797–799; (b) Sasaki, K.; Kusakabe, Y.; Esumi, S. *J. Antibiot.* **1972**, *25*, 151–154; (c) Kusakabe, Y.; Nagatsu, J.; Shibuya, M.; Kawaguchi, O.; Hirose, C.; Shirato, S. *J. Antibiot.* **1972**, *25*, 44–47; (d) Kupchan, S. M.; Komoda, Y.; Court, W. A.; Thomas, G. J.; Smith, R. M.; Karim, A.; Gilmore, C. J.; Haltivanger, R. C.; Bryan, R. F. *J. Am. Chem. Soc.* **1972**, *94*, 1354–1356; (e) Wani, M. C.; Taylor, H. L.; Wall, M. E. *J. Chem. Soc., Chem. Commun.* **1973**, 390–390; (f) Johnson, P. Y.; Silver, R. B. *J. Heterocycl. Chem.* **1975**, *10*, 1029–1030; (g) Renullard, S.; Rebhun, L. I.; Havic, G. A.; Kupchan, S. M. *Science* **1975**, *189*, 1002–1005; (h) Lesher, G. Y.; Surrey, A. R. *J. Am. Chem. Soc.* **1955**, *77*, 636–641; (i) Mosher, H. S.; Frankel, M. B.; Gregory, M. *J. Am. Chem. Soc.* **1953**, *75*, 5326–5328.
5. Peglion, J. L.; Vian, J.; Gourment, B.; Despaux, N.; Audinot, V.; Millan, M. *Bioorg. Med. Chem. Lett.* **1997**, *7*, 881–886.
6. (a) Balázs, Á.; Szakonyi, Z.; Fülöp, F. *J. Heterocycl. Chem.* **2009**, *44*, 403–406; (b) Nikam, S. S.; Yuen, P.-W.; Kornberg, B. E.; Tobias, B.; Rafferty, M. F. *J. Org. Chem.* **1997**, *62*, 9331–9334; (c) Kehagia, K.; Dömling, A.; Ugi, I. *Tetrahedron* **1995**, *51*, 139–144; (d) Delaney, P. M.; Huang, J.; Macdonald, S. J. F.; Harrity, J. P. A. *Org. Lett.* **2008**, *10*, 781–783; (e) Yadav, L. D. S.; Rai, A.; Rai, V. K.; Awasthi, C. *Synlett* **2008**, 529–534; (f) Yadav, L. D. S.; Awasthi, C.; Rai, V. K.; Rai, A. *Tetrahedron Lett.* **2008**, *49*, 2377–2380; (g) Yadav, L. D. S.; Awasthi, C.; Rai, V. K.; Rai, A. *Synlett* **2008**, 2257–2262.
7. Abbas, T. R.; Cadogan, J. I. G.; Doyle, A. A.; Gosney, I.; Hodgson, P. K. G.; Howells, G. E.; Hulme, A. N.; Parsons, S.; Sadler, I. H. *Tetrahedron Lett.* **1997**, *38*, 4917–4920. and references cited therein.
8. Damodiran, M.; Selvam, N. P.; Perumal, P. T. *Tetrahedron Lett.* **2009**, *50*, 5474–5478.
9. Bertolini, G.; Aquino, M.; Ferrario, F.; Pavich, G.; Zaliani, A.; Sala, A. *J. Org. Chem.* **1996**, *61*, 3358–3361.
10. Alizadeh, A.; Zohreh, N.; Zhu, L.-G. *Synthesis* **2008**, 2073–2076.
11. Sugiura, M.; Kumahara, M.; Nakajima, M. *Chem. Commun.* **2009**, 3585–3587.
12. Chen, G.; Fu, C.; Ma, S. *Org. Lett.* **2009**, *11*, 2900–2903.
13. Badiang, J. G.; Aubé, J. *J. Org. Chem.* **1996**, *61*, 2484–2487.
14. François-Endelmond, C.; Carlin, T.; Thuery, P.; Loreau, O.; Taran, F. *Org. Lett.* **2010**, *12*, 40–42.
15. Butler, J. D.; Solano, D. M.; Robins, L. I.; Haddadin, M. J.; Kurth, M. J. *J. Org. Chem.* **2008**, *73*, 234–240.
16. Larksarp, C.; Alper, H. *J. Org. Chem.* **1999**, *64*, 4152–4158.
17. Manning, J. R.; Davies, H. M. L. *Tetrahedron* **2008**, *64*, 6901–6908.

18. (a) Tumtin, S.; Phucho, I. T.; Nongpiur, A.; Nongrum, R.; Vishwakarma, J. N.; Myrboh, B.; Nongkhlaw, R. L. *J. Heterocycl. Chem.* **2010**, *47*, 125–130; (b) Maheswari, C. U.; Kumar, G. S.; Venkateshwar, M.; Kumar, R. A.; Kantam, M. L.; Reddy, K. R. *Adv. Synth. Catal.* **2010**, *352*, 341–346; (c) Cao, H.; Jiang, H.-F.; Qi, C.-R.; Yao, W.-J.; Chen, H.-J. *Tetrahedron Lett.* **2009**, *50*, 1209–1214; (d) Mathew, B. P.; Nath, M. *J. Heterocycl. Chem.* **2009**, *46*, 1003–1006; (e) Zhang, M.; Jiang, H.; Wang, A. *Synlett* **2007**, 3214–3218.
19. (a) Yadav, L. D. S.; Rai, A.; Rai, V. K.; Awasthi, C. *J. Chem. Res.* **2009**, 520–526; (b) Yadav, L. D. S.; Rai, V. K. *Nucleosides, Nucleotides Nucleic Acids* **2008**, *27*, 1227–1237; (c) Yadav, L. D. S.; Srivastava, V. P.; Rai, V. K.; Patel, R. *Tetrahedron* **2008**, *64*, 4246–4253; (d) Yadav, L. D. S.; Rai, V. K. *Synlett* **2007**, 1227–1230; (e) Yadav, L. D. S.; Rai, V. K. *Tetrahedron Lett.* **2006**, *47*, 395–397; (f) Yadav, L. D. S.; Kapoor, R. *J. Org. Chem.* **2004**, *69*, 8118–8120.
20. Yong, S. R.; Ung, A. T.; Pyne, S. G.; Skelton, B. W.; White, A. H. *Tetrahedron* **2007**, *63*, 5579–5586.
21. (a) Palacios, F.; Alonso, C.; Rubiales, G.; Villegas, M. *Tetrahedron* **2009**, *65*, 1119–1124; (b) Palacios, F.; Herrán, E.; Rubiales, G.; Ezpeleta, J. M. *J. Org. Chem.* **2002**, *67*, 2131–2135; (c) Palacios, F.; Alonso, C.; Rubiales, G. *J. Org. Chem.* **1997**, *62*, 1146–1154.
22. Rai, A. *Synlett* **2008**, 784–785.
23. (a) Yadav, L. D. S.; Rai, V. K.; Singh, S.; Singh, P. *Tetrahedron Lett.* **2010**, *51*, 1657–1662; (b) Yadav, L. D. S.; Singh, S.; Rai, V. K. *Synlett* **2010**, 240–246; (c) Yadav, L. D. S.; Rai, A. *Carbohydr. Res.* **2009**, *344*, 2329–2335; (d) Yadav, L. D. S.; Rai, A. *Synthesis* **2009**, 2802–2808; (e) Yadav, L. D. S.; Singh, S.; Rai, V. K. *Green Chem.* **2009**, *11*, 878–882.
24. *General procedure for the synthesis of 1,3-oxazines* **3**: A mixture of imine **1** (1 mmol), enone **2** (1 mmol), *N*-iodosaccharin (0.2 mmol) in 10 mL of THF was stirred at room temperature for 2–4 h (Table 2). After completion of the reaction (monitored by TLC), water (10 mL) was added and the product was extracted with ethyl acetate (3 × 15 mL). The organic extract was dried under vacuum and the residue thus obtained was dissolved in THF. The crude NISac which also get dissolved in THF was precipitated by addition of pentane, the yellowish crystalline precipitate was filtered and dried under vacuum in the dark to recover NISac for further reuse. The filtrate was dried over Na_2SO_4, filtered, concentrated under reduced pressure and the crude product thus obtained was purified by silica gel column chromatography using EtOAc–hexane (2:5) as eluent to afford an analytically pure sample of **3**.
Physical data of representative compounds. Compound **3a**: Yellowish solid, yield 90%, mp 110–112 °C. IR (KBr) ν_{max} 3012, 1620, 1605, 1582, 1516, 1350, 1310, 1459, 1140, 1050, 964, 735, 705 cm^{-1}. ^1H NMR (400 MHz; DMSO-d_6/TMS) δ: 2.42 (s, 3H, CH_3), 5.65 (d, J = 3.7 Hz, 1H, 4-H), 5.91 (m, 1H, 2-H), 6.41 (d, J = 3.7 Hz, 1H, 5-H), 7.30 (d, 2H, J = 8.1 Hz, Ts), 7.34–7.55 (m, 10H, Ph), 7.65–7.70 (m, 2H, 4-Cl-Ph), 7.72 (d, 2H, J = 8.3 Hz, Ts), 8.10–8.17 (m, 2H, 4-Cl-Ph). ^{13}C NMR (100 MHz, DMSO-d_6/TMS) δ: 24.5, 43.1, 78.1, 84.7, 123.4, 124.1, 124.9, 125.8, 126.7, 127.4, 128.0, 128.7, 129.4, 130.2, 131.1, 132.6, 133.3, 136.8, 138.0, 141.5, 149.6. EIMS (m/z) 501 (M^+). Anal. Calcd for $C_{29}H_{24}ClNO_3S$: C, 69.38; H, 4.82; N, 2.79. Found: C, 69.76; H, 4.61; N, 2.49.
Compound **3b**: Yellowish solid, yield 95%, mp 97–99 °C. IR (KBr) ν_{max} 3018, 1621, 1602, 1585, 1514, 1355, 1319, 1456, 1144, 1052, 966, 731, 708 cm^{-1}. ^1H NMR (400 MHz; DMSO-d_6/TMS) δ: 2.40 (s, 3H, CH_3), 5.50 (d, 1H, J = 4 Hz, 4-H), 5.97 (m, 1H, 2-H), 6.36 (d, 1H, J = 4 Hz, 5-H), 7.30 (d, 2H, J = 8.0 Hz, Ts), 7.60–7.69 (m, 2H, 4-ClPh), 7.63–7.72 (m, 2H, 4-ClPh), 7.66–7.71 (m, 5H, Ph), 7.74 (d, 2H, J = 8.2 Hz, Ts), 8.09–8.13 (m, 2H, 4-ClPh), 8.10–8.17 (m, 2H, 4-ClPh). ^{13}C NMR (100 MHz, DMSO-d_6/TMS) δ: 24.3, 43.8, 78.6, 84.1, 123.5, 124.2, 125.1, 125.8, 126.8, 127.5, 128.3, 129.0, 129.8, 130.9, 131.9, 132.7, 133.5, 136.1, 136.9, 141.6, 149.7. EIMS (m/z) 535 (M^+). Anal. Calcd for $C_{29}H_{23}Cl_2NO_3S$: C, 64.93; H, 4.32; N, 2.61. Found: C, 64.61; H, 4.70; N, 2.41.
Compound **3i**: Yellowish solid, yield 94%, mp 112–115 °C. IR (KBr) ν_{max} 3014, 1624, 1601, 1583, 1516, 1352, 1310, 1457, 1146, 1054, 964, 736, 706 cm^{-1}. ^1H NMR (400 MHz; DMSO-d_6/TMS) δ: 2.41 (s, 3H, CH_3), 3.85 (s, 3H, OCH_3), 5.74 (d, 1H, J = 4.0 Hz, 4-H), 5.93 (m, 1H, 2-H), 6.32 (d, 1H, J = 4.0 Hz, 5-H), 7.30 (d, 2H, J = 8.0 Hz, Ts), 7.36–7.56 (m, 10H, Ph), 7.66–7.68 (m, 2H, 4-OCH_3Ph), 8.01–8.03 (m, 2H, 4-OCH_3Ph), 7.72 (d, 2H, J = 8.5 Hz, Ts). ^{13}C NMR (100 MHz, DMSO-d_6/TMS) δ: 24.1, 34.5, 55.6, 78.4, 84.4, 114.7, 124.1, 124.9, 125.6, 126.5, 127.2, 128.0, 128.7, 129.6, 130.4, 131.3, 132.4, 136.7, 138.1, 141.4, 149.6, 159.2. EIMS (m/z) 497 (M^+). Anal. Calcd for $C_{30}H_{27}NO_4S$: C, 72.41; H, 5.47; N, 2.81. Found: C, 72.62; H, 5.15; N, 3.19.
Compound **3k**: Yellowish solid, yield 90%, mp 108–110 °C. IR (KBr) ν_{max} 3015, 1624, 1602, 1584, 1518, 1351, 1312, 1461, 1140, 1054, 961, 735, 708 cm^{-1}. ^1H NMR (400 MHz; DMSO-d_6/TMS) δ: 2.42 (s, 3H, CH_3), 3.82 (s, 3H, OCH_3), 5.75 (d, 1H, J = 4.2 Hz, 4-H), 5.91 (m, 1H, 2-H), 6.34 (d, 1H, J = 4.2 Hz, 5-H), 7.34 (d, 2H, J = 8.1 Hz, Ts), 7.64–7.66 (m, 2H, 4-OCH_3Ph), 7.67–7.70 (m, 2H, 2-ClPh), 7.74 (d, 2H, J = 8.2 Hz, Ts), 8.02–8.05 (m, 2H, 4-OCH_3Ph), 8.10–8.15 (m, 2H, 2-ClPh), 7.36–7.56 (m, 5H, Ph). ^{13}C NMR (100 MHz, DMSO-d_6/TMS) δ: 24.4, 34.6, 55.5, 78.3, 84.1, 114.5, 124.0, 124.8, 125.5, 126.4, 127.1, 127.9, 128.8, 129.5, 130.5, 131.3, 132.0, 132.9, 133.7, 136.7, 137.5, 141.6, 149.5, 159.0. EIMS (m/z) 531 (M^+). Anal. Calcd for $C_{30}H_{26}ClNO_4S$: C, 67.72; H, 4.93; N, 2.63. Found: C, 68.00; H, 5.22; N, 2.41.
25. Aloui, M.; Fairbanks, A. J. *Synlett* **2001**, 797–799.
26. Cherkauskas, J. P.; Klos, A. M.; Borzilleri, R. M.; Sisko, J.; Weinreb, S. M. *Tetrahedron* **1996**, *52*, 3135–3152.