ISSN 1070-4280, Russian Journal of Organic Chemistry, 2019, Vol. 55, No. 3, pp. 412–414. © Pleiades Publishing, Ltd., 2019.

SHORT COMMUNICATIONS

Green and Facile Synthesis of New 3-(Phenylallylideneamino)indeno[1,2-*d*]imidazoles

R. M. Ghalib[a]

[a] *Department of Chemistry, Faculty of Sciences and Arts-Khulais, University of Jeddah, Jeddah, P.O. Box 355, 21921 Kingdom of Saudi Arabia*
e-mail: raza2005communications@gmail.com

Received November 26, 2018; revised November 29, 2018 accepted December 17, 2018

Abstract—A green and facile strategy has been proposed for the synthesis of previously unknown 3a,8a-dihydroxy-3-[(3-phenylprop-2-en-1-ylidene)amino]-2-sulfanylidene-2,3,3a,8a-tetrahydro-1*H*-indeno[1,2-*d*]imidazol-8-one and 3a,8a-dihydroxy-3-[(3-phenylprop-2-en-1-ylidene)amino]-1,3,3a,8a-tetrahydroindeno[1,2-*d*]-imidazole-2,8-dione in excellent yields by condensation of cinnamaldehyde thiosemicarbazone and semicarbazone, respectively, with ninhydrin in boiling dioxane. The reaction is clean, simple, and free of work-up and column chromatography.

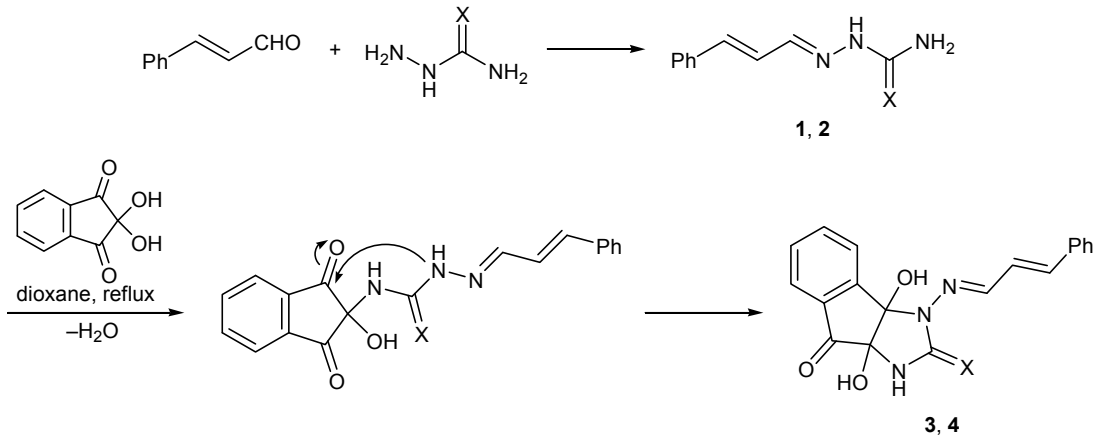
Keywords: green synthesis, semicarbazones, thiosemicarbazones, 3-phenylallylideneamine, ninhydrin, cinnamaldehyde, indeno[1,2-*d*]imidazol-8-ones.

DOI: 10.1134/S107042801903028X

Ninhydrin undergoes electrophilic substitution at the C^2 atom. It has been utilized as a building block in the synthesis of many heterocyclic compounds such as indenoimidazoles, quinoxalines, and benzazocines. Hydrazones exhibit biological activity and play a key role in the synthesis of heterocyclic compounds [1, 2]. Indenoimidazoles are heterocyclic molecules of extensive biological significance [3, 4]. The synthesis and supramolecular and crystal structures of several indenoimidazoles with antimicrobial and cholinesterase inhibitory activities were reported in [5–8]. These compounds were prepared by reaction of ninhydrin with urea, phenylurea, and phenylthiourea at a molar ratio of 1 : 1 in acetic acid [5, 6]. 3a,8a-Dihydroxy-2-sulfanylidene-1,3,3a,8a-tetrahydroindeno[1,2-*d*]imidazol-8(2*H*)-one showed antimicrobial activity against gram positive and gram negative bacterial strains, as well as the fungal strain *Candida albicans* [8]. Ninhydrin reacted with *o*-phenylenediamine at a molar ratio of 1 : 1 to give 11*H*-indeno[1,2-*b*]quinoxalin-11-one [9]. Biindenoquinoxaline was synthesized from ninhydrin; its structure was established by spectral methods and single crystal X-ray analysis. It showed good anticancer and antibacterial activities, selective inhibitory activity against acetylcholinesterase, and moderate inhibitory activity against butyrylcholinesterase [10]. Novel anticancer benzazocine derivatives were synthesized by a green and facile strategy starting from ninhydrin, and their structures were determined by spectral analysis and single crystal X-ray analysis [11]. A literature survey revealed no published data on 3-(phenylallylideneamino)indeno-[1,2-*d*]imidazoles **3** and **4**.

The target products were synthesized in two steps. In the first step, (thio)semicarbazones **1** and **2** were prepared in 100% yield by condensation of cinnamaldehyde with thiosemicarbazide and semicarbazide, respectively. The spectral parameters of compounds **1** and **2** were fully consistent with the previously published data [12–16]. The second step was the reaction of **1** and **2** with ninhydrin in boiling dioxane. Indenoimidazoles **3** and **4** were obtained in 90–92% yield in a short time (2 h). The reaction is likely to involve nucleophilic addition of the terminal nitrogen of (thio)-semicarbazone **1** or **2** to C^2 of ninhydrin, followed by attack from the same side of the internal nitrogen on C^1 of ninhydrin [2]. The structure of compounds **3** and **4** was assigned on the basis of their FT-IR, ^{1}H NMR, ^{13}C NMR, DEPT-135, ^{13}C–H HSQC, and mass spectra and elemental analyses.

General procedure for the synthesis of compounds 3 and 4. A mixture of cinnamaldehyde



1, **3**, X = S; **2**, **4**, X = O.

(1 mmol) and thiosemicarbazide (1 mmol) or semicarbazide hydrochloride (1 mmol) in double-distilled water (50 mL) containing a catalytic amount of acetic acid (1 mL) was refluxed for 30 min with stirring to obtain thiosemicarbazone **1** or semicarbazone **2**, respectively, in quantitative yield. A mixture of ninhydrin (1 mmol) and (thio)semicarbazone **1** or **2** (1 mmol) in dioxane (50 mL) was refluxed with stirring for 2 h, the progress of the reaction being monitored by TLC.

3a,8a-Dihydroxy-3-[(3-phenylprop-2-en-1-ylidene)amino]-2-sulfanylidene-2,3,3a,8a-tetrahydro-1*H*-indeno[1,2-*d*]imidazol-8-one (3). Yield 3.3 g (90%), yellowish solid, mp 138.6°C. IR spectrum, ν, cm^{-1}: 3519 (NH), 3325 (OH), 3082 (C–H_{arom}), 2949 (=C–H), 2108, 1718 (C=O), 1607 (C=C_{arom}), 1497, 1410, 1267, 1110, 970. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 6.99–6.96 t (1H, J = 9 Hz), 7.12–7.10 d (1H, J = 15.66 Hz), 7.96–7.34 m (12H), 9.01–8.99 d (1H, J = 6.6 Hz). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 86.83 (COH), 91.43 (COH), 123.41 (CH), 124.80 (CH), 125.38 (CH), 126.60 (2C, CH), 128.24 (2C, CH), 128.30 (CH), 130.38 (CH), 131.26, 135.30, 136.98 (CH), 139.06 (CH), 149.57, 149.93 (CH), 175.57 (C=S), 193.37 (C=O). Mass spectrum: m/z 366.0920 $[M + H]^+$. Found, %: C 62.49; H 4.09; N 11.71; O 13.3; S 8.61. $C_{19}H_{15}N_3O_3S$. Calculated, %: C 62.45; H 4.14; N 11.50; O 13.14; S 8.78.

3a,8a-Dihydroxy-3-[(3-phenylprop-2-en-1-ylidene)amino]-1,3,3a,8a-tetrahydro-1*H*-indeno-[1,2-*d*]imidazole-2,8-dione (4). Yield 3.22 g (92%), yellowish solid, mp 179.8°C. IR spectrum ν, cm^{-1}: 3533 (NH), 3330 (OH), 3083 (C–H_{arom}), 2950 (=C–H), 2108, 1718 (C=O), 1596 (C=C_{arom}), 1404, 1351, 1186, 1126, 966. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 6.94–6.90 m (2H), 7.92–6.99 m (11H), 8.84–8.83 d (1H, J = 8.7 Hz), 8.90 br.s (1H). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 83.45 (COH), 88.76 (COH), 123.19 (CH), 124.45 (CH), 125.98 (CH), 126.36 (2C, CH), 127.99 (CH), 128.21 (2C, CH), 129.99 (CH), 131.13, 135.51, 136.59 (CH), 137.30 (CH), 147.21 (CH), 150.64, 151.43 (C=O), 194.43 (C=O). Mass spectrum: m/z 350.1145 $[M + H]^+$. Found, %: C 65.48; H 4.41; N 12.21; O 18.40. $C_{19}H_{15}N_3O_4$. Calculated, %: C 65.32; H 4.33; N 12.03; O 18.32.

Ninhydrin (Sigma-Aldrich) and solvents (Merck) were purchased commercially and used without further purification. Thin-layer chromatography was done on silica gel 60 F_{254} plates (Merck). The IR spectra were recorded on a Perkin Elmer Spectrum II FT IR spectrometer in potassium bromide discs. The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance 600 spectrometer (600 MHz for ^{1}H; 150 MHz for ^{13}C) with tetramethylsilane as an internal standard. The mass spectra were obtained on an Agilent 6520 Q-TOF mass spectrometer. Elemental analysis was performed with a Perkin Elmer 240 analyzer. The melting points were taken on a Stuart SMP30 Digital Melting Point Apparatus by open capillary method and are uncorrected.

ACKNOWLEDGMENTS

The author thanks Faculty of Sciences & Arts, University of Jeddah, Khulais, Kingdom of Saudi Arabia, for providing research facilities.

CONFLICT OF INTERESTS

The author declares the absence of conflict of interests.

REFERENCES

1. Samus, N.M., Gulya, A.P., Tsapkov, V.I., Chumakov Y.M., and Roshu, T., *Russ. J. Gen. Chem*., 2006, vol. 76, p. 1100.
2. Yeshwinder, S., Rajni, K., Ramneet, K., Sanjana, K., Tanwi, S., Suruchi, G., Vivek, K.G., Rajni, K., and Kamal, K.K., *Synth. Commun*., 2017, vol. 47, p. 1159.
3. Roberts, L.R., Bryans, J., Conlon, K., McMurray, G., Stobie, A., and Whitlock, G.A., *Bioorg. Med. Chem. Lett*., 2008, vol. 18, p. 6437.
4. Sarra, J.D. and Stephani, R.A., *Med. Chem. Res*., 2000, vol. 10, p. 81.
5. Ghalib, R.M., Mehdi, S.H., Hashem, R., Solhe, F.A., and Sulaiman, O., *J. Chem. Sci*., 2016, vol. 128, p. 1841.
6. Ghalib, R.M., Hashim, R., Mehdi, S.H., Quah, C.K., and Fun, H-K., *Acta Crystallogr., Sect. E*, 2011, vol. 67, p. o1525.
7. Ghalib, R.M., Hashim, R., Alshahateet, S.F., Mehdi, S.H. Sulaiman, O. Chan, K-L., Murugaiyah, V., and Jawad, A., *J. Chem. Crystallogr*., 2012, vol. 42, p. 783.
8. Ghalib, R.M., Hashim, R., Alshahateet, S.F., Mehdi, S.H., Sulaiman, O., Murugaiyah, V., and Aruldass, C.A., *J. Mol. Struct*., 2011, vol. 1005, p. 152
9. Ghalib, R.M., Hashim, R., Sulaiman, O., Hemamalini, M., and Fun, H-K., *Acta Crystallogr., Sect. E*, 2010, vol. 66, p. o1494.
10. Ghalib, R.M., Hashim, R., Mehdi, S.H., Sulaiman, O., Silva, P.S.P., Jassbi, A.R., Firuzi, O., Kawamura, F., Chan, K., and Murugaiyah, V., *Lett. Drug Des. Discovery*, 2012, vol. 9, p. 767.
11. Ghalib, R.M., Hashim, R., Mehdi, S.H., Sulaiman, O., Jawad, A., Bogdanović, G.A., Srećko, R.T., Kawamura, F., Khadeer Ahamed, B.M., and Abdul-Majid, A.M.S., *Curr. Org. Synth*., 2017, vol. 14, p. 127.
12. Janardhan, B. and Rajitha, B., *Acta Chim. Pharm. Indica*, 2013, vol. 3, p. 26.
13. Naimi-Jamal, M.R., Mokhtari, J., Dekamin, M.G., and Javanshir, S., *Iran. J. Chem. Chem. Eng*., 2012, vol. 31, p. 1.
14. Kiasat, A.R., Kazemi, F., and Mehrjardia, M.F., *J. Chin. Chem. Soc*., 2007, vol. 54, p. 1337.
15. Krishna, P.M., and Reddy, K.H., *Pharma Chem*,, 2013, vol. 5, p. 258.
16. Leite, A.C.L., Moreira, D.R.M., Coelho, L.C.D., Menezes, F.D., and Brondani, D.J., *Tetrahedron Lett*., 2008, vol. 49, p. 1538.