Cover Page

INTERNATIONAL JOURNAL OF MULTIDISCIPLINARY EDUCATIONAL RESEARCH
ISSN:2277-7881; IMPACT FACTOR :7.816(2022); IC VALUE:5.16; ISI VALUE:2.286
Peer Reviewed and Refereed Journal: VOLUME:11, ISSUE:3(6), March: 2022
Online Copy of Article Publication Available (2022 Issues): www.ijmer.in
Digital Certificate of Publication: http://ijmer.in/pdf/e-Certificate%20of%20Publication-IJMER.pdf
Scopus Review ID: A2B96D3ACF3FEA2A
Article Received: 2nd March 2022
Publication Date:10th April 2022
Publisher: Sucharitha Publication, India

DOI: http://ijmer.in.doi./2022/11.03.117

SYNTHESIS AND CHARACTERIZATION OF LSOFLAVONE: GENESTEIN

Anupam Vibha
Assistant Teacher
+2 Sarvoday High School
Gangasagar, Darbhanga, Bihar, India

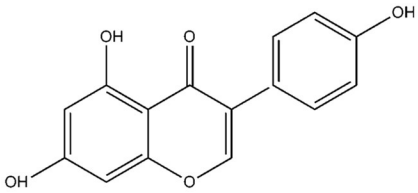
Abstract

Genistein was efficiently synthesized from (2,4,6Ptrihy-droxyphenyl) ethanone by a novel five-step procedure involving the formation of an enamino ketone, followed by ring closure and a Suzuki coupling reaction using palladium acetate and poly (ethyleneglycol).

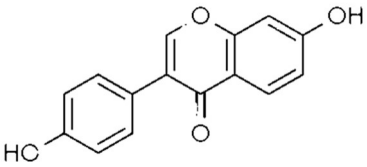
Keywords: Ring Closure, Coupling, Heterocycle, Genistein, Isoflavone, Green Chemistry.

INTRODUCTION

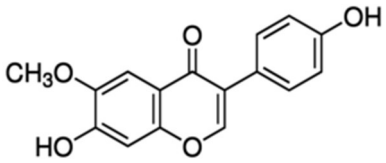
lsofiavones are found naturally in many plant species, particularly those of the legume family. lsoflavones are often produced by the plant as a defense mechanism to ward off microbes or other pathogens, and to reduce oxidative stress caused by reactive-oxygen species (ROS). The soy isoflavones consist of three compounds: genistein, daidzein, and, less commonly, glycitein. These compounds are usually O-glycosylated within the plant and are metabolized into the active aglycone forms by bacterial or digestive action.[1]



Isoflavone: Genestein



lsoflavone:Daidzein



lsoflavone: Glyecitein

Our synthesis began from commercially available (2,4,6- trihydroxyphenyl)ethanone. However initial attempts to form an enamino ketone were not successful, presumably because (dimethoxy methyl) dimethylamine is capable of reacting with phenols. We therefore considered it necessary to protect two of the hydroxy substituents in the triol.[2]

Initially, triol was protected as its dibenzyl derivative, albeit in moderate yield (64%). However, this protection did not permit the subsequent ring closure and halogenation reactions. Protection as the methoxymethyl (MOM) ether by treatment with chloromethyl methyl ether and N, N-diisopropylethylamine in dichloromethane gave the desired protected acetophenone 6 (94%) without addition-al purification. This was subsequently treated with (dimethoxymethyl)dimethylamine to form the enamino ketone in 99% yield after column chromatography. On stirring in methanol with excess diiodine, the MOM-protected.[3] enamino ketone

Cover Page

INTERNATIONAL JOURNAL OF MULTIDISCIPLINARY EDUCATIONAL RESEARCH
ISSN:2277-7881; IMPACT FACTOR :7.816(2022); IC VALUE:5.16; ISI VALUE:2.286
Peer Reviewed and Refereed Journal: VOLUME:11, ISSUE:3(6), March: 2022
Online Copy of Article Publication Available (2022 Issues): www.ijmer.in
Digital Certificate of Publication: http://ijmer.in/pdf/e-Certificate%20of%20Publication-IJMER.pdf
Scopus Review ID: A2B96D3ACF3FEA2A
Article Received: 2nd March 2022
Publication Date:10th April 2022
Publisher: Sucharitha Publication, India

DOI: http://ijmer.in.doi./2022/11.03.117

underwent tandem cyclization and iodination to afford 3-iodo-5,7-bis(meth-oxymethoxy)-4H-1- benzopyran-4-one. During this reaction, two distinct bands were observed by thin-layer chromatography. The blue fluorescent band was isolated and shown, by means of NMR spectroscopy, to contain the non-iodinated ring product. The upper band contained the required iodinated product. This provided evidence that the halogenation reaction succeeded the ring-closure reaction.[4]

A Suzuki coupling reaction[5] was next used to attach the final ring of the isoflavone. A green approach to this procedure has recently been demonstrated that uses polylethylene glycol) (PEG 4000), methanol, sodium carbonate, and palladium diacetate as a source of palladium at a mild temperature of 50°C. We replaced PEG 4000 with PEG 10000 in our reaction, which gave 5,7-bis(meth0xymethoxy)-3-[4- (methoxymethoxy)phenyl]-4H-1-benzopyran-4-one in 88% yield. The PEG and palladium diacetate could be reused without further addition of a palladium source.

It was necessary to protect two of the hydroxy substituents in the triol 5. initially, triol was protected as its dibenzyl derivative. albeit in Chloromethyl ether and desired protected[6] acetophenone 6 (94%) without additional purification. This was subsequently treated with (dimethoxymethyl) dimethyiamine to form the enamino ketone in 99% yield after column chromatography. On stirring in methanol with excess diiodine, the MOM-protected enamino ketone 7 underwent tandem cycliztion and iodination to afford 3- iodo-5,7-bis (meth- oxymethoxy)-4H-1- benzopyran-4-one. During this reaction, two distinct bands were observed by thin layer chromatography. The blue fluorescent band[7] was isolated and shown, by means of NMR spectroscopy, to contain the non-iodinated ring product. The upper band contained the required iodinated product. This provided evidence that the halogenation reaction succeeded the ring-closure reaction.

A Suzuki coupling reaction was next used to attach the final ring of the isoflavone. A green approach to this procedure has recently been demonstrated that uses poly (ethylene glycol) (PEG 4000), methanol, sodium carbonate, and palladium diacetate as a source of palladium at a mild temperature of 50 °C. We replaced moderate yield (64%). However, this protection did not permit the subsequent ring closure and halogenation reactions. Protection as the methoxymethyl (MOM) ether by treatment with PEG 4000 with PEG 10000 in our reaction, which gave 5,7- bis(methoxymethoxy)-3- {4- (methoxymethoxy)phenyl]- 4H-1- benzopyran-4-one in 88% yield. The PEG and palladium diacetate could be reused without further addition of a palladium source.

Experimental

Purchased chemicals were reagent grade. Melting points were obtained on a Gallenkamp apparatus and are uncorrected.[8] NMR (400 MHz) and C NMR (100 MHz) spectra were recorded on a Varian instrument in the solvent indicated, and they are referenced to TMS or residual undeuterated solvent. HRMS were recorded on a ThermoFinnigan MAT 95XL with ESl II source for electrospray ionization.

1- [2-Hydroxy-4,6- bis (methoxymethoxylpheny) pllethanone

A fmale-dries were charged with CH_2Cl_2 MOMCI (1.15 g, 14.3 mmol) was added dropwise. The mixture was maintained at 0 °C for 20 min, then brought to r.t. The reaction was quenched with H_20 (40 mL). The organic layer was removed, and the aqueous layer was extracted with $CHCI_3$ (3 x 40 mL). The combined organic layers were dried ($MgSO_4$) and concentrated; yield: 1.46 g (94%); mp 39-42 °C.

1HNMR (CDCL[3]): d= 13.69 (S, 1H, COH), 6.27 (s,1H, Ar-H), 6.24 (s, 1 H, Ar-H), 5.25 (5, 2 H, OCH_2OCH_3), 5.16 (5, 2 $HOCH_2OCH_3$), 3.51 (s, 3 H $HOCH_2OCH_3$), 3.46 (s, 3 $HOCH_2OCH_3$), 2.65 (5, 3 H, $COCH_3$). C NMR (col_3): d = 203.3, 190.0, 166.9, 163.6, 160.5, 107.0, 97.3, 94.6, 94.1, 56.8, 56.5, 33.1.

Genisteln: A mixture of the benzopyranone 9 (0.650g, 1.81 mmol), $CHCl_3$ (5 mL),

CONCLUSION

In conclusion, we have demonstrated a novel synthetic route for the total synthesis of the isoflavone genistein. This five-step pathway, with an overall yield of 63%, also permits the preparation of numerous derivatives of genistein. The use of PEG introduces an aspect of green chemistry into the synthesis. MeOH (5 mL), and concd HCI (1 mL) was refluxed for 1 h. The reaction was quenched with H_2O, and the mixture was extracted with $CHCl_3$ (210 mL). The extracts were washed with H_2O (10 mL) and purified by column chromatography [Et0Ac—-hexanes—4% EtOH (1:2.5)]; yield: 0.451 g (92%); mp 292-297 °C (Lit. 291- 296 °C). C NMR (DMSO—ds): d =180.3, 164.4, 162.1, 157.7, 157.5, 154.1,130.3, 122.4, 121.3, 115.2, 104.5, 99.1, 93.8. HRMS (ESJ); m/z $[M + H\}^+$ calcd for C1sH11Os: 271.0601; found:271.0602.

Cover Page

INTERNATIONAL JOURNAL OF MULTIDISCIPLINARY EDUCATIONAL RESEARCH
ISSN:2277-7881; IMPACT FACTOR :7.816(2022); IC VALUE:5.16; ISI VALUE:2.286
Peer Reviewed and Refereed Journal: VOLUME:11, ISSUE:3(6), March: 2022
Online Copy of Article Publication Available (2022 Issues): www.ijmer.in
Digital Certificate of Publication: http://ijmer.in/pdf/e-Certificate%20of%20Publication-IJMER.pdf
Scopus Review ID: A2B96D3ACF3FEA2A
Article Received: 2nd March 2022
Publication Date:10th April 2022
Publisher: Sucharitha Publication, India

DOI: http://ijmer.in.doi./2022/11.03.117

References

1. Vasselin, D. A.; Westwell, A. D.; Matthews, C. S.; Bradshaw, T. D.; Stevens, M. F. G. J. Med. Chem. 2006, 49, 3973.
2. Setchell, K. D.; Brown, N. M.; _Desai, P.; Zimmer Nechemias, L.; Wolfe, B. E.; Brashear, W. T.; Kirschner, A. S.; Cassidy, A.; Heubi, J. E. J. Nutr. 2001, 131, 1362.
3. Scholar, E. M.; Toews, M. L. Cancer Lett. (Shannon, lrel.)
4. Merlino, G. T.; Xu, Y. H.; lshii, S.; Clark, A. J.; Semba, K.; Toyoshima, K.; Yamamoto, T.; Pastan, l. Science 1984, 224, 417.
5. Messina, M. J.; Persky, V.; Setchell, K. D.; Barnes, S. Nutr.
6. Zhou, J.-R. Nutr. Cancer Prev. 2006, 325.
7. Wietrzyk, J.; Opolski, A.; Madej, J.; Radzikowski, C. In
8. Wang, S. Y.; Yang, K. W.; Hsu, Y. T.; Chang, C. L.; Yang, Y. C. Neoplasma 2001, 3, 227.