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Iodine mediated mild and efficient method for the synthesis of tatrahydropyrans via cross-cyclization between epoxides and homoallylic alcohols

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ABSTRACT

Epoxides undergo cyclization with homoallylic alcohols in the presence of iodine under mild conditions to afford the corresponding Iodotetrahydropyran derivatives in excellent yields under mild condition.

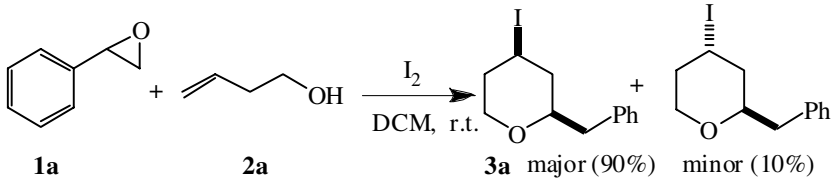
Key words: Epoxides, homoallylic alcohols, tetrahydropyrans, Iodine**.**

INTRODUCTION

Tetrahydro pyrans occupy an important role in the field of organic synthesis because of their biological activity as bio-heterocycles.[1] Aplysiapyranoids A-D, which contain tetrahydropyran core structure were the most active compounds against Moser cells.[2] Especially, 4-Iodotetrahydropyrans are having more synthetic value, since iodine is easy leaving group, they could be easily converted to various functionalities. Despite their potential importance to build up structurally complex molecules, the synthesis of tetrahydropyrans remains underutilized. Although other methods are available[3], its importance prompted us to study extensively on the synthesis of tetrahydropyran derivatives. However, the development of inexpensive, efficient and versatile catalytic methods would be more useful. Epoxides are the most convenient starting materials for the preparation of various compounds because of their ease of formation, wide reactivity and ability to undergo regioselective ring opening reactions contribute largely to their synthetic value.[4] Iodine, which is available as a crystalline solid, is easier to handle and its ability to act as a Lewis acid has been exploited in the cyclization of epoxides and homoallylic alcohols.[5] The use of iodine in cyclization of epoxides and homoallylic alcohols to tetrahydropyrans, however, has not been reported. We set out to investigate this. Herein, we describe iodine mediated cross-cyclization between aryl-substituted epoxides and homoallylic alcohols for the formation of tetrahydropyran derivatives.

MATERIAL AND METHODS

In order to delineate the standard operating conditions, a mixture of styrene oxide and 3-buten-1-ol was treated with iodine in dry methylene chloride. The mixture was stirred at room temperature for 30 min. to achieve the quantitative yield. After work-up, the crude product was purified over silica gel provided the product in 80% yield. By the spectroscopic data the product was confirmed as 3a (Scheme 1).



Scheme 1.

With these encouraged results, the reaction was performed with wide range of epoxides and all were reacted smoothly with 3-buten-1-ol under similar condition to afford the corresponding tetrahydropyran derivatives in good yield ranging from 60-80% (Table 1). In all cases, the reactions proceeded efficiently in good yields at ambient temperature under mild conditions showing the generality of the reaction. The role of Iodine in catalyzing the opening of epoxide ring with alcohol and providing iodide nucleophile.

In summary, we have described a simple and highly efficient protocol for the preparation of 4-Iodotetrahydropyran derivatives through the reaction between epoxides and homoallylic alcohols using iodine. The attractive features of this process are mild reaction conditions, inexpensive reagents, short reaction times and cleaner reactions with good yields, which make it a useful process for the synthesis of iodotetrahydropyrans.General procedure: To a stirred solution of 3-buten-1-ol (0.144 g, 2 mmol) and styrene oxide (0.360 g, 3 mmol) in dry methylene chloride (20 mL) was added iodine (1.012 g, 4 mmol) at room temperature. The mixture was stirred under a nitrogen atmosphere for 2 h. After work-up, the solution was concentrated and the crude mixture was separated by column chromatography over silica gel (ethyl acetate–hexane, 1:9).

RESULTS AND DISCUSSION

Spectral data

Compound 3a

^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.12-7.26 (m, 5H), 4.10-4.21 (m, 1H), 3.79-3.86 (m, 1H), 3.68-3.75 (m, 1H), 3.31-3.47 (m, 2H), 2.58-2.88 (m, 2H), 2.18-2.31 (m, 2H), 1.90-2.00 (m, 1H). IR (neat) ν 3026, 1252, 752 cm^{-1}; ^{13}C NMR ($CDCl_3$, 50 MHz): δ: 135.0, 127.2, 125.1, 73.5, 65.8, 41.1, 39.9, 35.8, 21.9; HRMS: Calcd. for $C_{12}H_{15}IO$ (M^++Na): 325.005. Found: 325.0065.

Compound 3b

^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.14-7.23 (m, 2H), 4.53 (dt, *J* = 3.47 and 7.81 Hz, 1H), 3.77 (dd, J= 3.47 and 11.28 Hz, 1H), 3.59 (dd, *J* = 3.47 and 9.54 Hz), 3.33 (dt, *J* = 2.60, 12.15 and 13.88 Hz), 2.80-2.91 (m, 2H), 2.59 (dd, *J* = 4.34 and 14.75 Hz, 1H), 2.24-2.30 (m, 1H), 1.82-1.97 (m, 2H), 1.35-1.45 (m, 8H), 0.95 (t, *J* = 6.07 Hz, 3H). IR (neat) ν 3027, 1256, 747 cm^{-1}; ^{13}C NMR ($CDCl_3$, 50 MHz): δ: 139.3, 128.1, 127.6, 124.2, 77.7, 64.5, 40.5, 39.1, 35.1, 31.4, 26.8, 25.7, 23.4, 22.6, 14.8; HRMS: Calcd. for $C_{17}H_{25}IO$ (M^++Na): 395.0847. Found: 395.0865.

Compound 3c

^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.16-7.24 (m, 10H), 4.12-4.29 (m, 1H), 3.80-3.99 (m, 3H), 3.34-3.47 (m, 1H), 2.12-2.26 (m, 3H), 1.83-2.01 (m, 1H). IR (neat) ν 3027, 1257, 746 cm^{-1}; ^{13}C NMR ($CDCl_3$, 50 MHz): δ: 142.2, 130.1, 127.8, 125.8, 80.5, 66.3, 54.1, 38.4, 35.7, 23.9, 21.3,; HRMS: Calcd. for $C_{18}H_{19}IO$ (M^++Na): 401.0378. Found: 401.0477.

Compound 3d

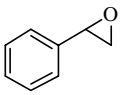
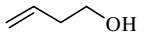
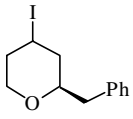
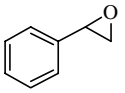
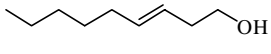
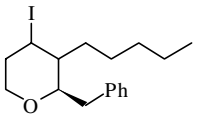
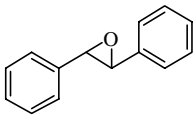
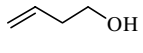
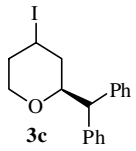
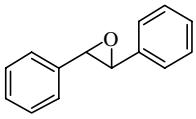
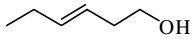
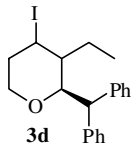
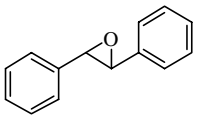
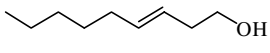
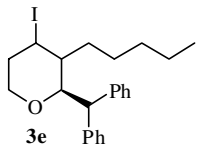
^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.17-7.37 (m, 10H), 4.30-4.35 (m, 1H), 4.24 (d, *J* = 2.26 Hz, 1H), 3.37-3.89 (m, 2H), 3.27-3.31 (m, 1H), 2.37-2.57 (m, 2H), 1.78-1.89 (m, 3H), 0.95 (t, 3H). IR (neat) ν 3026, 1248, 740 cm^{-1}; ^{13}C NMR ($CDCl_3$, 50 MHz): δ: 142.6, 130.4, 127.6, 80.7, 65.6, 50.5, 41.2, 34.8, 22.5, 20.6, 12.1; HRMS: Calcd. for $C_{20}H_{23}IO$ (M^++Na): 429.0691. Found: 429.0700.

Compound 3e

^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.25-7.03 (m, 10H), 4.50 (dt, *J* = 3.67 and 7.34 Hz, 1H), 4.07-3.64 (m, 3H), 3.29 (dt, *J* = 2.93 and 11.75 Hz, 1H), 2.15-2.43 (m, 1H), 1.52-1.95 (m, 2H), 1.10-1.44 (m,

8H), 0.82 (t, *J* = 5.87 Hz, 3H). IR (neat) ν 3029, 1204, 758 cm^{-1}; ^{13}C NMR ($CDCl_3$, 50 MHz): δ: 142.2, 128.1, 126.6, 81.5, 65.4, 50.4, 38.2, 33.9, 31.3, 27.2, 26.3, 22.6, 21.8, 15.5,; HRMS: Calcd. for $C_{23}H_{29}IO$ (M^++Na): 471.1161. Found: 471.1171.

Table 1: Iodine mediated cyclization of epoxides with homoallylic alcohols

Entry	Epoxide	Alcohol	Products[a]	Yield(%)[b]
1	 **1a**	 **2a**	 **3a**	80
2	 **1a**	 **2b**	 **3b**	68
3	 **1b**	 **2a**	 **3c**	65
4	 **1b**	 **2c**	 **3d**	65
5	 **1b**	 **2b**	 **3e**	60

a) All the products were characterized by ^1H NMR and mass spectroscopy

b) Yields are isolated after column chromatography

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