One Pot Green Synthesis of N- substituted Succinimide

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Abstract

Sequential one pot method for the synthesis of 1-(4-substitutedphenyl)pyrrolidine-2,5-dione has been described. Series of five member cyclic N-substituted succinimides were synthesized using succinic anhydride and various aromatic as well as aliphatic amines as precursors using cheap and readily available reagents zinc and acetic acid.

Keyword:
Succinic anhydride,1-(4-substitutedphenyl)pyrrolidine-2,5-dione and N-substituted succinimides.

INTRODUCTION

It is the challenges work in organic chemistry to develop general and efficient synthetic green methods for widely used organic compounds from readily available reagent. Among the organic compounds five member cyclic N-aryl imides have attracted the attention of many researchers, as these imides have found numerous applications in antifungal agent[1], biology[1-6], herbicides [7], pesticides [7], material science[8,9], pharmacology[18], synthetic[10-21] and polymer chemistry[22,23]. Large numbers of biologically active natural products are also synthesized from N-substitued succinimides[18-21]. N-substitued succinimides are also used for the synthesis of different heterocyclic compounds.

Numbers of synthetic methods for N-aryl succinimides are available in literature [24-33]. Among these methods many are two steps, first step used for dehydrative condensation of an anhydride and an amine at high temperature yield succianilic acid [4], where second step used for cyclization of succianilic acids to N-substituted succinimides by using various reagents. The of choice reagents in these methods are (i) Ac_2O/NaOAc[31],(ii)Et_3N/Ac_2O/acetone or ethyl methyl ketone[30], (iii) DMS/Na_2CO_3/TBAB[22], (iv) cyanuric chloride/Et_3N [25].

However, each of these routes has its own synthetic limitations when applied to range of derivatives, such as (a) use excess of acetic anhydride (b) use of hazardous reagent (c) low yield and (d) tedious workup and purification process. Therefore, an efficient synthesis of functionalized imide derivatives is still a challenging endeavor.

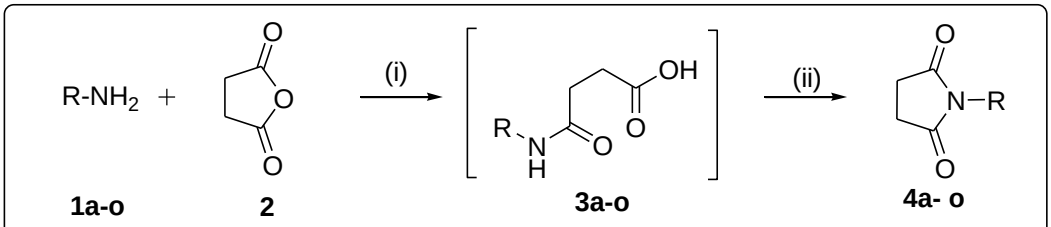
We herein describe an efficient green, approach towards sequential one pot synthesis of (1-(4-substitutedphenyl)pyrrolidine-2,5-dione) by using very common table top reagent zinc and solvent acetic acid, with easy workup and high yield (Table 1).

RESULT AND DISCUSSIONS

In previous work we have reported one pot synthesis of imides by using acetic acid in presence of sulfuric acid[34, 35]. Acetic acid is considered environmentally friendly solvent but sulfuric acid even though readily available, it is corrosive and contains sulfur. Therefore we thought to use another reagent

to substitute sulfuric acid. As we came across one green reaction [36] where zinc is used for acetylation of amine. We thought to replace sulfuric acid by Zn.

We prepared N-aryl succianilic acid (**3a-o**) in acetic acid. Succinic anhydride was dissolved in acetic acid and reacted with substituted aromatic amines and aliphatic amines to afford the corresponding succianilic acids (**3a-o**). Zinc powder was added to the reaction mixture containing succianilic acid (**3a-o**), temperature increases to 55° C and maintain it further for 1.5 hour. On aqueous workup furnished the sodium bicarbonate insoluble solid turned out to be imides (4**a-o**) in high yield (Table 1; Scheme-I). The imides were characterized by IR, NMR and Mass spectroscopy.



Reagents and Reaction Condition: (i) AcOH, rt, 10 min. (iv) Zn, 60°C 1.5 h

Scheme-1

The present reaction offers a highly efficient and cost effective method for synthesis of N-aryl succinimide **(4a-o).** IR spectra of imides (**4a-o**) displays 1695-1720 cm^{-1} atributed to imide carbonyls and absence of signal for hydroxyl group in arylamic acid (**3a-o**).

In summary we have demonstrated an economical and practical one pot method for the synthesis of a wide range of N-substitited succinimide derivatives by using cheap and readily available reagents under mild condition. In view of its operational simplicity, simple purification procedure and high efficiency, the procedure is expected to have broad utility, especially the synthesis of N-Aryl five member imide for future synthetic and biological application.

Table-1.4: Physical Constants for *N*-Substituted succinamide (4a-o)

	R	mp.°C (lit.)
4a	C_6H_5	155 (156)[29]
4b	4-MeO C_6H_4	144
4c	4-MeC_6H_4	154 (154.8)[29]
4d	2-MeC_6H_4	92
4e	4-BrC_6H_4	172
4f	4-ClC_6H_4	163 (163.1)[29]
4g	3-ClC_6H_4	108
4h	3-Cl,6-MeC_6H_3	146
4i	4-Br,5-ClC_6H_3	152
4j	3-$O_2NC_6H_4$	170
4k	4-$O_2NC_6H_4$	208 (209.9)[29]
4l	2-$O_2NC_6H_4$	150
4m	$C_6H_4CH_2$	102 (98-99)[29]
4n	*n*-C_4H_9	Colorless oil (Colorless oil)[29]
4o	$HOCH_2CH_2$	Colorless oil

EXPERIMENTAL

Melting points were determined on Gallenkamp apparatus Mod. MFB 595 using one end open capillaries and are uncorrected. ^{1}HNMR spectra were recorded in $CDCl_3$ on VarianXL-300 Spectrometer (300 $MH_{Z)}$. Chemical shift were recorded in ppm using tetramethylsilaneas a internal standard. Infrared spectra were recorded on Shimadzu FTIR-408 instrument in potassium bromide pellets.

General Procedure: N-Substituted Succinimide(4a-o)

Amines (0.040 mole) were dissolved in acetic acid (35mL). Succinic anhydride (0.044mole) was added at once with stirring and it was stirred vigorously for another 10 minute at room temperature. To this reaction mixture zinc (2 mole) was added at once. The temperature increases by 55^{o}C. The reaction mixture was stirred further for 1.5 hour to same temperature and later allowed to cool to room temperature. It was filtered to remove unreacted zinc. The filtrate was poured onto crushed ice (150gm). The solid separated was filtered and wash with water. The solid was transferred to the aqueous solution of sodium bicarbonate and stirred for 10 minute to remove succianilic acid if present. Then filtered and washed with water.

All compounds were purified by recrystalization in ethyl alcohol to prepare analytical samples.

Spectral Data

N-Phenylsuccinimide (4a): Yield 82 %, mp 155 °C, IR (cm^{-1}): 1712, 1498, 1186, 815, 673.^{1}H NMR (300 MHz, $CDCl_3$): 2.86 (4H, s, 2 X CH_2), 7.25 (2H, d, J= 8.7 Hz, ArH), 7.40-7.50 (3H, m, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): 28.7, 30.9, 118.8, 122.8, 128.6, 139.2, 170.0, 173.7. LC-MS (M+1): 176.4.

N-(4-Methoxyphenyl)succinimide (4b): Yield 85 %, mp 144 °C, IR (cm^{-1}): 2953, 1710, 1603, 830, 685. ^{1}H NMR (300 MHz, $CDCl_3$): 2.88(4H, s, 2 X CH_2), 3.82 (3H, s, OCH_3), 6.97 (2H, d, J=8.7 Hz, ArH), 7.19 (2H, d, J=8.7 Hz, ArH). LC-MS (M+1):

N-(4-Methylphenyl)succinimide (4c): Yield 83 %, mp 154°C, IR (cm^{-1}): 2932, 1702, 1516, 1179, 828, 668. ^{1}H NMR (300 MHz, $CDCl_3$): 2.38 (3H, s, CH_3), 2.87 (4H, s, 2 X CH_2), 7.15 (2H, d, J=8.1 Hz, ArH), 7.28 (2H, d, J=8.1 Hz, ArH). LC-MS (M+1): 190.4.

N-(2-Methylphenyl)succinimide (4d): Yield 87 %, mp 92°C, IR (cm^{-1}): 1703, 1494, 1190, 767, 661. ^{1}H NMR (300 MHz, $CDCl_3$): 2.15 (3H, s, CH_3), 2.92 (4H, s, 2 X CH_2), 7.08 (1H, d, J=7.2 Hz, ArH), 7.26-7.35 (3H, m, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ 17.53, 28.43, 126.81, 127.81, 129.39, 130.94, 131.01, 135.44, 176.07. LC-MS (M+1): 190.6.

N-(4-Bromophenyl)succinimide (4e): Yield 85 %, mp 172 °C, IR (cm^{-1}): 1700, 1486, 1188, 824, 672. ^{1}H NMR (300 MHz, $CDCl_3$): 2.90 (4H, s, 2 X CH_2), 7.20 (2H, d, J=8.7 Hz, ArH), 7.61 (2H, d, J=8.7 Hz, ArH). LC-MS (M+1): 256.5.

N-(4-Chlorophenyl)succinimide (4f): Yield 82 %, mp 163 °C, IR (cm^{-1}): 1710, 1491, 1166, 833, 665. ^{1}H NMR (300 MHz, $CDCl_3$): 2.90 (4H, s, 2 X CH_2), 2.89 (4H, s, 2 X CH_2), 7.25 (2H, d, J=8.7 Hz, ArH), 7.45 (2H, d, J=8.7 Hz, ArH). LC-MS (M+1): 210.2.

N-(3-Chlorophenyl)succinimide (4g): Yield 80 %, mp 108°C, IR (cm^{-1}): 1708, 1583, 1186, 819, 690. ^{1}H NMR (300 MHz, $CDCl_3$): 2.92 (4H, s, 2 X CH_2), 7.37-7.45 (4H, m, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ 28.67, 124.65, 126.72, 128.83, 130.13, 132.91, 134.68, 175.76. LC-MS (M+1): 222.5.

N-(2-Chloro-6-methylphenyl)succinimide (4h): Yield 79 %, mp 146°C, IR (cm^{-1}): 2995, 1708, 1465, 1180, 777, 676, ^{1}H NMR (300 MHz, $CDCl_3$): 2.17 (3H, s, CH_3), 2.95 (4H, s, 2 X CH_2), 7.21-7.38 (3H, m, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ 18.00, 28.60, 127.58, 128.98, 129.24, 130.37, 132.37, 138.41, 175.20. LC-MS (M+1): 224.1

N-(4-Bromo-3-chlorophenyl)succinimide (4i): Yield 80 %, mp 152 °C, IR (cm^{-1}): 1704, 1178, 829,661. ^{1}H NMR (300 MHz, $CDCl_3$): 2.89 (4H, s, 2 X CH_2), 7.18-7.28 (2H, m, ArH), 7.40 (1H, dd, J= 1.8 & 8.4 Hz, ArH). LC-MS (M+1): 289.1.

N-(3-Nitrophenyl)succinimide (4j): Yield 85 %, mp170 °C, IR (cm^{-1}): 1710, 1529, 1377, 1353, 817, 682. ^{1}H NMR (300 MHz, $CDCl_3$): 2.95 (4H, s, 2 X CH_2), 7.63-8.26 (4H, m, ArH), ^{13}C NMR (100 MHz, $CDCl_3$): δ 28.35, 121.61, 123.21, 129.93, 132.22, 132.87, 148.43, 175. 35. LC-MS (M+1): 221.2.

N-(4-Nitrophenyl)succinimide (4k): Yield 86 %, mp 208°C, IR (cm^{-1}): 1703, 1629, 1503, 1332, 840, 630. ^{1}H NMR (300 MHz, $CDCl_3$): 4.38 (4H, s, 2 X CH_2), 6.62 (2H, d, J=9 Hz, ArH), 8.07 (2H, d, J=9Hz, ArH). LC-MS (M+1): 221.0

N-(2-Nitrophenyl)succinimide (4l): Yield 88 %, mp 150°C, IR (cm^{-1}): 1728, 1716, 1525, 1386, 1357, 1176, 707. ^{1}H NMR (300 MHz, $CDCl_3$): 2.93 (4H, t, 2 X CH_2), 7.30 (1H, d, J=8 Hz, ArH), 7.50 (1H, dd, J=7.8 &8.1 Hz, ArH), 7.75 (1H, dd, J=8.1 & 7.8 Hz, ArH), 8.15 (1H, d, J = 8 Hz, ArH). LC-MS (M+1): 221.2.

N-Benzylsuccinimide (4m): Yield 86 %, mp 102 °C, IR (cm^{-1}): 2945, 2923, 1770, 1691, 821. ^{1}H NMR (300 MHz, $CDCl_3$): 2.64 (2H, s, 2 X CH_2), 4.61 (2H, s, CH_2), 7.26-7.34 (5H, m, ArH). ^{13}C NMR (100 MHz, $CDCl_3$): δ 28.1, 42.3, 127.9, 128.5, 128.8, 135.7, 176.8. LC-MS (M+1): 190.1.

N-Butylsuccinimide (4n): Yield 83 %, Thick oil, IR (cm^{-1}): 3026, 2660, 2933, 1772, 1704, 1693. ^{1}H NMR (300 MHz, $CDCl_3$): 0.87 (3H, t, J=7.2 Hz., CH_3), 1.20-1.30 (2H, m, CH_2), 1.46-1.55 (2H, m, CH_2), 2.65 (4H, s, 2 X CH_2), 3.45(2H, t, J=7.6 Hz., CH_2). ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.4, 19.9, 28.0, 29.6, 38.4, 177.2. LC-MS (M+1): 156.1.

N-(1-Hydroxyethyl)succinimide (4o): Yield 86 %, Thick Oil, IR (cm^{-1}): 3445, 2960, 1774, 1735, 1701. ^{1}H NMR (300 MHz, $CDCl_3$): 2.06 (1H, s,OH), 2.73 (4H, s, 2 X CH_2), 3.78 (2H, t, J= 5.2 Hz., CH_2), 4.24 (2H, t, J= 5.2 Hz., CH_2). ^{13}C NMR (100 MHz, $CDCl_3$): δ 20.37, 27.79, 37.49, 60.50, 170.57, 176.88. LC-MS (M+1): 144.2.

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