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New synthetic methodology for construction of the 3,4-dihydroquinolin-2-one skeleton

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Abstract: We hereby report a new method for preparation of 3,4-dihydroquinolin-2(2*H*)-one starting from the methyl 2-(2-carboxyethyl)benzoic acid. The acid functionality, adjacent to the methylene, was regiospecifically converted to the desired methyl ester and the remaining acid functionality was transferred into acyl azide. Curtius rearrangement of acyl azide followed by trapping with aniline and alcohols provided the corresponding urea and urethane derivatives. Hydrolysis of methyl ester groups gave the acids. Ring closure in the presence of thionyl chloride resulted in the formation of the 3,4-dihydroquinolin-2(2*H*)-one skeleton.

Key words: Quinolinone, dihydroquinolinone, acyl azide, Curtius rearrangement

1. Introduction

The 3,4-dihydroquinolin-2-one scaffold is a crucial element in a number of pharmacologically and biologically active compounds. Many pharmaceutical agents such as carteolol (**1**) (a beta-adrenergic blocking agent with intrinsic sympathetic activity used in the treatment of glaucoma and ocular hypertension),[1] cilostazol (**2**) (used in the treatment of peripheral vascular disease),[2] NMDA (*N*-methyl-D-aspartate) antagonist (**3**),[3] HIV reverse transcriptase inhibitor (**4**),[4] and meloscine (**5**), a representative of the *melodinus* alkaloids,[5] contain a dihydroquinolinone ring structure (Figure 1).

In view of the various biological activities of compounds having the dihydroquinolinone motif, various synthetic methods have been developed for the synthesis of dihydroquinolin-2-one and its derivatives. These methods include Friedel–Crafts cyclization,[6] tandem reaction combining radical and ionic processes,[7] manganese(III)-mediated intramolecular cyclization,[8] condensation reactions of aryl aldehydes with *o*-aminoacetophenone in the presence of *L*-proline catalyst,[9] rhodium catalysis,[10] Heck reduction–cyclization reaction,[11] and others.[12]

In this paper, we describe a novel route for the synthesis of the 3,4-dihydroquinolin-2-one skeleton based upon Curtius rearrangement of the acyl azide derived from 2-(2-carboxyethyl)benzoic acid (**8**).

2. Experimental

General: Infrared spectra were obtained from a solution ($CHCl_3$) in 0.1 mm cells or KBr pellets on an FT-IR Bruker Vertex 70 instrument. The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker-Biospin (DPX-400)

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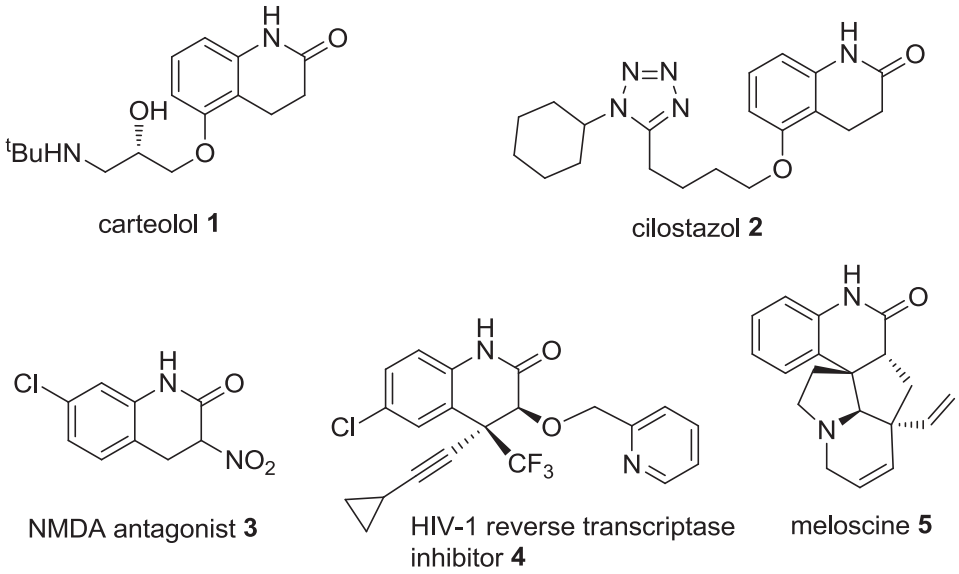


Figure 1. Examples of 3,4-dihydroquinolin-2-one skeleton-containing natural and unnatural products.

instrument. Apparent splitting is given in all cases. Column chromatography was performed on silica gel (60-mesh, Merck); TLC was carried out on Merck 0.2 mm silica gel 60 F_{254} analytical aluminum plates.

2-(3-Methoxy-3-oxopropyl)benzoic acid (9): 2-(2-carboxyethyl)benzoic acid (**8**) (4.98 g, 25.6 mmol) was dissolved in methanol (100 mL), concentrated sulfuric acid (2.5 mL) was added, and the solution was stirred at room temperature for 30 min. The solution was concentrated at 30 °C to about 1/10 of the solution. The residue was dissolved in water (60 mL), and 1 M NaOH (60 mL) was added during stirring. The pH was brought to 8 by saturated $NaHCO_3$ and more 1 M NaOH. The aqueous solution was washed with diethyl ether (2 × 100 mL) and the ether phases were discarded. The aqueous phase was acidified with concentrated HCl to pH 1–2 and the acidic product extracted 4 times with diethyl ether. The combined organic layers were dried over Na_2SO_4 and the solvents removed by a rotary evaporator at 30 °C to give **9** (5.04 g, 95%) as a colorless solid, mp 78–79 °C (Lit. mp 80–82 °C).[1] ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (dd, J = 7.9, 1.4 Hz, 1H, H-6), 7.43 (dt, J = 7.5, 1.4 Hz, 1H, H-4), 7.30–7.20 (m, 2H), 3.60 (s, 3H, OCH_3), 3.28 (t, J = 7.6 Hz, 2H, H-2'), 2.65 (t, J = 7.6 Hz, 2H, H-1'). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.7, 171.6, 142.4, 132.2, 130.9, 130.4, 127.1, 125.6, 50.6, 34.5, 28.9.

Methyl 3-(2-(chlorocarbonyl)phenyl)propanoate (10): To a stirred suspension of half-ester **9** (0.96 g, 4.61 mmol) in CH_2Cl_2 (50 mL) was added oxalyl chloride (0.44 mL, 5.07 mmol) and DMF (2 drops) as catalyst. The resulting solution was stirred at room temperature for 1 h. After completion of the reaction, the solvent was evaporated to give **10**[2] (0.97 g, 93%) as a viscous oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (d, J = 8.0 Hz, 1H, H-3), 7.47 (t, J = 7.5 Hz, 1H, H-4), 7.31 (t, J = 7.7 Hz, 1H, H-5), 7.27 (d, J = 7.7 Hz, 1H, H-6), 3.57 (s, 3H, OCH_3), 3.13 (t, J = 7.6 Hz, 2H, H-3'), 2.54 (t, J = 7.6 Hz, 2H, H-2'); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.9, 167.8, 143.3, 134.5, 134.1, 132.3, 131.4, 127.1, 51.7, 34.8, 29.7. IR (ATR, cm^{-1}) 2952, 1770, 1736, 1437, 1188, 868, 650.

Methyl 3-(2-(azidocarbonyl)phenyl)propanoate (11): To a solution of acyl chloride **10** (0.90 g, 3.97 mmol) in acetone (25 mL) was added a solution of NaN_3 (0.52 g, 7.94 mmol) in H_2O (10 mL) dropwise at 0 °C and the mixture was stirred at 0 °C for 1 h. After the addition of H_2O (25 mL) the mixture was

extracted with EtOAc (3 × 25 mL), and the combined extracts were washed with sat. $NaHCO_3$ and H_2O, and dried ($MgSO_4$). After concentration of the solvent, acyl azide **11** (0.82 g, 89%), unstable at room temperature, was obtained as a colorless oil, which was used for the next step without purification. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, J = 7.6 Hz, 1H, H-6), 7.42 (t, J = 7.3 Hz, 1H, H-4), 7.30–7.10 (m, 2H), 3.58 (s, 3H, OCH_3), 3.23 (t, J = 7.8 Hz, 2H, 2'), 2.59 (t, J = 7.8 Hz, 2H, 1'); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.4, 173.1, 143.6, 133.7, 131.7, 131.3, 129.1, 126.7, 51.6, 35.3, 29.9; IR (ATR, cm^{-1}) 2952, 2277, 2133, 1736, 1689, 1436, 1224, 1175, 976.

Methyl 3-(2-isocyanatophenyl)propanoate (12): Acyl azide **11** (0.5 g, 2.14 mmol) was dissolved in anhydrous benzene (50 mL) and the mixture was refluxed for 1 h. After completion of the reaction, the reaction mixture was concentrated under reduced pressure to give the isocyanate **12** as a colorless oil, which was directly used for the next step without further purification; yield: 0.37 g (84%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.15–6.95 (m, 4H), 3.58 (s, 3H, OCH_3), 2.88 (t, J = 7.6 Hz, 2H, H-2'), 2.54 (t, J = 7.6 Hz, 2H, H-3'); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.0, 134.6, 132.1, 130.0, 128.4, 127.7, 126.1, 125.0, 51.7, 34.1, 27.4; IR (ATR, cm^{-1}) 2952, 2268, 1736, 1510, 1158, 754.

Methyl 3-{2-[(anilinocarbonyl)amino]phenyl} propanoate (13a): A solution of aniline (0.34 g, 3.70 mmol) in benzene (5 mL) was added dropwise to a stirred solution of isocyanate 12 (0.69 g, 3.36 mmol) in anhydrous CH_2Cl_2 (50 mL) at room temperature and the mixture was stirred for 12 h. The formed urea **12** was collected by filtration and washed with CH_2Cl_2 (5–10 mL) to give a white solid (0.79 g, 79%), mp 138.5–140 °C from EtOH. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (s, 1H, NH), 7.54 (br d, J = 8.0 Hz, 1H), 7.24 (br d, J = 7.5 Hz, 2H), 7.20–7.05 (m, 5H), 7.00 (dt, J = 7.5 and 1.1 Hz, 1H), 6.93 (t, J = 7.3 Hz, 1H), 3.52 (s, 3H, OCH_3), 2.81 (t, J = 7.1 Hz, 2H, H-3'), 2.56 (t, J = 7.1 Hz, 2H, H-2'); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.6, 154.2, 138.6, 135.9, 133.7, 129.8, 129.0, 127.5, 125.4, 125.2, 123.3, 120.2, 52.0, 34.5, 25.9; IR (ATR, cm^{-1}) 3275, 1739, 1638, 1547, 1451, 1209, 1155, 753; HRMS: m/z $(M+H)^+$ Calcd for $C_{17}H_{19}N_2O_3$: 299.13902; Found: 299.14181; Anal. Calcd for $C_{17}H_{18}N_2O_3$: C, 68.44; H, 6.08; N, 9.39. Found: C, 67.99; H, 5.78; N, 9.62.

General procedure for 13b–c: A solution of acyl azide **11** (2.27 mmol) in alcohol (100 mL) was heated at reflux temperature for 24–48 h with TLC monitoring. After completion of the reaction, the solvent was removed under vacuum. Chromatography of the residue (silica gel, 50 g, EtOAc–hexane, 1:2) afforded **13b–c**.

Methyl 3-{2-[(metoxycarbonyl)amino]phenyl} propanoate (13b): 0.46 g (isolated yield), 86% as a white solid; mp 69–71 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (br s, 1H, NH), 7.71 (br s, 1H, H-3), 7.24 (dt, J = 7.9, 1.7 Hz, 1H, H-4), 7.16 (dd, J = 7.7, 1.6 Hz, 1H, H-6), 7.09 (dt, J = 7.5 and 1.0 Hz, 1H, H-5), 3.80 (s, 3H, OCH_3), 3.67 (s, 3H, OCH_3), 2.90 (t, J = 6.7 Hz, 2H, H-3'), 2.71 (t, J = 6.7 Hz, 2H, H-2'); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.5, 155.0, 135.7, 131.8, 129.6, 127.3, 124.8, 123.5, 52.3, 52.0, 34.9, 25.3; IR (ATR, cm^{-1}) 3290, 1743, 1693, 1527, 1453, 1252, 1151, 754; HRMS: m/z $(M+H)^+$ Calcd for $C_{12}H_{16}NO_4$: 238.10738; Found: 238.10904; HRMS(2): m/z $(M+Na)^+$ Calcd for $C_{12}H_{15}NO_4Na$: 260.08933; Found: 260.09524; Anal. Calcd for $C_{12}H_{15}NO_4$: C, 60.75; H, 6.37; N, 5.90. Found: C, 60.72; H, 6.29; N, 6.11.

Methyl 3-{2-[(*tert*-butoxycarbonyl)amino]phenyl} propanoate (13c): 0.66 g, (isolated yield 82%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (br d, J = 8.0 Hz, 1H), 7.18–7.07 (m, 2H), 7.06 (dd, J = 7.6, 1.6 Hz, 1H), 6.98 (dt, J = 7.5, 1.2 Hz, 1H), 3.60 (s, 3H, OCH_3), 2.82 (t, J = 7.1 Hz, 2H, H-3'),

2.61 (t, J = 7.1 Hz, 2H, H-2'), 1.46 [s, 9H, $OC(CH_3)_3$]; ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.0, 153.7, 136.0, 131.5, 129.3, 127.1, 124.4, 123.4, 80.2, 51.9, 34.6, 28.4, 25.6; IR (ATR, cm^{-1}) 3343, 1720, 1589, 1516, 1447, 1233, 1153, 752; HRMS: m/z $(M+Na)^+$ Calcd for $C_{15}H_{21}NO_4Na$: 302.13628; Found: 302.14348.

General procedure for 15a–c: To a solution of ester **13a–c** (2.41 mmol) in MeOH–H_2O (1:1, 50 mL) was added K_2CO_3 (0.40 g, 2.89 mmol) and the mixture was heated at reflux temperature for 45 min. The mixture was cooled to rt and H_2O was added. To remove the unreacted ester **13a–c**, the aqueous phase was extracted with EtOAc. The aqueous phase was acidified with 1 M HCl and extracted with EtOAc. Evaporation of the solvent gave pure **15a–c**.

3-{2-[(Anilino-carbonyl)amino]phenyl} propanoic acid (15a): Pale yellow solid; 0.62 g (91%); mp 159.5–161.0 °C from EtOAc. ^1H NMR (400 MHz, DMSO-d_6) δ 12.21 (br s, 1H), 9.01 (br s, 1H), 7.97 (br s, 1H), 7.77 (d, J = 8.1 Hz, 1H), 7.47 (d, J = 8.3 Hz, 2H), 7.29 (t, J = 7.9 Hz, 2H), 7.22–7.05 (m, 2H), 7.02–6.88 (m, 2H), 2.84 (t, J = 7.8 Hz, 2H), 2.55 (t, J = 7.8 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 173.8, 152.9, 139.9, 136.8, 131.4, 128.9, 128.8, 126.4, 123.3, 122.6, 121.7, 118.1, 33.6, 25.9; IR (ATR, cm^{-1}) 3283, 3037, 1699, 1639, 1548, 1443, 1236, 748. HRMS: m/z $(M+H)^+$ Calcd for $C_{16}H_{17}N_2O_3$: 285.12337; Found: 285.12822. Anal. Calcd for $C_{16}H_{16}N_2O_3$: C, 67.59; H, 5.67; N, 9.85. Found: C, 66.49; H, 5.31; N, 9.89.

3-{2-[(Methoxycarbonyl)amino]phenyl} propanoic acid (15b): White solid, 0.46 g (96%); mp 158–159 °C from EtOAc. ^1H NMR (400 MHz, DMSO-d_6) δ 12.20 (br s, 1H), 8.93 (br s, 1H), 7.32 (d, J = 7.7 Hz, 1H), 7.25–7.15 (m, 2H), 7.11 (d, J = 7.4 Hz, 1H), 3.64 (s, 3H, OCH_3), 2.80 (t, J = 7.7 Hz, 2H), 2.48 (t, J = 7.7 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 172.8, 153.8, 134.6, 133.6, 127.9, 125.1, 124.3, 123.9, 50.4, 32.6, 24.5; IR (ATR, cm^{-1}) 3290, 2949, 1710, 1692, 1533, 1246, 1067; HRMS: m/z (M-H) Calcd for $C_{11}H_{12}NO_4$: 222.07718; Found: 222.07551. RMS(2): m/z $(M+Na)^+$ Calcd for $C_{11}H_{13}NO_4Na$: 246.07368; Found: 246.07798; Anal. Calcd for $C_{11}H_{13}NO_4$: C, 59.19; H, 5.87; N, 6.27. Found: C, 58.48; H, 5.69; N, 6.55.

3-{2-[(tert-Butoxycarbonyl)amino]phenyl} propanoic acid (15c): White solid, 0.36 g (91%), mp 112.5–114 °C from EtOAc. ^1H NMR (400 MHz, $CDCl_3$) δ 12.00-10.00 (br s, 1H), 7.65 (br s, 1H), 7.25–7.15 (m, 3H), 7.09 (t, J = 7.5 Hz, 1H), 2.93 (t, J = 7.2 Hz, 2H), 2.80–2.65 (m, 2H), 1.53 (s, 9H, $OC(CH_3)_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.6, 154.6, 135.8, 132.0, 129.4, 127.1, 124.9, 124.0, 80.9, 34.4, 28.3, 25.6; IR (ATR, cm^{-1}) 3394, 2983, 1702, 1523, 1458, 1157, 742; HRMS: m/z $(M+H)^+$ Calcd for $C_{14}H_{20}NO_4$: 266.13868; Found: 266.14289; Anal. Calcd for $C_{14}H_{19}NO_4$: C, 63.38; H, 7.22; N, 5.28. Found: C, 63.20; H, 7.19; N, 5.43.

General procedure for 14a–c: To a solution of acid **15a–c** (1.76 mmol) in 50 mL of dry THF was added thionyl chloride (0.26 mL, 3.52 mmol) and the resulting mixture was heated at reflux temperature for 8–12 h. The reaction was checked by TLC. After completion of the reaction, evaporation of the solvent gave a crude product, which was purified by chromatography (silica gel, 50 g, EtOAc-hexane) to afford **14a–c**.

2-Oxo-N-phenyl-3,4-dihydroquinoline-1(2H)-carboxamide (14a): Purification by chromatography (silica gel, 50 g, EtOAc-hexane, 1:2) to afford 14a (0.39 g, 84%) as a white solid, mp 117–119 °C from $CHCl_3$-n-hexane. ^1H NMR (400 MHz, $CDCl_3$) δ 10.82 (br s, 1H), 7.52 (d, J = 7.6 Hz, 2H), 7.40 (d, J = 8.2 Hz, 1H), 7.33–7.00 (m, 6H), 2.84 (t, J = 6.7 Hz, 2H), 2.70 (t, J = 6.7 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.6, 150.7, 137.5, 135.9, 130.2, 129.1, 127.2, 126.8, 125.7, 124.5, 124.2, 120.5, 35.8, 25.0; IR (ATR, cm^{-1}) 3180, 2916, 1717, 1592, 1548, 1445, 1160, 751. HRMS: m/z $(M+H)^+$ Calcd for $C_{16}H_{15}N_2O_2$: 267.11280; Found: 267.11518; HRMS(2): m/z $(M+Na)^+$ Calcd for $C_{16}H_{14}N_2O_2Na$: 289.09475; Found: 289.10048. Anal.

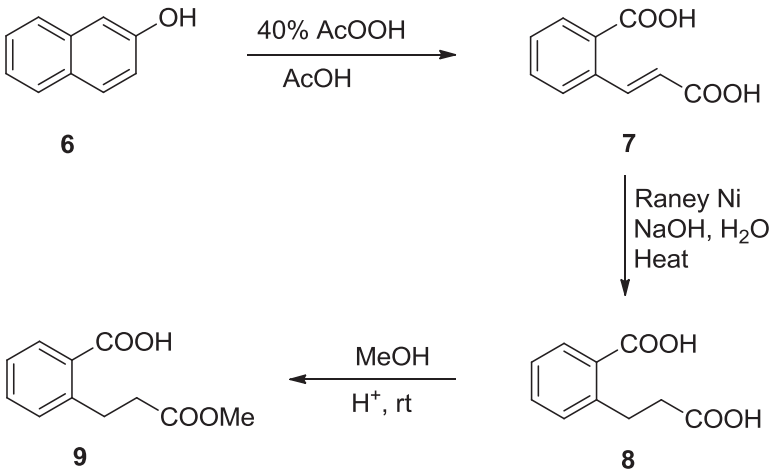
Calcd for $C_{16}H_{14}N_2O_2$: C, 72.16; H, 5.30; N, 10.52. Found: C, 71.68; H, 5.04; N, 10.31.

Methyl 2-oxo-3,4-dihydroquinoline-1(2H)-carboxylate (14b): Purification by chromatography (silica gel, 50 g, EtOAc-hexane, 1:1.5) afforded **14b** (0.35 g, 76%) as a white solid, mp 149–151 °C from $CHCl_3$/n-hexane. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30–7.18 (m, 2H), 7.11 (dt, J = 7.4, 1.0 Hz, 1H), 7.02 (d, J = 8.0 Hz, 1H), 4.01 (s, 3H, OCH_3), 2.97 (t, J = 7.1 Hz, 2H), 2.71 (t, J = 7.1 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.9, 154.0, 136.8, 127.9, 127.4, 127.0, 124.8, 118.6, 54.9, 33.0, 25.5; IR (ATR, cm^{-1}) 3336, 2954, 1701, 1526, 1460, 1237, 758; HRMS: m/z $(M+H)^+$ Calcd for $C_{11}H_{12}NO_3$: 206.08117; Found: 206.08277; HRMS(2): m/z $(M+H)^+$ Calcd for $C_{11}H_{12}NO_3$: 206.08117; Found: 206.08532.

3,4-Dihydroquinolin-2(1H)-one (14c): Purification by chromatography (silica gel, 50 g, EtOAc–hexane, 1:1) afforded 14c (0.17 g, 68%) as a white solid. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.08 (br s, 1H, NH), 7.25-7.05 (m, 2H), 6.90 (t, J = 7.4 Hz, 1H), 6.84 (d, J = 7.9 Hz, 1H), 2.86 (t, J = 7.5 Hz, 2H), 2.44 (t, J = 7.5 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 170.2, 138.2, 127.7, 127.0, 123.5, 121.9, 114.9, 30.4, 24.7.

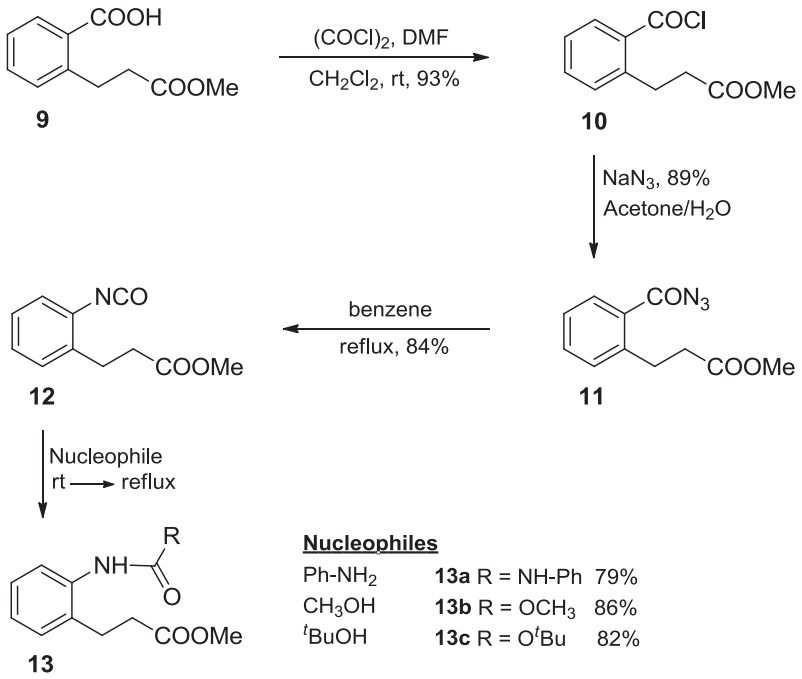
3. Results and discussion

The starting material **9** was synthesized from commercially available β-naphthol (**6**). First **6** was oxidized to o-carboxycinnamic acid (**7**) by reaction with peroxyacetic acid (Scheme 1). Diacid **7** was then reacted with Raney nickel in basic aqueous solution to give the desired acid **8**, as described in the literature.[13] The corresponding starting material **9** was synthesized by dissolving diacid **8** in methanol in the presence of concentrated sulfuric acid at room temperature.[14] Recently, we reported that reactivity of the ester groups connected to benzene or furan rings is different from the reactivity of ester groups connected to alkyl groups.[15] The ester functionality connected to the -CH_2- group is more reactive than the others. Similarly, carboxylic acid functionality adjacent to the methylene group in diacid **8** is more reactive than the aromatic one. Therefore, it was possible to convert one of the acid groups in **8** regiospecifically to the corresponding monoester **9**.



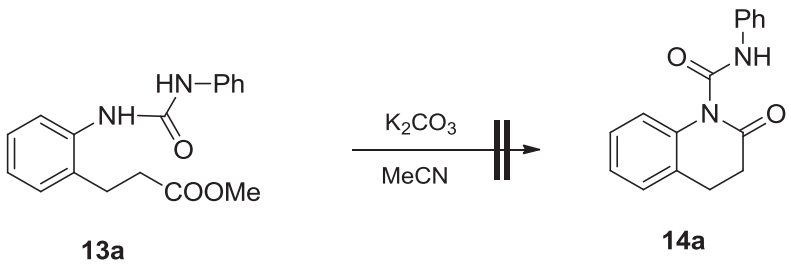
Scheme 1. Synthesis of methyl 2-(3-Methoxy-3-oxopropyl)benzoic acid **9**.

Our plan for the construction of the desired heterocyclic ring system, 3,4-dihydroquinolin-2-one, involved an intramolecular cyclization reaction of the isocyanate **12**, generated by Curtius rearrangement of the corresponding acyl azide **11**.



Scheme 2. Synthesis of urea and urethane derivatives **13a-c** starting from the monoester **9.**

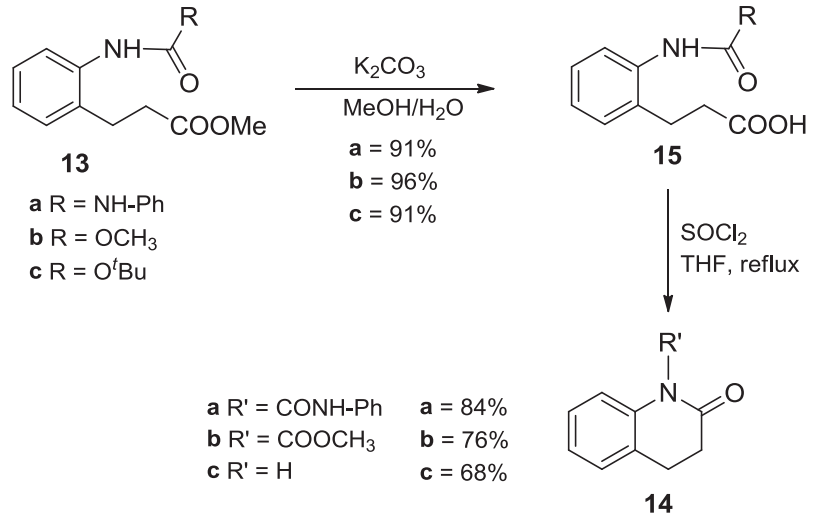
For the synthesis of acyl azide **11**, the monoester **9** was treated with oxalyl chloride in the presence of N,N-dimethylformamide in dichloromethane, followed by addition of a solution of sodium azide in a mixture of acetone and water. After the successful synthesis of acyl azide **11**, we turned our attention to the Curtius rearrangement.[16] Our plan for the construction of the desired heterocyclic ring system involved an intramolecular cyclization reaction of the isocyanate **12**, which can be generated by the Curtius reaction. Thus, acyl azide **11** was allowed to reflux in benzene for 1 h to effect the transformation of the acyl azide functionality to the corresponding isocyanate group in 84% yield. Isocyanate was chosen as a model to explore further reactions. The isocyanate can be trapped by a variety of nucleophiles. Treatment of the resulting isocyanate **12** with aniline in dichloromethane at room temperature for 12 h gave the expected urea derivative **13a** in 79% yield (Scheme 2). When the acyl azide was heated in MeOH at the reflux temperature for 12 h urethane derivative **13b** was isolated in 86% yield. Boc-protected urethane derivative **13c** was obtained in 82% yield after heating for 48 h at reflux temperature of ^{t}BuOH (Scheme 2).



Scheme 3. Base-promoted ring-closure reaction of **13a**.

After successful synthesis of urea and urethanes, we focused our efforts on the base-promoted ring-closure reaction of **13a** already bearing the necessary functionalities (Scheme 3). When urea **13a** was treated with potassium carbonate in acetonitrile or other bases such as NaH, ring formation was not achieved. We assume

the amide anion formed by abstraction of one of the NH protons stabilized by delocalization over the carbonyl group and the benzene ring.



Scheme 4. Synthesis of target 3,4-dihydroquinolin-2-one derivatives **14a–c.**

After the failure of the ring-closure reaction of **13** under basic conditions, we turned our attention to the synthesis of the carboxylic acids **15a–c**. To increase the reactivity of the ester C=O groups in **13**, which is necessary for the cyclization reaction, the ester functionalities in **13** should be converted into acyl chlorides. The ester derivatives **13** were first hydrolyzed to the corresponding acids **15a–c** by treatment with potassium carbonate in a MeOH–H_2O mixture at reflux temperature for 45 min (Scheme 4).

The acids **16–18** were then treated with $SOCl_2$ in THF and the resulting mixture was heated to the reflux temperature. The in situ formed acyl chlorides were cyclized to the desired 3,4-dihydroquinolinone derivatives **14a–c**. The Boc-protected acid **15c** was hydrolyzed to the parent compound, 3,4-dihydroquinolin-2(1*H*)-one (**14c**), by in situ formed HCl.

In conclusion, cyclization of acyl azides is a valuable method for the synthesis of heterocyclic compounds. The present study resulted in the preparation of 3,4-dihydroquinolin-2-one derivative **14c** and its derivatives by application of a new synthetic methodology, where Curtius rearrangement was involved as the key step. This methodology may be applied to the synthesis of various benzene ring substituted 3,4-dihydroquinolin-2-one derivatives.

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