

## Efficient one-pot synthesis of substituted propanamide derivatives by a three-component reaction of 2-oxopropyl benzoate, 1,1,3,3-tetramethylbutyl isocyanide and aromatic carboxylic acids in water

A. Jafari, A. Ramazani\*, M. Rouhani

Department of Chemistry, University of Zanjan, Zanjan, Iran

Received February 11, 2014; Revised March 24, 2014

In the present paper, we have performed the synthesis of fully substituted propane dibenzoate derivatives *via* the reactions of 2-oxopropyl benzoate with 1,1,3,3-tetramethylbutyl isocyanide and various aromatic acids in aqueous media in 83–92% yields at room temperature. This procedure provides several advantages such as operational simplicity, high yield, safety and environment friendly protocol. The resulting products were characterized on the basis of  $^1\text{H}$  NMR,  $^{13}\text{C}$  NMR, IR and mass spectral (in one case) data.

**Keywords:** 2-oxopropyl benzoate, 1,1,3,3-tetramethylbutyl isocyanide, aromatic acids, aqueous media.

### INTRODUCTION

Multicomponent reactions (MCRs) are convergent reactions between three or more reactants in which all or most of the atoms in the starting materials form part of the final product [1]. They are inherently atom-economical processes. Enhanced complex products can be obtained in a one-pot reaction from simple starting materials and thus exemplify many of the desired features of an “ideal synthesis”. Within multicomponent reactions, isocyanide-based multicomponent reactions (IMCRs) have provided a wealth of highly useful sequences for the assembly of compound libraries of particular interest to the pharmaceutical industry. Also products which incorporate amino acid or hydroxyacid motifs through the use of the well known Ugi [2] and Passerini [3] reactions have proven to be very valuable. The replacement of the carbonyl component in these reactions with a cyclic acetal unit could provide access to alternative multicomponent pathways. To date, reactions have been limited to simple isocyanide insertion into one of the C-O bonds [4-7]. However, the application of bis-secondary diamines [8,9], *N,O*-acetals [10] and glycolaldehyde dimer [11-13] in new IMCRs has been reported. In recent years numerous papers on the development and application of isocyanide-based multicomponent reactions provide evidence of the growing interest in this rapidly evolving research area [14-19].

The chemical industry is one of the major

contributors to environmental pollution, owing to the use of hazardous materials, in particular large amounts of volatile, flammable and often toxic organic solvents. With burgeoning interest in green chemistry concept, such toxic organic solvents are being replaced by alternative non-toxic, non-volatile and nonflammable media such as supercritical fluids, ionic liquids and water or the reactions are carried out under solvent free conditions [20]. Water is a safe, readily available, cheap and environmentally benign solvent. Therefore, significant interest has been evinced in the development of organic reactions in water in recent years [21-24].

Multi-component one-pot reactions are always resource effective and environmentally acceptable and, hence, greener as compared to multi-step reactions. They offer significant advantages over conventional linear step syntheses by saving money, energy, raw materials and reducing time, thus resulting in both environmental and economical benefits. Diversity can be achieved for building up libraries by simply varying each component [25-37].

### EXPERIMENTAL

Starting materials were obtained from Merck (Germany) and Fluka (Switzerland) and were used without further purification. The methods used to follow the reactions are TLC and NMR. TLC and NMR indicated that there are no side products. IR spectra were measured on a Jasco 6300 FTIR spectrometer.  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were measured ( $\text{CDCl}_3$  solution) with a BRUKER DRX-400 AVANCE spectrometer at 400.0 and 100.0 MHz, respectively. Mass spectra were recorded on a FINNIGAN-MATT 8430 mass spectrometer operating at an ionization potential of 70 eV. 2-

\* To whom all correspondence should be sent:  
E-mail: aliramazani@gmail.com

Oxopropyl benzoate **3** was prepared based on known procedure [28].

*General Procedure for the Preparation of Compounds (4)*

To a stirred solution of aromatic acid (**2**) (1 mmol) and 2-oxopropyl benzoate (**3**) (1 mmol) in water (7 mL), 1,1,3,3-tetramethylbutyl isocyanide (**1**) (1 mmol) was added dropwise (5 mL) at room temperature over 15 min. The mixture was stirred for 24 h. The solvent was removed under reduced pressure, and the products were obtained without any purification. The characterization data of the compounds are given below:

**2-methyl-3-oxo-3-(2,4,4-trimethylpentan-2-ylamino)propane-1,2-diyl dibenzoate (4a)**. Yellow oil, yield (85%); IR: 710.68, 1274.52, 1451.55, 1601.62, 1686.41, 1727.45, 2953.41, 3447.14  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR( $\text{CDCl}_3$ )  $\delta$ : 0.95 (s, 9H,  $\text{CMe}_3$ ), 1.44 and 1.46 (6 H,  $\text{Me}_2\text{CNH}$ ), 1.61 and 1.78 (AB quartet, 2H,  $^2J_{\text{HH}} = 12$  Hz,  $\text{CH}_2\text{CMe}_3$ ), 1.86 (s, 3H  $\text{CH}_3\text{C}$ ), 4.84 and 5.04 (AB quartet, 2H,  $^2J_{\text{HH}} = 12$  Hz,  $\text{CH}_2\text{CO}_2\text{Ph}$ ), 6.28 (s, 1H, NH), 7.29-8.02 (m, 10 H, CH of arom);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$ : 19.92 ( $\text{CH}_3\text{C}$ ), 28.39 and 28.71 ( $\text{CMe}_2$ ), 31.48 ( $\text{CMe}_3$ ), 31.78 ( $\text{CMe}_3$ ), 55.51 ( $\text{CH}_2\text{CMe}_3$ ), 55.94 ( $\text{Me}_2\text{C}$ ), 66.37 ( $\text{CH}_2\text{CCH}_3$ ), 83.03 ( $\text{CH}_3\text{C}$ ), 128.52, 128.91, 129.65, 129.68, 129.91, 130.15, 130.58, 133.21, 133.46, 133.50 (10 CH and C of arom), 164.66 (COPh), 165.66 (COPh), 168.71 (CONH). MS: m/e (%) 439 ( $\text{M}^+$ , 5), 408 (45), 252 (85), 145 (20), 119 (100), 91 (23), 57 (55).

**3-(benzoyloxy)-2-methyl-1-oxo-1-(2,4,4-trimethylpentan-2-ylamino)propan-2-yl-4-methylbenzoate (4b)**. Yellow oil, yield (87%); IR: 711.21, 1275.00, 1611.51, 1687.84, 1748.08, 2953.22, 3445  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR( $\text{CDCl}_3$ )  $\delta$ : 0.94 (s, 9H,  $\text{CMe}_3$ ), 1.43 and 1.45 (6 H,  $\text{Me}_2\text{CNH}$ ), 1.60 and 1.77 (AB quartet, 2H,  $^2J_{\text{HH}} = 12$  Hz,  $\text{CH}_2\text{CMe}_3$ ), 1.85 (s, 3H  $\text{CH}_3\text{C}$ ), 2.41 (Ph $\text{CH}_3$ ), 4.82 and 5.02 (AB quartet, 2H,  $^2J_{\text{HH}} = 12$  Hz,  $\text{CH}_2\text{CO}_2\text{Ph}$ ), 6.30 (s, 1H, NH), 7.24-8.00 (m, 9 H, CH of arom);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$ : 19.93 ( $\text{CH}_3\text{C}$ ), 21.69 (Ph $\text{CH}_3$ ), 28.39 and 28.71 ( $\text{CMe}_2$ ), 31.48 ( $\text{CMe}_3$ ), 31.75 ( $\text{CMe}_3$ ), 55.45 ( $\text{CH}_2\text{CMe}_3$ ), 55.88 ( $\text{Me}_2\text{C}$ ), 66.38 ( $\text{CH}_2\text{CCH}_3$ ), 82.81 ( $\text{CH}_3\text{C}$ ), 127.38, 128.39, 128.50, 128.98, 129.34, 129.56, 129.63, 129.71, 129.88, 130.01, 133.19, 133.47 (9 CH and 3 C of arom), 168.85 (CONH), 165.63 (COPh), 164.69 (COPh).

**3-(benzoyloxy)-2-methyl-1-oxo-1-(2,4,4-trimethylpentan-2-ylamino)propan-2-yl-3-methylbenzoate (4c)**. Pale Yellow oil, yield (86%); IR: 711.56, 1287.22, 1602.75, 1688.70, 1728.08, 2953.27, 3446.83  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR( $\text{CDCl}_3$ )  $\delta$ : 0.96 (s, 9H,  $\text{CMe}_3$ ), 1.45 and 1.47 (6 H,  $\text{Me}_2\text{CNH}$ ), 1.62

and 1.79 (AB quartet, 2H,  $^2J_{\text{HH}} = 12$  Hz,  $\text{CH}_2\text{CMe}_3$ ), 1.86 (s, 3H  $\text{CH}_3\text{C}$ ), 2.39 (Ph $\text{CH}_3$ ), 4.82 and 5.06 (AB quartet, 2H,  $^2J_{\text{HH}} = 12$  Hz,  $\text{CH}_2\text{CO}_2\text{Ph}$ ), 6.32 (s, 1H, NH), 7.35-8.01 (m, 9 H, CH of arom);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$ : 19.91 ( $\text{CH}_3\text{C}$ ), 21.28 (Ph $\text{CH}_3$ ), 28.45 and 28.71 ( $\text{CMe}_2$ ), 31.50 ( $\text{CMe}_3$ ), 31.77 ( $\text{CMe}_3$ ), 55.49 ( $\text{CH}_2\text{CMe}_3$ ), 55.88 ( $\text{Me}_2\text{C}$ ), 66.31 ( $\text{CH}_2\text{CCH}_3$ ), 83.00 ( $\text{CH}_3\text{C}$ ), 126.65, 127.01, 128.21, 128.39, 128.52, 129.65, 129.71, 130.11, 130.13, 133.21, 134.21, 138.43 (9 CH and 3 C of arom), 168.83 (CONH), 165.65 (COPh), 164.82 (COPh).

**3-(benzoyloxy)-2-methyl-1-oxo-1-(2,4,4-trimethylpentan-2-ylamino)propan-2-yl-3,4-dimethylbenzoate (4d)**. Yellow oil, yield (89%); IR: 759.30, 1278.24, 1603.35, 1687.70, 1733.04, 2923.53, 3445.79  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR( $\text{CDCl}_3$ )  $\delta$ : 0.95 (s, 9H,  $\text{CMe}_3$ ), 1.43 and 1.44 (6 H,  $\text{Me}_2\text{CNH}$ ), 1.62 and 1.79 (AB quartet, 2H,  $^2J_{\text{HH}} = 12$  Hz,  $\text{CH}_2\text{CMe}_3$ ), 1.83 (s, 3H  $\text{CH}_3\text{C}$ ), 2.28 and 2.32 (2  $\text{CH}_3$  of Ph( $\text{CH}_3$ ) $_2$ ), 4.80 and 5.03 (AB quartet, 2H,  $^2J_{\text{HH}} = 12$  Hz,  $\text{CH}_2\text{CO}_2\text{Ph}$ ), 6.30 (s, 1H, NH), 7.07-8.00 (m, 8 H, CH of arom);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$ : 19.86 ( $\text{CH}_3\text{C}$ ), 19.69 and 20.03 (2  $\text{CH}_3$  of Ph( $\text{CH}_3$ ) $_2$ ), 28.44 and 28.70 ( $\text{CMe}_2$ ), 31.57 ( $\text{CMe}_3$ ), 31.78 ( $\text{CMe}_3$ ), 55.40 ( $\text{CH}_2\text{CMe}_3$ ), 55.88 ( $\text{Me}_2\text{C}$ ), 66.38 ( $\text{CH}_2\text{CCH}_3$ ), 82.86 ( $\text{CH}_3\text{C}$ ), 127.08, 127.72, 128.23, 128.32, 128.54, 129.65, 129.84, 130.63, 133.09, 133.22, 136.96, 138.42 (8 CH and 4 C of arom), 168.88 (CONH), 165.65 (COPh), 164.82 (COPh).

**3-(benzoyloxy)-2-methyl-1-oxo-1-(2,4,4-trimethylpentan-2-ylamino)propan-2-yl-4-tert-butylbenzoate (4e)**. Yellow oil, yield (88%); IR: 710.43, 1365.85, 1684.05, 1727.87, 2960.30, 3445.93  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR( $\text{CDCl}_3$ )  $\delta$ : 0.94 (s, 9H,  $\text{CMe}_3$ ), 1.31 (PhC( $\text{CH}_3$ ) $_3$ ), 1.42 and 1.44 (6 H,  $\text{Me}_2\text{CNH}$ ), 1.61 and 1.77 (AB quartet, 2H,  $^2J_{\text{HH}} = 12$  Hz,  $\text{CH}_2\text{CMe}_3$ ), 1.83 (s, 3H  $\text{CH}_3\text{C}$ ), 4.80 and 5.02 (AB quartet, 2H,  $^2J_{\text{HH}} = 12$  Hz,  $\text{CH}_2\text{CO}_2\text{Ph}$ ), 6.32 (s, 1H, NH), 7.34-7.97 (m, 9 H, CH of arom);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$ : 19.93 ( $\text{CH}_3\text{C}$ ), 28.57 and 28.80 ( $\text{CMe}_2$ ), 31.30 (PhC( $\text{CH}_3$ ) $_3$ ), 31.56 ( $\text{CMe}_3$ ), 31.72 ( $\text{CMe}_3$ ), 35.12 (PhC( $\text{CH}_3$ ) $_3$ ), 55.41 ( $\text{CH}_2\text{CMe}_3$ ), 55.82 ( $\text{Me}_2\text{C}$ ), 66.35 ( $\text{CH}_2\text{CCH}_3$ ), 82.83 ( $\text{CH}_3\text{C}$ ), 125.60, 127.34, 128.21, 128.36, 128.51, 129.44, 129.62, 129.69, 130.19, 133.17, 133.95, 157.21 (9 CH and 3 C of arom), 168.84 (CONH), 165.57 (COPh), 164.62 (COPh).

**3-(benzoyloxy)-2-methyl-1-oxo-1-(2,4,4-trimethylpentan-2-ylamino)propan-2-yl-4-chlorobenzoate(4f)**. Yellow oil, yield (92%); IR: 711.56, 1278.22, 1602.75, 1688.70, 1728.08, 2953.27, 3446.83  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR( $\text{CDCl}_3$ )  $\delta$ : 0.92 (s, 9H,  $\text{CMe}_3$ ), 1.42 and 1.44 (6 H,  $\text{Me}_2\text{CNH}$ ), 1.60 and 1.75 (AB quartet, 2H,  $^2J_{\text{HH}} = 12$  Hz,  $\text{CH}_2\text{CMe}_3$ ), 1.83 (s, 3H  $\text{CH}_3\text{C}$ ), 4.80 and 4.98 (AB quartet, 2H,  $^2J_{\text{HH}} = 12$  Hz,  $\text{CH}_2\text{CO}_2\text{Ph}$ ), 6.14 (s, 1H, NH), 7.37-8.11 (m, 9 H, CH

of arom);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ) $\delta$ : 19.84 ( $\text{CH}_3\text{C}$ ), 28.25 and 28.63 ( $\text{CMe}_2$ ), 31.56 ( $\text{CMe}_3$ ), 31.58 ( $\text{CMe}_3$ ), 55.58 ( $\text{CH}_2\text{CMe}_3$ ), 55.83 ( $\text{Me}_2\text{C}$ ), 66.36 ( $\text{CH}_2\text{CCH}_3$ ), 83.19 ( $\text{CH}_3\text{C}$ ), 128.54, 128.76, 128.94, 129.36, 129.61, 129.88, 130.91, 131.48, 131.87, 133.28, 133.46, 139.94 (9 CH and 3 C of arom), 163.82 (COPh), 165.64 (COPh), 168.41 (CONH).

**3-(benzoyloxy)-2-methyl-1-oxo-1-(2,4,4-trimethylpentan-2-ylamino)propan-2-yl-3-chlorobenzoate (4g).** Pale Yellow oil, yield (89%); IR: 711.21, 1271.62, 1601.79, 1686.27, 1730.43, 2953.48, 3450.30  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR( $\text{CDCl}_3$ )  $\delta$ : 0.93 (s, 9H,  $\text{CMe}_3$ ), 1.41 and 1.44 (6 H,  $\text{Me}_2\text{CNH}$ ), 1.60 and 1.75 (AB quartet, 2H,  $^2J_{\text{HH}} = 12$  Hz,  $\text{CH}_2\text{CMe}_3$ ), 1.84 (s, 3H  $\text{CH}_3\text{C}$ ), 4.80 and 5.00 (AB quartet, 2H,  $^2J_{\text{HH}} = 12$  Hz,  $\text{CH}_2\text{CO}_2\text{Ph}$ ), 6.21 (s, 1H, NH), 7.36-8.01 (m, 9 H, CH of arom);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ) $\delta$ : 19.88 ( $\text{CH}_3\text{C}$ ), 28.34 and 28.62 ( $\text{CMe}_2$ ), 31.47 ( $\text{CMe}_3$ ), 31.73 ( $\text{CMe}_3$ ), 55.61 ( $\text{CH}_2\text{CMe}_3$ ), 55.80 ( $\text{Me}_2\text{C}$ ), 66.17 ( $\text{CH}_2\text{CCH}_3$ ), 83.39 ( $\text{CH}_3\text{C}$ ), 127.69, 128.46, 129.52, 129.59, 129.62, 129.87, 129.99, 131.85, 133.32, 133.44, 134.71. (9 CH and 3 C of arom). 163.54 (COPh), 165.62 (COPh), 168.38 (CONH).

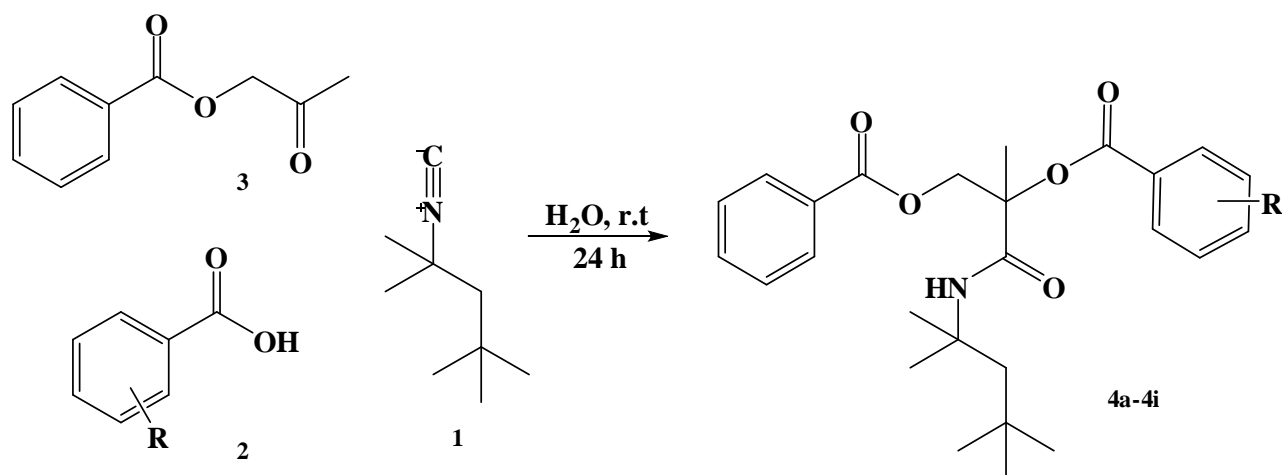
**3-(benzoyloxy)-2-methyl-1-oxo-1-(2,4,4-trimethylpentan-2-ylamino)propan-2-yl-1-naphthoate (4h).** Yellow oil, yield (83%); IR: 710.57, 1192.28, 1510.76, 1685.15, 1731.44, 2925.00, 3439.82  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR( $\text{CDCl}_3$ )  $\delta$ : 0.87 (s, 9H,  $\text{CMe}_3$ ), 1.40 and 1.44 (6 H,  $\text{Me}_2\text{CNH}$ ), 1.55 and 1.76 (AB quartet, 2H,  $^2J_{\text{HH}} = 12$  Hz,  $\text{CH}_2\text{CMe}_3$ ), 1.94 (s, 3H  $\text{CH}_3\text{COCOPh}$ ), 4.88 and 5.23 (AB quartet, 2H,  $^2J_{\text{HH}} = 12$  Hz,  $\text{CH}_2\text{CO}_2\text{Ph}$ ), 6.39 (s, 1H, NH), 7.43-8.07 (m, 9 H, CH of arom);  $^{13}\text{C}$  NMR

( $\text{CDCl}_3$ ) $\delta$ : 20.08 ( $\text{CH}_3\text{C}$ ), 28.49 and 28.64 ( $\text{CMe}_2$ ), 31.38 ( $\text{CMe}_3$ ), 31.50 ( $\text{CMe}_3$ ), 55.47 ( $\text{CH}_2\text{CMe}_3$ ), 55.78 ( $\text{Me}_2\text{C}$ ), 66.14 ( $\text{CH}_2\text{CCH}_3$ ), 83.59 ( $\text{CH}_3\text{C}$ ), 124.47, 1278.78, 125.38, 126.42, 127.92, 128.35, 128.69, 129.24, 129.67, 129.78, 130.95, 133.16, 133.35, 133.52, 133.81 (11 CH and 4 C of arom), 165.64 (COPh), 165.74 (COPh), 168.80 (CONH).

**3-(benzoyloxy)-2-methyl-1-oxo-1-(2,4,4-trimethylpentan-2-ylamino)propan-2-yl-4-fluorobenzoate (4i).** Pale Yellow oil, yield (91%); IR: 711.55, 1278.21, 1601.76, 1687.71, 1728.12, 2953.26, 3446.53  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR( $\text{CDCl}_3$ )  $\delta$ : 0.89 (s, 9H,  $\text{CMe}_3$ ), 1.39 and 1.41 (6 H,  $\text{Me}_2\text{CNH}$ ), 1.57 and 1.71 (AB quartet, 2H,  $^2J_{\text{HH}} = 12$  Hz,  $\text{CH}_2\text{CMe}_3$ ), 1.81 (s, 3H  $\text{CH}_3\text{COCOPh}$ ), 4.79 and 4.95 (AB quartet, 2H,  $^2J_{\text{HH}} = 12$  Hz,  $\text{CH}_2\text{CO}_2\text{Ph}$ ), 6.18 (s, 1H, NH), 7.05-7.99 (m, 9 H, CH of arom);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$ : 19.88 ( $\text{CH}_3\text{C}$ ), 28.26 and 28.62 ( $\text{CMe}_2$ ), 31.52 ( $\text{CMe}_3$ ), 31.70 ( $\text{CMe}_3$ ), 55.52 ( $\text{CH}_2\text{CMe}_3$ ), 55.83 ( $\text{Me}_2\text{C}$ ), 66.36 ( $\text{CH}_2\text{CCH}_3$ ), 82.93 ( $\text{CH}_3\text{C}$ ), 126.31, 126.34, 128.21, 128.43, 129.57, 129.83, 130.11, 132.08, 132.17, 133.29, 138.43 (9 CH and 3 C of arom), 164.65 (COPh), 165.60 (COPh), 168.50 (CONH).

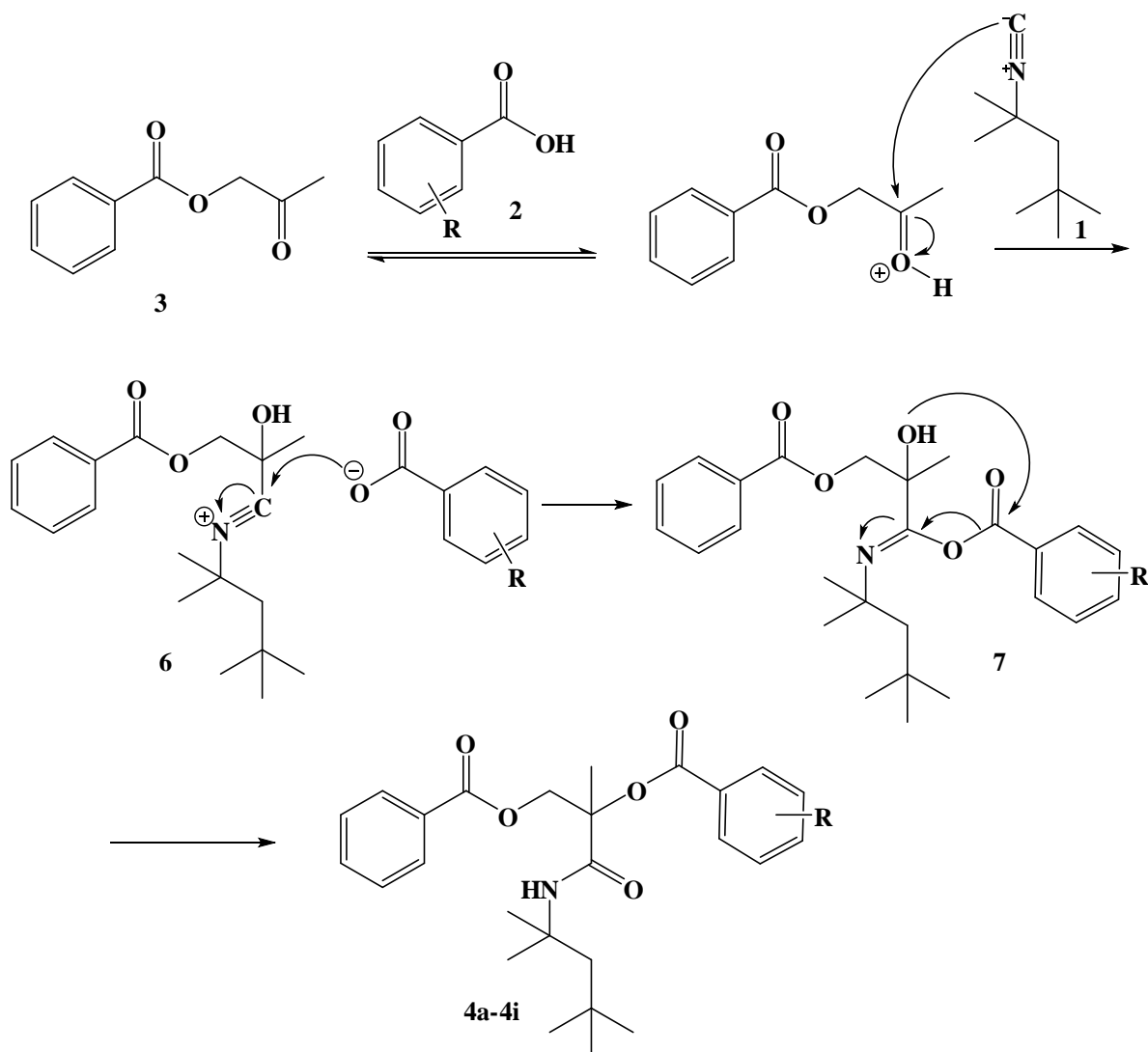
## RESULTS AND DISCUSSION

As part of our program aimed at developing new isocyanide-based multi-component reactions [28-37] herein we describe for the first time an efficient synthetic approach to substituted propanamide derivatives preparation by an isocyanide-based three-component reaction between 2-oxopropyl benzoate (**3**), 1,1,3,3-tetramethylbutyl isocyanide (**1**) and various aromatic acids (**2**) in aqueous media at ambient temperature in excellent yields (Scheme 1).



**4a:** R=H; **4b:** R=4-methyl; **4c:** R= 3-methyl; **4d:** R= 3,4-dimethyl, **4e:** 4-*t*-butyl, **4f:** R= 4-chloro; **4g:** R= 3-chloro; **4h:** 1-naphthyl; **4i:** R= 4-flouro

**Scheme 1:** Three-component synthesis of substituted propanamide derivatives (**4a-i**).



**Scheme 2.** Proposed mechanism for the formation of substituted propanamide derivatives (4a-i).

The structures of the products were deduced from their  $^1\text{H}$  NMR,  $^{13}\text{C}$  NMR, mass and IR spectra. The mass spectra of these compounds displayed molecular ion peaks at the appropriate  $m/z$  values. The  $^1\text{H}$  NMR spectrum of (**4a**) consists of a singlet at  $\delta = 0.95$  ppm for  $\text{CMe}_3$ , two peaks at 1.44 and 1.46 for  $\text{Me}_2\text{CNH}$ , an AB-quartet for  $\text{CH}_2$  of  $\text{CH}_2\text{CMe}_3$  at  $\delta = 1.61$  ppm and 1.78 ppm ( $^2J_{\text{HH}} = 12$  Hz), a singlet at  $\delta = 1.86$  ppm for  $\text{CH}_3\text{C}$ , an AB-quartet for  $\text{CH}_2$  of  $\text{CH}_2\text{CO}_2\text{Ph}$  at  $\delta = 4.84$  ppm and 5.04 ppm ( $^2J_{\text{HH}} = 12$  Hz), a singlet at  $\delta = 6.28$  ppm for NH and a multiplet at  $\delta = 7.29$ -8.02 ppm for aromatic protons of phenyls. The  $^1\text{H}$ -decoupled  $^{13}\text{C}$  NMR spectrum of **4a** is in agreement with the proposed structure. In view of the success of the above-mentioned reaction, we explored the scope of this promising reaction by varying the structure of the carboxylic acid component.

As indicated in Scheme 1, the reaction proceeds very cleanly under mild reaction conditions at room temperature, and no undesirable byproducts are

observed. Owing to the great diversity of substitution patterns, this reaction may be used in the production of combinatorial libraries. A mechanistic rationalization for this reaction is provided in Scheme 2. On the basis of the chemistry of isocyanides, it is reasonable to assume that the first step may involve protonation of 2-oxopropyl benzoate **3** with the acid **2** followed by the nucleophilic addition of the isocyanide **1** to it leading to the nitrilium intermediate **6**. This intermediate may be attacked by a conjugate base of the acid to form the 1:1:1 adduct **7**. This adduct may undergo Mumm rearrangement to afford the isolated sterically congested propanamide derivatives **4** (Scheme 2).

## CONCLUSION

In conclusion, an efficient, clean, and simple method for the preparation of fully substituted propane dibenzoate derivatives using readily available starting materials is reported. The advantage of our work is that the reaction proceeds under neutral

conditions with no bases or catalysts in high yield and no purification of the products. The simplicity of the present procedure makes it an interesting alternative to the complex multistep approaches.

**Acknowledgment:** The authors thank the University of Zanjan for the support and guidance.

## REFERENCES

1. J. Zhu, H. Bienayme, (Eds), Multicomponent Reactions, Wiley-VCH, Weinheim, 2005.
2. I. Ugi, *Angew. Chem. Int. Ed. Engl.* **1**, 8 (1962).
3. M. Passerini, *Gazz. Chim. Ital.*, **61**, 964 (1931).
4. H. Pellissier, A. Meou, G. Gil, *Tetrahedron Lett.*, **27**, 2979 (1986).
5. H. Pellissier, G. Gil, *Tetrahedron Lett.* **29**, 6773 (1988).
6. S. Yoshioka, M. Oshita, M. Tobisui, *Org. Lett.*, **7**, 3697 (2005).
7. M. Tobisu, A. Kitakima, S. Yoshioka, *J. Am. Chem. Soc.*, **129**, 11431 (2007).
8. G.B. Giovenzana, G.C. Tron, S. Di Paola, *Angew. Chem. Int. Ed.*, **45**, 1099 (2006).
9. T. Pirali, G. Callipari, E. Ercolano, *Org. Lett.*, **10**, 4199 (2008).
10. L.J. Diorazio, W.B. Motherwell, T.D. Sheppard, R.W. Waller, *Synlett*, **2281** (2006).
11. Y. B. Kim, E. H. Choi, G. Keum, *Org. Lett.*, **3**, 4149 (2001).
12. L. Banfi, A. Basso, G. Guanti, *Mol. Divers.*, **12**, 187 (2008).
13. R. Mossetti, T. Pirali, G.C. Tron *J. Org. Chem.*, **74**, 4890 (2009).
14. A. Ramazani, F. ZeinaliNasrabadi, Z. Karimi, M. Rouhani, *Bull. Korean Chem. Soc.*, **32**, 2700 (2011).
15. A. Ramazani, A. Rezaei, A. Mahyari, *Helv. Chim. Acta.*, **93**, 2033 (2010).
16. A. Ramazani, A. Tofangchi Mahyari, M. Rouhani, *Tetrahedron Lett.*, **50**, 5625 (2009).
17. A. Ramazani, K. Dastanra, F. ZeinaliNasrabadi, *Turk. J. Chem.*, **36**, 467 (2012).
18. A. Ramazani, F. ZeinaliNasrabadi, B. Abdian, M. Rouhani, *Bull. Korean Chem. Soc.* **33**, 453 (2012).
19. A. Ramazani, M. Rouhani, A. Rezaei, *Helv. Chim. Acta.*, **94**, 282 (2011).
20. C. J. Li, *Chem. Rev.* **93**, 2033 (1993) 2023.
21. N. Azizi, F. Aryanasab, L. Torkiyan, *J. Org. Chem.*, **71**, 3634 (2006).
22. U.K. Roy, S. Roy, *Tetrahedron*, **62**, 678 (2006).
23. J. Safaei-ghomi, A. Kakavand-Qalenoee, M.A. Ghasemzadeh, *Turk. J. Chem.*, **36**, 852 (2012).
24. C. Yildirim, C. Yollacan, F. Aydogan, *Turk. J. Chem.*, **36**, 101 (2012).
25. N.K. Terret, M. Gardener, D.W. Gordon, *Tetrahedron*, **51**, 8135 (1995).
26. L. A. Thompson, J. A. Ellman, *Chem. Rev.*, **96**, 555 (1996).
27. J. A. Ellman, *Acc. Chem. Res.*, **29**, 132 (1996).
28. A. Ramazani, Y. Ahmadi, A. Mashhadi Malekzadeh, A. Rezaei, *Heteroat. Chem.*, **22**, 692 (2011).
29. A. Ramazani, A. Souldozi, *Phosphorus Sulfur Silicon Relat. Elem.*, **184**, 2344 (2009).
30. A. Ramazani, A. Souldozi, *Arkivoc* *xvi*, 235 (2008)
31. A. Ramazani, S. Salmanpour, A. Souldozi, *Phosphorus Sulfur Silicon Relat. Elem.*, **18**, 97 (2010).
32. A. Souldozi, A. Ramazani, K. Slepokura, T. Lis, *Z. Naturforsch.*, **62b**, 835 (2007).
33. A. Ramazani, A. Rezaei, *Org. Lett.* **12**, 2852 (2010).
34. A. Ramazani, Z. Karimi, A. Souldozi, Y. Ahmadi, *Turk. J. Chem.*, **36**, 81 (2012).
35. A. Massoudi, I. Amini, A. Ramazani, F. Zeinali-Nasrabadi, *Turk. J. Chem.*, **36**, 537 (2012).
36. M. Valizadeh-Holagh, A.M.O. Maharramov, M.A.O. Allahverdiyev, *Turk. J. Chem.*, **36**, 179 (2012).
37. M. Valizadeh-Holagh, A. M. O. Maharramov, M. A. O. Allahverdiyev, A. Ramazani, Y. Ahmadi, F. Zeinali-Nasrabadi, A. Souldozi, *Turk. J. Chem.*, **36**, 671 (2012).

## ЕФЕКТИВНА ЕДНОСТАДИЙНА СИНТЕЗА НА ЗАМЕСТЕНИ ПРОПАНАМИДНИ ПРОИЗВОДНИ ЧРЕЗ ТРИКОМПОНЕНТНА РЕАКЦИЯ НА 2-ОКСОПРОПИЛОВ БЕНЗОАТ, 1,1,3,3-ТЕТРАМЕТИЛБУТИЛ ИЗОЦИАНИД И АРОМАТНИ КАРБОКСИЛНИ КИСЕЛИНИ ВЪВ ВОДА

А. Джафари, А. Рамазани \*, М. Рухани

Катедра по химия в Университета на Занджиан, Занджиан, Иран

Получена на 11 февруари, 2014 г.; коригирана на 24 март, 2014 г.

(Резюме)

В настоящата статия, ние извършихме синтеза на напълно заместени пропан дибензоат производни чрез реакции на 2-оксопропил бензоат с 1,1,3,3-тетраметилбутил изоцианид и различни ароматни киселини във водна среда, с добив 83-92% при стайна температура. Тази процедура осигурява няколко предимства, като например оперативна простота, висок добив, безопасност и благоприятен за околната среда протокол. Получените продукти бяха характеризирани на основата на  $^1\text{H}$  NMR,  $^{13}\text{C}$  NMR, IR и мас-спектрални (в един случай) данни.