NRC Research Press

ARTICLE

Direct and facile synthesis of acyl azides from carboxylic acids using the trichloroisocyanuric acid–triphenylphosphine system

Batool Akhlaghinia and Hamed Rouhi-Saadabad

Abstract: A mild, efficient, and practical method for the one-step synthesis of acyl azides from carboxylic acids using a safe and inexpensive mixed reagent, trichloroisocyanuric acid–triphenylphosphine, is described.

Key words: carboxylic acid, acyl azide, trichloroisocyanuric acid, triphenylphosphine, sodium azide.

Résumé : On décrit une méthode de synthèse en une étape des azotures d'acyles à partir d'acides carboxyliques; la méthode est à la fois douce, efficace et pratique et elle implique l'utilisation d'un réactif sécuritaire et pas cher, soit un mélange d'acide trichloroisocyanurique et de triphénylphosphine. [Traduit par la Rédaction]

Mots-clés : acide carboxylique, azoture d'acyle, acide trichloroisocyanurique, triphénylphosphine, sodium.

Introduction

Acyl azides are important intermediates in organic chemistry and especially in pharmaceuticals,[1–4] dyes,[5] and agrochemicals.[6–9] They have been extensively used in the synthesis of amides, nitriles, cycloaddition reactions, peptide bond formation,[10,11] and in heterocyclic chemistry.[12–15] Many single-step and multistep protocols have been developed to convert carboxylic acids to acyl azides.[16–29] Acyl azides are usually prepared from acid derivatives such as acid chlorides, acyl hydrazides,[16] or mixed anhydrides.[26,30–36] Acid chlorides are not always easy to access or store. They are highly sensitive to moisture and require care in handling. Acyl hydrazides require the availability of the hydrazide.[37–44] Mixed anhydrides need to be generated from a carboxylic acid and alkyl chloroformate. There are few reports on the direct conversion of carboxylic acids to acyl azides using acid activators such as $SOCl_2$–dimethylformamide (DMF),[28,45–47] trichloroacetonitrile–triphenylphosphine,[48] bis(2-methoxyethyl)aminosulfur trifluoride,[49] benzotriazole,[50] 2-azido-1,3-dimethylimidazolinium chloride (ADMC),[51] benzotriazole-1-yl-oxy-tris-(dimethylamino)-phosphonium hexafuorophosphate (BOP),[50] and di-*tert*-butyl dicarbonate.[52]

Various methods have been reported in the literature for the direct conversion of aldehydes into acyl azides, which include chromic anhydride–trimethylsilylazide,[53,54] $PhI(OAc)_2$,[55] triazidochlorosilane activated MnO_2,[56,57] and Dess–Martin periodinane.[58,59] Modified methods in which carbamoyl azides were formed directly from aldehydes via acyl azides in a one-pot synthesis have been also reported.[60,61]

In continuation of our recent work on the use of triphenylphosphine (TPP) in the synthesis of alkyl azides, cyanides, thiocyanates, isocyanates, and nitrites,[62–70] and by considering the activity of trichloroisocyanuric acid (TCCA) as an electron deficient and *N*-halo reagent towards TPP, in this paper, we wish to report a more simplified one-step method for the conversion of carboxylic acids to acyl azides.

Results and discussion

Since carboxylic acids are more readily available commercially than acyl azides, herein we propose a more robust, mild, and highly efficient procedure for the direct conversion of carboxylic acids to acyl azides using the triphenylphosphine–trichloroisocyanuric acid–NaN_3 system (Scheme 1).

At first, the reaction of *p*-nitrobenzoic acid was initially performed in the presence of different molar ratios of RCO_2H–TPP–TCCA–NaN_3 at 0 °C to room temperature. The effect of different solvents was also studied (Table 1). Employing the ratio of 1:1:0.3:3 in CH_2Cl_2 at room temperature gave the best results and produced *p*-nitrobenzoyl azide in a quantitative yield after 40 min (Table 1, entry 9). By performing the reaction at reflux, *p*-nitrobenzoyl azide and some byproducts were obtained at a longer reaction time (Table 1, entries 6 and 10). In refluxing CH_3CN and CH_2Cl_2, *p*-nitrobenzoyl azide was converted to *p*-nitrobenzene isocyanate (as a Curtius rearrangement product) by losing N_2.

The conversion of carboxylic acid to corresponding acyl azides exhibits high efficiency. Applying the optimized conditions, different aryl, alkyl, and heteroaryl carboxylic acids on reaction with triphenylphosphine–trichloroisocyanuric acid in the presence of sodium azide undergo smooth conversion to corresponding acyl azides with excellent yields (Table 2). The carboxylic acids were rapidly converted into their corresponding products in a very short reaction time (45–120 min) with 100% conversion.

The mechanism of these transformations is not obvious. A plausible mechanism is depicted in Scheme 2. The initial attack at the halogen in TCCA by triphenylphosphine leads to the halogen–phosphonium salt (**I**). The reaction of **I** with carboxylic acid yields **II** and [1,3,5]triazine-2,4,6-triol (**III**), which is in equilibrium with [1,3,5]triazinane-2,4,6-trione (**IV**; Scheme 2). A rapid reaction of **II** with sodium azide yields triphenylphosphine oxide and the corresponding acyl azide (at room temperature). Nevertheless, at the moment there is no experimental evidence for **I**. Further mechanistic studies require confirming this mechanism.

On the basis of the previously mentioned mechanism, triphenylphosphine plays an important role in this transformation. The reaction of *p*-nitrobenzoic acid with sodium azide was carried out in the absence of triphenylphosphine but after long period of time no benzoyl azide was obtained. It is noteworthy that no evidence for the formation of carboxylic acid chlorides as

Received 21 December 2011. Accepted 25 September 2012.

B. Akhlaghinia and H. Rouhi-Saadabad. Department of Chemistry, Faculty of Sciences, Ferdowsi University of Mashhad, Mashhad, 9177948974, Iran.

Corresponding author: Batool Akhlaghinia (e-mail: akhlaghinia@um.ac.ir).

Can. J. Chem. **91**: 181–185 (2013) dx.doi.org/10.1139/cjc-2011-0493

Scheme 1.

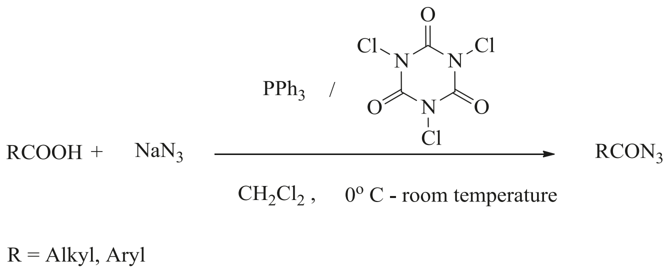


Table 1. The conversion of *p*-nitrobenzoic acid to *p*-nitrobenzoyl azide with a TPP–TCCA–NaN_3 system under different reaction conditions.

Entry	Solvent	Molar ratio RCO_2 H–TPP–TCCA–NaN_3	Time	Conversion (%)	Isolated yield (%)[a]
1	CH_3CN	1:1:1:1	12 h	100	90
2	CH_3CN	1:1:1:1.5	8.5 h	100	92
3	CH_3CN	1:1:1:2	4 h	100	94
4	CH_3CN	1:1:1:2.5	40 min	100	95
5	CH_3CN	1:1:1:3	40 min	100	95
6[b]	CH_3CN	1:1:0.3:3	1 h	100	Trace
7	CH_2Cl_2	1:1:1:3	40 min	100	98
8	CH_2Cl_2	1:1:0.5:3	40 min	100	97
9	CH_2Cl_2	1:1:0.3:3	40 min	100	98
10[b]	CH_2Cl_2	1:1:0.3:3	1 h	100	Trace

[a] Isolated yield of *p*-nitrobenzoyl azide.

[b] The temperature was raised from 0 °C to reflux.

a byproduct of the reaction was observed. The products were obtained in pure form after aqueous workup and purification. As the temperature was retained between 0–5 °C before adding sodium azide, any tendency between **II** and the chloride ion to form acyl chloride can be prohibited.

According to the results in Table 2 and the proposed mechanism in Scheme 2, aromatic carboxylic acids with electron-withdrawing groups require a shorter reaction time compared with aromatic carboxylic acids with electron-donating groups. Electron-withdrawing groups increase the acidity of carboxylic acid, which leads to an easier formation of **II**. Cinnamic acid (pK_a = 4.44) is converted to cinnamoyl azide more slowly than benzoic acid (pK_a = 4.21) and 4-nitro benzoic acid (pK_a = 3.41) (compare entries 1, 2, and 11 in Table 2). By substitution of an electron-releasing group, such as the methoxy group in the para position of phenyl moiety, the acidity of 4-methoxy benzoic acid decreases. Then, 4-methoxy benzoic acid produces the corresponding acyl azide at a longer reaction time compared to benzoic acid (compare entries 1 and 10 in Table 2). Because of steric effects, *o*-chlorobenzoic acid reacts more slowly than the *p*-chlorobenzoic acid with the TPP–TCCA–NaN_3 mixed reagent (Table 2, entries 5, 6). In similar conditions, 3-nitrocinnamoyl azide can be obtained from 3-nitro cinnamic acid in a short reaction time compared to 4-chloro cinnamic acid (Table 2, entries 12, 13).

A ^{13}C nuclear magnetic resonance (NMR) signal at around 170 ppm is assigned to the quaternary carbon of CON_3. In the Fourier transform (FT)-IR spectrum, a strong sharp absorption band at 2150–2129 cm^{-1} and a medium absorption band at 2194–2170 cm^{-1} are assigned to N_3 (asymmetrical) stretching vibration. The symmetric vibration frequency of the azido group appears at 1292–1194 cm^{-1} as a strong band. Also, the carbonyl group shows a strong sharp absorption band at 1705–1670 cm^{-1} and a weak absorption band at 1599–1550 cm^{-1}.

Conclusions

In conclusion, the present method for the preparation of acyl azides is very simple without requiring any drastic experimental conditions. Also, the trichloroisocyanuric acid–triphenylphosphine system is a very mild and efficient general mixed reagent for the conversion of carboxylic acids to the corresponding acyl azides without the formation of any Curtius rearrangement products.

It is important to note that triphenylphosphine–trichloroisocyanuric acid is a safe and inexpensive mixed reagent compared with the recently reported use of hazardous and expensive *N*-methylmorpholine and triphosgene.[56,60]

Experimental

General

The products were purified by column chromatography and characterized by spectroscopic data (IR, ^1H NMR, and ^{13}C NMR). The purity determinations of the products were accomplished by thin-layer chromatography (TLC) on silica gel polygram STL G/UV 254 plates. Melting points were determined with an Electrothermal Type 9100 melting point apparatus. Elemental analyses were made by a Thermo Finning Flash EA1112 CHNO-S analyzer and agreed with the calculated values. The FT-IR spectra were recorded on an Avatar 370 FT-IR Therma Nicolet spectrometer. The NMR spectra were recorded on a Bruker Avance 100 and 400 MHz instrument in $CDCl_3$. The ^1H and ^{13}C NMR chemical shifts (δ) in ppm were downfield from tetramethylsilane ($CDCl_3$: δ_C = 77.0 ppm; residual $CHCl_3$ in $CDCl_3$: δ_H = 7.26 ppm). Caution: Azido compounds may represent an explosion hazard when being concentrated under vacuum or stored neat. A safety shield and appropriate handling procedures are recommended.

Typical procedure for the preparation of *p*-nitrobenzoyl azide

To a solution of trichloroisocyanuric acid (0.0775 g, 0.3 mmol) in dichloromethane (3–5 mL), triphenylphosphine (0.2623 g, 1 mmol) was added at 0–5 °C with stirring. A white suspension was formed to which *p*-nitrobenzoic acid (0.1671 g, 1 mmol) was added and stirring continued for 15 min. NaN_3 (0.1950 g, 3 mmol) was added and the temperature was raised to room temperature. Stirring was continued for 45 min at room temperature. After completion of the reaction (TLC), the mixture was washed with cold distilled water (2 × 10 mL). The organic layer was dried with anhydrous Na_2SO_4, passed through a short silica-gel column using *n*-hexane–ethyl acetate (10:1) as the eluent. *p*-Nitrobenzoyl azide was obtained with 98% yield after removing the solvent under reduced pressure.

Benzoyl azide (Table 2, entry 1)

Oil (lit. report:[71] oil). IR (neat, cm^{-1}) υ: 3067, 2173 (2179),[59] 2129 (2127),[59] 1695 (1682),[59] 1599, 1582, 1450, 786, 695.

4-Nitrobenzoyl azide (Table 2, entry 2)

Solid; mp 64–65 °C (lit. value[71] mp 65 °C). IR (KBr, cm^{-1}) υ: 3108, 3092, 2185 (2180),[59] 2140 (2127),[59] 1727, 1694 (1690),[59] 1600, 1535, 847. ^1H NMR (400 MHz, $CDCl_3$, 25 °C, ppm) δ: 8.34 (d, 2H, *J* = 8.4 Hz), 8.24 (d, 2H, *J* = 8.8 Hz). ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, ppm) δ: 170.9 (170.9 –CON_3),[59] 151.2, 123.8, 135.7, 130.6.

3-Nitrobenzoyl azide (Table 2, entry 3)

Solid; mp 65–67 °C (lit. value[29] mp 67 °C). IR (KBr, cm^{-1}) υ: 3092, 2203, 2154 (2137),[59] 1697 (1700),[59] 1686, 1632, 900, 730, 708. ^1H NMR (400 MHz, $CDCl_3$, 25 °C, ppm) δ: 8.9 (s, 1H), 8.5 (ddd, 1H, *J* = 8.2 Hz, *J* = 1.2 Hz, *J* = 0.8 Hz), 8.39 (dt, 1H, *J* = 8.0 Hz, *J* = 1.2 Hz), 7.72 (t, 1H, *J* = 8.0 Hz). ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, ppm) δ: 170.6 (170.6 –CON_3),[59] 148.4, 134.9, 132.3, 130.0, 128.5, 124.4.

Table 2. The synthesis of acyl azides from carboxylic acids using a triphenylphosphine–trichloroisocyanuric acid–sodium azide system.

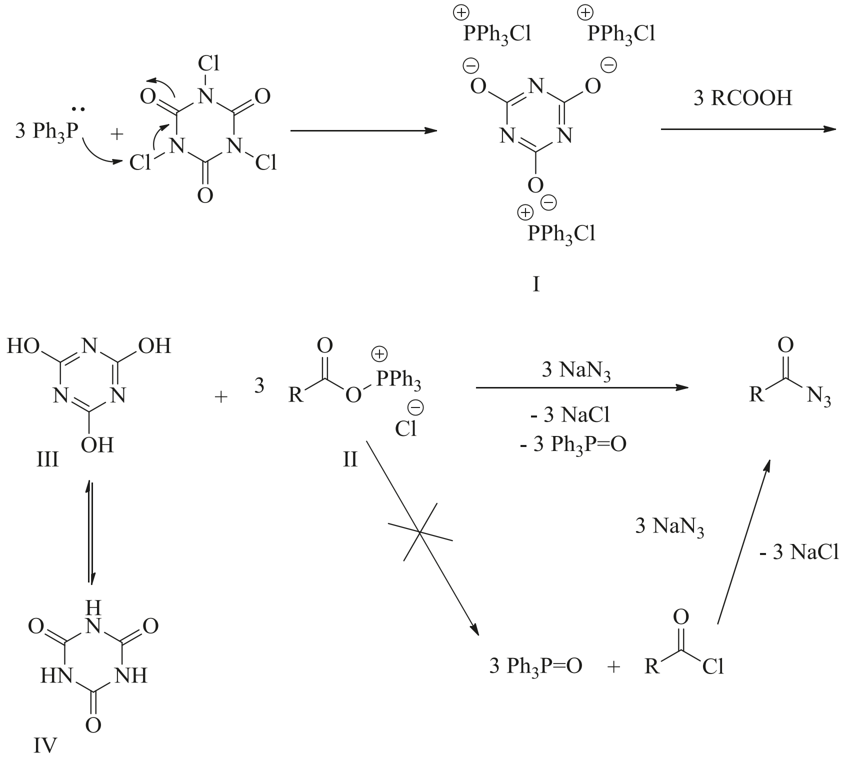
Entry	Carboxylic acid	Acyl azide[a]	Time (min)	Molar ratio[b]	Isolated yield (%)
1	Benzoic acid	Benzoyl azide	60	1:1:0.3:3	97
2	4-Nitrobenzoic acid	4-Nitrobenzoyl azide	40	1:1:0.3:3	98
3	3-Nitrobenzoic acid	3-Nitrobenzoyl azide	50	1:1:0.3:3	95
4	3,4-Dichlorobenzoic acid	3,4-Dichlorobenzoyl azide	120	0.5:1:0.3:3	98
5	4-Chlorobenzoic acid	4-Chlorobenzoyl azide	70	1:1:0.3:3	96
6	2-Chlorobenzoic acid	2-Chlorobenzoyl azide	110	0.5:1:0.3:3	97
7	4-Bromobenzoic acid	4-Bromobenzoyl azide	75	1:1:0.3:3	93
8	4-Methylbenzoic acid	4-Methylbenzoyl azide	70	1:1:0.3:3	95
9	3,5-Dimethylbenzoic acid	3,5-Dimethylbenzoyl azide	85	0.5:1:0.3:3	97
10	4-Methoxybenzoic acid	4-Methoxybenzoyl azide	90	1:1:0.3:3	98
11	Cinnamic acid	Cinnamoyl azide	90	0.5:1:0.3:3	95
12	3-Nitrocinnamic acid	3-Nitrocinnamoyl azide	80	0.5:1:0.3:3	93
13	4-Chlorocinnamic acid	4-Chlorocinnamoyl azide	110	0.5:1:0.3:3	94
14	Phenylethanoic acid	Phenylethanoyl azide	70	0.5:1:0.3:3	95
15	2,2-Diphenylethanoic acid	2,2-Diphenylethanoyl azide	75	0.5:1:0.3:3	96
16	Hexanoic acid	Hexanoyl azide	40	0.5:1:0.3:3	85
17	Oleic acid	Octadec-9(*Z*)-enoyl azide	30	0.5:1:0.3:3	68
18	Stearic acid	Stearoyl azide	40	0.5:1:0.3:3	94
19	Thiophene-3-carboxylic acid	Thiophene-3-carbonyl azide	60	0.5:1:0.3:3	95
20	Pyridine-4-carboxylic acid	Pyridine-4-carbonyl azide	55	0.5:1:0.3:3	93
21	Pyridine-2,6-dicarboxylic acid	Pyridine-2,6-dicarbonyl diazide	60	1:2:0.6:4	95

Note: The products were characterized by ^{1}H nuclear magnetic resonance (NMR), ^{13}C NMR, melting points, and infrared (IR) data.

[a] Identified by comparison data with authentic samples.

[b] Molar ratio: RCO_2H–TPP–TCCA–NaN_3.

Scheme 2.



3,4-Dichlorobenzoyl azide (Table 2, entry 4)

Solid; mp 56–58 °C (lit. value[72] mp 58–59 °C). IR (KBr, cm^{-1}) υ: 3091, 2194, 2152, 1698, 1585, 826, 784. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, ppm) δ: 8.12 (d, 1H, *J* = 1.6 Hz), 7.87 (dd, 1H, *J* = 8.4 Hz, *J* = 1.6 Hz), 7.56 (d, 1H, *J* = 8.4 Hz). ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, ppm) δ: 170.6, 139.1, 133.4, 130.8, 130.4, 128.4. Anal. calcd. for $C_7H_3Cl_2N_3O$ (%): C 38.92, H 1.40, N 19.45; found: C 39.70, H 1.46, N 19.06.

4-Chlorobenzoyl azide (Table 2, entry 5)

Solid; mp 38–41 °C (lit. value[24] mp 39–42 °C). IR (KBr, cm^{-1}) υ: 3088, 2177 (2174),[59] 2134 (2132),[59] 1680 (1680),[59] 1588, 1486, 849.

2-Chlorobenzoyl azide (Table 2, entry 6)

Oil. (lit. report:[58] oil). IR (KBr, cm^{-1}) υ: 3289, 2138, 1682, 1645, 1585, 757.

4-Bromobenzoyl azide (Table 2, entry 7)

Solid; mp 45–47 °C (lit. value[71] mp 47 °C). IR (KBr, cm^{-1}) υ: 3020, 2172, 2132, 1679, 1582, 846. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, ppm) δ: 7.91 (d, 2H, *J* = 8.4 Hz), 7.63 (d, 2H, *J* = 8.4 Hz). ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, ppm) δ: 171.8 (171.8), [49] 132.1, 130.9, 129.8, 129.5.

4-Methylbenzoyl azide (Table 2, entry 8)

Solid; mp 33–35 °C (lit. value[71] mp 35 °C). IR (KBr, cm^{-1}) υ: 3043, 2924, 2868, 2181, 2131(2180, 2150),[58] 1693 (1690),[58] 1608, 832.

3,5-Dimethylbenzoyl azide (Table 2, entry 9)

Solid; mp 29–31 °C. IR (KBr, cm^{-1}) υ: 3050, 2930, 2921, 2905, 2138, 1696, 1607, 885, 650. ^{1}H NMR (100 MHz, $CDCl_3$, 25 °C, ppm) δ: 7.65 (2H), 7.25 (1H), 2.39 (s, 6H).

4-Methoxybenzoyl azide (Table 2, entry 10)

Solid; mp 68–70 °C (lit. value[71] mp 70–71 °C). IR (KBr, cm^{-1}) υ: 3016, 2990, 2186 (2179),[59] 2135 (2127),[59] 1677, 1597, 1509, 849. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, ppm) δ: 8.00 (d, 2H, *J* = 9.2 Hz), 6.96 (d, 2H, *J* = 9.2 Hz), 3.89 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, ppm) δ: 171.7 (171.69 $-CON_3$),[59] 164.6, 131.7 123.2, 113.9, 55.5.

Cinnamoyl azide (Table 2, entry 11)

Solid; mp 81–83 °C (lit. value[24] mp 82–84 °C). IR (KBr, cm^{-1}) υ: 3064, 2150 (2148),[29] 2099 (2103),[29] 1681 (1683),[29] 1632, 1450, 760, 700. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, ppm) δ: 7.78 (d, 1H, *J* = 16.0 Hz), 7.57 (d, 2H, *J* = 7.6 Hz), 7.46 (m, 3H), 6.46 (d, 1H, *J* = 15.6 Hz). ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, ppm) δ: 172.1 (172.0 $-CON_3$),[29] 146.8, 133.8, 131.2, 129.1, 128.6, 119.1. Anal. calcd. for $C_9H_7N_3O$ (%): C 62.42, H 4.07, N 24.27; found: C 63.59, H 4.18, N 24.33.

3-Nitrocinnamoyl azide (Table 2, entry 12)

Solid; mp 118–120 °C (lit. value[29] mp 120 °C). IR (KBr, cm^{-1}) υ: 3080, 2142, 1674, 1626, 1614, 1528, 1159, 910, 860, 747.

4-Chlorocinnamoyl azide (Table 2, entry 13)

Solid; mp 138–140 °C (lit. value[29] mp 140 °C). IR (KBr, cm^{-1}) υ: 3068, 2146 (2150),[73] 1680 (1685),[73] 1629, 1588, 1498, 826. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, ppm) δ: 7.72 (d, 1H, *J* = 16 Hz), 7.49 (d, 2H, *J* = 8.4 Hz), 7.40 (d, 2H, *J* = 8.4 Hz), 6.41 (d, 1H, *J* = 16.0 Hz). ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, ppm) δ: 171.9, 145.2, 137.1, 132.3, 129.7, 129.4, 119.6.

Phenylethanoyl azide (Table 2, entry 14)

Oil (lit. report:[25] oil). IR (neat, cm^{-1}) υ: 3039, 2989, 2267, 2138 (2137),[59] 1713 (1714),[59] 1492, 1454, 719.

2,2-Diphenylethanoyl azide (Table 2, entry 15)

Oil (lit. report:[74] oil). IR (neat, cm^{-1}) υ: 3059, 3031, 2985, 2257, 1778, 1748, 1493, 1451, 742, 698.

Hexanoyl azide (Table 2, entry 16)

Oil (lit. report:[75] oil). IR (neat, cm^{-1}) υ: 2962, 2933, 2869, 2137 (2135),[59] 1697 (1722),[59] 1533, 1232.

Octadec-9(Z)-enoyl azide (Table 2, entry 17)

Oil (lit. report:[49] oil). IR (neat, cm^{-1}) υ: 3006, 2960, 2921, 2853, 2133, 1722, 1644, 1465, 1353.

Stearoyl azide (Table 2, entry 18)

Solid; mp 37–39 °C (lit. value[76] mp 38–40 °C). IR (KBr, cm^{-1}) υ: 2923, 2852, 2272, 2135 (2145),[77] 1716 (1710),[77] 1464, 1192, 722.

Thiophene-3-carbonyl azide (Table 2, entry 19)

Oil (lit. report:[78] oil). IR (neat, cm^{-1}) υ: 3108, 2928, 2201 (2273),[76] 2139 (2139),[76] 1686, 1516, 728. ^{1}H NMR (100 MHz, $CDCl_3$, 25 °C, ppm) δ: 8.2 (dd, 1H), 7.6 (dd, 1H), 7.4 (dd, 1H).

Pyridine-4-carbonyl azide (Table 2, entry 20)

Oil (lit. report:[78] oil). IR (neat, cm^{-1}) υ: 2928, 2853, 2190, 2140, 1705, 1564, 1407, 690.

Pyridine-2,6-dicarbonyl diazide (Table 2, entry 21)

Solid; mp 109–111 °C (lit. value[79] mp 110–111 °C). IR (KBr, cm^{-1}) υ: 3066, 2194, 2142, 1712, 1574. ^{1}H NMR (100 MHz, $CDCl_3$, 25 °C, ppm) δ: 8.4 (d, 2H), 7.9–8.1 (t, 1H). Anal. calcd. for $C_7H_3N_7O_2$ (%): C 38.91, H 1.42, N 45.49; found: C 38.72, H 1.39, N 45.15.

Supplementary data

Supplementary data are available with the article through the journal Web site at http://nrcresearchpress.com/doi/suppl/10.1139/cjc-2011-0493.

Acknowledgments

We gratefully acknowledge the partial support of this study by the Ferdowsi University of Mashhad Research Council (grant No. p/3/19312).

References

(1) Valiaeva, N.; Bartley, D.; Konno, T.; Coward, J. K. *J. Org. Chem.* **2001**, *66* (15), 5146. doi:10.1021/jo010283t.

(2) Chiyoda, T.; Iida, K.; Takatori, K.; Kajiwara, M. *Synlett* **2000**, (10), 1427. doi:10.1055/s-2000-7648.

(3) Kubo, K.; Kohara, Y.; Imamiya, E.; Sugiura, Y.; Inada, Y.; Furukawa, Y.; Nishikawa, K.; Naka, T. *J. Med. Chem.* **1993**, *36* (15), 2182. doi:10.1021/jm00067a016.

(4) Burger, A.; Yost, W. L. *J. Am. Chem. Soc.* **1948**, *70* (6), 2198. doi:10.1021/ja01186a062.

(5) Mallakpour, S.; Nasr-Isfahani, H. *Indian J. Chem.* **2002**, *41B*, 169.

(6) Wang, Y. G.; Wang, Z. Y.; Zhao, X. Y.; Song, X. J. *Youji Huaxue* **2004**, *24*, 1606.

(7) Wang, Y. G.; Wang, Z. Y.; Zhao, X. Y.; Song, X. J. *Chem. Abstr.* **2005**, *143*, 326296c.

(8) Kudis, S.; Baumann, E.; Von Deyn, W.; Langemann, K.; Mayer, G.; Misslitz, U.; Neidlein, U.; Witschel, M.; Westphalen, K. O.; Walter, H.; Kudis, S.; Baumann, E.; Von Deyn, W.; Langemann, K.; Mayer, G.; Misslitz, U.; Neidlein, U.; Witschel, M.; Westphalen, K. O.; Walter, H. *Chem. Abstr.* **2001**, *135*, 5609w.

(9) Crews, A.D., Jr.; Harrington, P. M.; Karp, G. M.; Gill, S. D.; Dieterich, P. *US pat. 5,519,133*, **1996**; (*CA., 125:114718v*).

(10) Jones, J.; *The Chemical Synthesis of Peptides*; Clarendon Press: Oxford, **1991**.

(11) Vommina, V.; Suresh Babu, V. V. S.; Ananda, K.; Vasanthakumar, G. R. J. Chem. Soc. Perkin Trans. *1* **2000**, 4328. doi:10.1039/b006756n.

(12) Brase, S.; Gill, C.; Knepper, K.; Zimmermann, V. *Angew Chem. Int. Ed. (Engl.)* **2005**, *44* (33), 5188. doi:10.1002/anie.200400657.

(13) Kangani, C. O.; Day, B. W.; Kelly, D. E. *Tetrahedron Lett.* **2008**, *49* (5), 914. doi:10.1016/j.tetlet.2007.11.090.

(14) Cano, I.; Alvarez, E.; Nicasio, M. C.; Perez, P , *J. Am. Chem. Soc.* **2011**, *133* (2), 191. doi:10.1021/ja109732s.

(15) Dengiz, C.; Özcan, S.; Sahin, E.; Balci, M. *Synthesis* **2010**, (8), 1365. doi:10.1055/s-0029-1218673.

(16) Ito, M.; Koyakumaru, K. I.; Ohta, T.; Takaya, H. *Synthesis* **1995**, (4), 376. doi:10.1055/s-1995-3928.

(17) Zhong, Z.; Hu, J.; Wang, X.; Liu, J.; Zhang, L. *Synth. Commun.* **2011**, *41* (16), 2461. doi:10.1080/00397911.2010.505698.

(18) Laszlo, P.; Polla, E. *Tetrahedron Lett.* **1984**, *25* (34), 3701. doi:10.1016/0040-4039(84)80109-4.

(19) Kaiser, C.; Weinstock, J. *Org. Synth.* **1971**, *51*, 48.

(20) Bolm, C.; Schiffers, I.; Dinter, C. L.; Defrère, L.; Gerlach, A.; Raabe, G. *Synthesis* **2001**, (11), 1719. doi:10.1055/s-2001-16745.

(21) Bolm, C.; Schiffers, I.; Atodiresei, I.; Hackenberger, C. P. R. *Tetrahedron: Asymmetry* **2003**, *14*, 3455. doi:10.1016/S0957-4166(03)00579-2.

(22) Shao, H.; Colucci, M.; Tong, S.; Zhang, H.; Castelhano, A. L. *Tetrahedron Lett.* **1998**, *39* (40), 7235. doi:10.1016/S0040-4039(98)01595-0.

(23) Froeyen, P. *Phosphorus, Sulfur Silicon Relat. Elem.* **1994**, *89* (1–4), 57. doi:10.1080/10426509408020432.

(24) Gumaste, V. K.; Bhawal, B. M.; Deshmukh, A. R. A. S. *Tetrahedron Lett.* **2002**, *43* (7), 1345. doi:10.1016/S0040-4039(01)02377-2.

(25) Bandgar, B. P.; Pandit, S. S. *Tetrahedron Lett.* **2002**, *43* (18), 3413. doi:10.1016/S0040-4039(02)00508-7.

(26) Kobayashi, S.; Kamiyama, K.; Iimori, T.; Ohno, M. *Tetrahedron Lett.* **1984**, *25* (24), 2557. doi:10.1016/S0040-4039(01)81230-2.

(27) Canonne, P.; Akssira, M.; Dahouh, A.; Kasmi, H.; Boumzebra, M. *Heterocycles* **1993**, *36* (6), 1305. doi:10.3987/COM-92-6296.

(28) Arrieta, A.; Aizpurua, J. M.; Palomo, C. *Tetrahedron Lett.* **1984**, *25* (31), 3365. doi:10.1016/S0040-4039(01)81386-1.

(29) Sridhar, R.; Perumal, P. T. *Synth. Commun.* **2003**, *33* (4), 607. doi:10.1081/SCC-120015815.

(30) Weinstock, J. *J. Org. Chem.* **1961**, *26* (9), 3511. doi:10.1021/jo01067a604.
(31) Overman, L. E.; Taylor, G. F.; Petty, C. B; Jessup, P. J. *J. Org. Chem.* **1978**, *43* (11), 2164. doi:10.1021/jo00405a017.
(32) Chorev, M.; MacDonald, S. A.; Goodman, M. *J. Org. Chem.* **1984**, *49*, 821. doi:10.1021/jo00179a014.
(33) Stefanuti, I.; Smith, S. A.; Taylor, R. J. K. *Tetrahedron Lett.* **2000**, *41* (19), 3735. doi:10.1016/S0040-4039(00)00477-9.
(34) Bolm, C.; Dinter, C. L.; Schiffers, I.; Defre‘re, L. *Synlett* **2001**, *2001* (12), 1875. doi:10.1055/s-2001-18753.
(35) Kuramochi, K.; Osada, Y.; Kitahara, T. *Tetrahedron* **2003**, *59* (47), 9447. doi:10.1016/j.tet.2003.09.011.
(36) Binder, D.; Habison, G.; Noe, C. R. *Synthesis* **1977**, *1977* (4), 255. doi:10.1055s-1977-24341.
(37) Wolf, G.; Friedman, O. M.; Dickinson, S. J.; Seligman, A. M. *J. Am. Chem. Soc.* **1950**, *72* (1), 390. doi:10.1021/ja01157a105.
(38) Rinderknecht, H.; Koechlin, H.; Niemann, C. *J. Org. Chem.* **1953**, *18* (8), 971. doi:10.1021/jo50014a011.
(39) Yale, H. L.; Losee, K.; Martins, J.; Holsing, M.; Perry, F. M.; Bernstein, J. *J. Am. Chem. Soc.* **1953**, *75* (8), 1933. doi:10.1021/ja01104a046.
(40) Saxena, S.; Haksar, C. N. *Curr. Sci.* **1979**, *48*, 63.
(41) Nettekoven, M. *Synlett* **2001**, *2001* (12), 1917. doi:10.1055/s-2001-18758.
(42) Tarabara, I. N.; Yarovoi, M. Y.; Kasyan, L. I. *Russ. J. Org. Chem.* **2003**, *39* (11), 1676. doi:10.1023/B:RUJO.0000013149.46416.76.
(43) Macor, J. E.; Mullen, G.; Verhoest, P.; Sampognaro, A.; Shepardson, B.; Mack, R. A. *J. Org. Chem.* **2004**, *69* (19), 6493. doi:10.1021/jo049404q.
(44) Papeo, G.; Posteri, H.; Vianello, P.; Varasi, M. *Synthesis* **2004**, *2004* (17), 2886. doi:10.1055/s-2004-831254.
(45) New, J. S.; Christopher, W. L.; Yevich, J. P.; Butler, R.; Schlemmer, R. F., Jr.; VanderMaelen, C. P.; Cipollina, J. A. *J. Med. Chem.* **1989**, *32* (6), 1147. doi:10.1021/jm00126a002.
(46) Chambers, J.; Reese, C. B. *Tetrahedron Lett.* **1975**, *16* (32), 2783. doi:10.1016/S0040-4039(00)75239-7.
(47) Padwa, A.; Crawford, K. R.; Rashatasakhon, P.; Rose, M. *J. Org. Chem.* **2003**, *68* (7), 2609. doi:10.1021/jo026757l.
(48) Gon, K.; Doo, O. J. *Synlett* **2008**, *2008* (13), 2072. doi:10.1055/s-2008-1077979.
(49) Kangani, C. O.; Day, B. W.; Kelley, D. E. *Tetrahedron Lett.* **2007**, *48*, 5933. doi:10.1016/j.tetlet.2007.06.119.
(50) Vasantha, B.; Sureshbabu, V. V. *Indian J. Chem.* **2010**, *49 B* (6), 812.
(51) Kitamura, M.; Tashiro, N.; Takamoto, Y.; Okauchi, T. *Chem. Lett,* **2010**, *39* (7), 732. doi:10.1246/cl.2010.732.
(52) Lebel, H.; Leogane, O. *Org. Lett.* **2005**, *7* (19), 4107. doi:10.1021/ol051428b.
(53) Lee, J. G.; Kwak, K. H. *Tetrahedron Lett.* **1992**, *33* (22), 3165. doi:10.1016/S0040-4039(00)79841-8.
(54) Reddy, P. S.; Yadgiri, P.; Lumin, S.; Falck, J. R. *Synth. Commun.* **1988**, *18* (5), 545. doi:10.1080/00397918808060749.
(55) Chen, D. J.; Chen, Z. C. *Tetrahedron Lett.* **2000**, *41* (38), 7361. doi:10.1016/S0040-4039(00)00990-4.
(56) Elmorsy, S. S. *Tetrahedron Lett.* **1995**, *36* (8), 1341. doi:10.1016/0040-4039(94)02472-N.
(57) Marinescu, L.; Thinggaard, J.; Thomsen, I. B.; Bols, M. *J. Org. Chem.* **2003**, *68* (24), 9453. doi:10.1021/jo035163v.
(58) Bose, D. S.; Narsimha Reddy, A. V. *Tetrahedron Lett.* **2003**, *44* (17), 3543. doi:10.1016/S0040-4039(03)00623-3.
(59) Arote, N. D.; Akamanchi, G. K. *Tetrahedron Lett.* **2007**, *48* (32), 5661. doi:10.1016/j.tetlet.2007.06.020.
(60) Pedersen, M. C.; Marinescu, L. G.; Bols, M. *Org. Biomol. Chem.* **2005**, *3*, 816. doi:10.1039/B500037H, Paper.
(61) Marinescu, L. G.; Pedersen, M. C.; Bols, M. *Tetrahedron* **2005**, *61* (1), 123. doi:10.1016/j.tet.2004.10.040.
(62) Iranpoor, N.; Firouzabadi, H.; Akhlaghinia, B.; Nowrouzi, N. *Tetrahedron Lett.* **2004**, *45* (16), 3291. doi:10.1016/j.tetlet.2004.02.141.
(63) Akhlaghinia, B. *Phosphorus, Sulfur Silicon Relat. Elem.* **2005**, *180* (7), 1601. doi:10.1080/104265090884292.
(64) Iranpoor, N.; Firouzabadi, H.; Akhlaghinia, B.; Nowrouzi, N. *J. Org. Chem.* **2004**, *69* (7), 2562. doi:10.1021/jo035238v.
(65) Akhlaghinia, B. *Phosphorus, Sulfur Silicon Relat. Elem.* **2004**, *179* (9), 1783. doi:10.1080/10426500490466463.
(66) Iranpoor, N.; Firouzabadi, H.; Akhlaghinia, B.; Azadi, R. *Synthesis* **2004**, *2004* (1), 92. doi:10.1055/s-2003-44369.
(67) Iranpoor, N.; Firouzabadi, H.; Azadi, R.; Akhlaghinia, B. *J. Sulfur Chem.* **2005**, *26* (2), 133. doi:10.1080/17415990500135228.
(68) Akhlaghinia, B. *Synthesis* **2005**, *2005* (12), 1955. doi:10.1055/s-2005-869906.
(69) Akhlaghinia, B.; Samiei, S. *Phosphorus, Sulfur Silicon Relat. Elem.***2009**, *184* (10), 2525. doi:10.1080/10426500802508212.
(70) Akhlaghinia, B.; Pourali, A. R. *Synthesis* **2004**, *2004* (11), 1747. doi:10.1055/s-2004-829122.
(71) Yukawa, Y.; Tsuno, Y. *J. Am. Chem. Soc.* **1957**, *79* (20), 5530. doi:10.1021/ja01577a054.
(72) Harvey, G. R. *J. Org. Chem.* **1966**, *31* (5), 1587. doi:10.1021/jo01343a063.
(73) Youssef, A. H. A.; Sharaf, S. M.; Abdel-Baki, S. A. *Journal fuer Praktische Chemie (Leipzig),* **1982**, *324* (3), 491.
(74) Hohenlohe, O. *Monatsh. Chem.* **1958**, *89*, 588.
(75) Swetha, M.; Shirodkar, S. G.; Ramana, P. Venkata. *Org. Prep. Proced. Int.* **2011**, *43*(4), 348. doi:10.1080/00304948.2011.594002.
(76) McGarvey, C. E.; Holden, D. A. *Langmuir,* **1990**, *6* (6), 1123. doi:10.1021/la00096a017.
(77) Holden, D. A. *Can. J. Chem.* **1984**, *62* (3), 574. doi:10.1139/v84-096.
(78) Breu, V.; Burri, K.; Cassal, J. M.; Clozel, M.; Hirth, G.; Loffler, B. M.; Muller, M.; Neidhart, W.; Ramuz, H.; *US pat. 5,541,186 A,* **1996.**
(79) Meyer, H. Mally. *Monatsh. Chem.***1912**, *33*, 403.