J. Chem. Sci. Vol. 127, No. 12, December 2015, pp. 2269–2282.
DOI 10.1007/s12039-015-0988-6

Synthesis of *N*-acylurea derivatives from carboxylic acids and *N,N′*-dialkyl carbodiimides in water

ALI RAMAZANI[a,*], FATEMEH ZEINALI NASRABADI[b], ARAM REZAEI[a], MORTEZA ROUHANI[c], HAMIDEH AHANKAR[d], PEGAH AZIMZADEH ASIABI[a], SANG WOO JOO[e,*], KATARZYNA ŚLEPOKURA[f] and TADEUSZ LIS[f]

[a]Department of Chemistry, University of Zanjan, P. O. Box 45195-313, Zanjan, Iran
[b]Chemistry Department, Payame Noor University, I. R. of Iran, P. O. Box 19395-3697, Tehran, Iran
[c]Young Researchers and Elite Club, Zanjan Branch, Islamic Azad University, Zanjan, Iran
[d]Department of Chemistry, Abhar Branch, Islamic Azad University, P. O. Box 22, Abhar, Iran
[e]School of Mechanical Engineering, Yeungnam University, Gyeongsan 712-749, Republic of Korea
[f]Faculty of Chemistry, University of Wrocław, 14 Joliot-Curie St., 50-383 Wrocław, Poland
e-mail: aliramazani@gmail.com; swjoo@yu.ac.kr

MS received 5 July 2015; revised 1 October 2015; accepted 10 October 2015

Abstract. Reactions of benzoic acid derivatives and (*E*)-cinnamic acid derivatives with *N*, *N′*-dialkyl carbodiimide proceed smoothly at room temperature and in neutral conditions to afford *N*-acylurea derivatives in high yields. The reaction proceeds smoothly and cleanly under mild conditions and no side reactions were observed.

Keywords. *N*, *N′*-dialkylcarbodiimide; benzoic acid derivatives; (*E*)-cinnamic acid derivatives; O→N acyl migration; *N*-acylurea.

1. Introduction

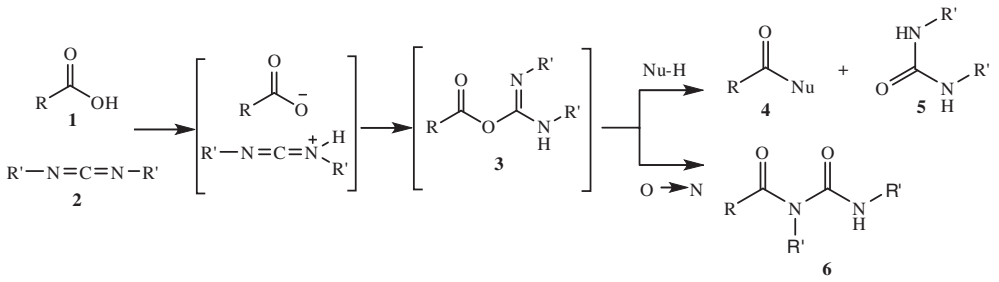
In recent years, there has been extreme interest on the applications of multicomponent reactions (MCRs) in modern synthetic organic chemistry.[1–6] With respect to the simplicity of one-pot synthetic methods and high atom efficiency, MCRs have a highly significant position in comparison with other reactions.[7] The reactions of carbodiimides with carboxylic acids are particularly interesting and have been studied extensively in the last few years. The mechanism and kinetics of these reactions have been extensively investigated.[8,9] The reaction sequence includes a proton transfer from the carboxylic acid **1** (scheme 1) to the basic nitrogen of the carbodiimide **2**, followed by addition of the carboxylate to form the *O*-acyl isourea **3**. It is known[10] that in low dielectric constant solvents such as CH_2Cl_2, formation of **3** occurs instantaneously and, in the absence of a nucleophile or a base, it can be stable for many hours. The intermediate **3** is a reactive species and in the presence of a nucleophile affords the coupling product **4**, along with a urea coproduct **5**. However, **3** can undergo a rearrangement, the so-called ON acyl migration, to give the *N*-acylurea **6**, which is frequently found as byproduct in these reactions.

As part of our ongoing program to develop efficient and robust methods for the preparation of organic compounds,[11–32] we studied ON acyl migration of carbodiimides with benzoic acid derivatives and (*E*)-cinnamic acid derivatives in water (schemes 2, 3 and tables 2, 3).

2. Experimental

Starting materials and solvents 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, which indicated that there was no side product. Melting points were measured on an Electrothermal 9100 apparatus and are uncorrected. IR spectra were measured on a Jasco 6300 FTIR spectrometer. ^{1}H and ^{13}C NMR spectra ($CDCl_3$) were recorded on a BRUKER DRX-250 AVANCE spectrometer at 250.0 and 62.5 MHz, respectively. Elemental analyses were performed using a Heraeus CHN-O-Rapid analyzer. Mass spectra were recorded on a FINNIGAN-MATT 8430 mass spectrometer operating at an ionization potential of 70 eV. Preparative layer chromatography (PLC) plates were prepared from Merck silica gel (F_{254}) powder.

*For correspondence



Scheme 1. Carbodiimide-promoted coupling of carboxylic acids.

2.1 *General Procedure for the Preparation of Compounds (**9,12**)*

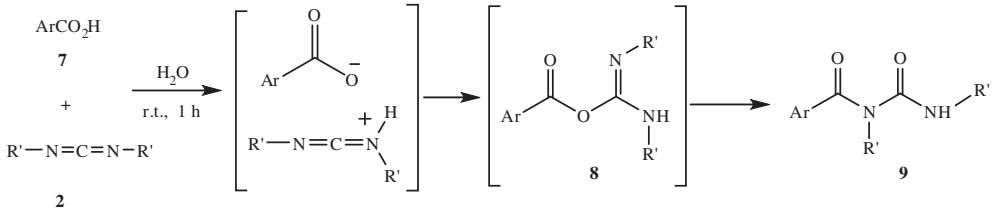
To a magnetically stirred solution of carboxylic acid (1 mmol) in H_2O was added 1 mmol of carbodiimide **2**. After total consumption of starting material (TLC monitoring), the organic solvent was evaporated under reduced pressure and the viscous residue was purified by preparative layer chromatography (PLC) (silica gel (F_{254}) powder; petroleum ether–ethyl acetate (4:1)). The characterization data of the compounds are given below.

2.1a *N-Benzoyl-N,N′-diisopropylurea (**9a**)*: White powder, (yield: 95%), M.p. 90-92°C. IR (KBr): ν = 3305 (NH), 3072, 2977, 1678, 1646, 1550, 1459, 1315, 700 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$) δ (ppm): 0.97 (d, 6H, J = 6.3 Hz, CH_3 isopropyl); 1.42 (d, 6H, J = 6.3 Hz, CH_3 isopropyl); 3.72-3.90 (m, 1H, CH isopropyl); 4.30-4.47 (m, 1H, CH isopropyl); 6.72 (d, 1H, J = 6.3 Hz, NH); 7.25-7.48 (m, 5H, CH_{arom}). ^{13}C NMR (62.5 MHz, $CDCl_3$) δ (ppm): 20.8, 22.2 ($4CH_3$, isopropyl); 42.7, 50.3 (2CH, isopropyl); 126.3, 128.6, 130.6 (5CH, arom); 137.1 (C, arom); 154.1, 173.1 (2C=O). MS, m/z (%): 248 (M^+), 247 (2), 162 (29), 105 (100), 77 (28), 57 (26), 42 (48). Analysis of $C_{14}H_{20}N_2O_2$ (248.32). (% calculation/ found): C: 67.71/67.76, H: 8.12/8.18, N: 11.28/11.23.

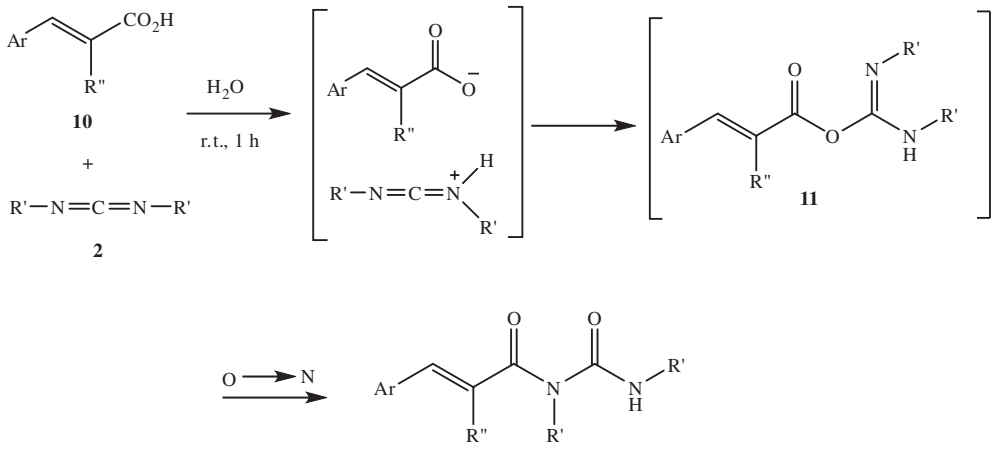
2.1b *N-(4-Bromobenzoyl)-N,N′-diisopropylurea (**9b**)*: Yellow powder, (yield: 94%), M.p. 125-127°C. IR (KBr): ν = 3327 (NH), 3077, 2973, 2855, 1708, 1639, 1550, 1376, 830 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$) δ (ppm): 1.00 (d, 6H, J = 6.3 Hz, CH_3 isopropyl); 1.41 (d, 6H, J = 6.5 Hz, CH_3 isopropyl); 3.75-3.90 (m, 1H, CH isopropyl); 4.30-4.43 (m, 1H, CH isopropyl); 6.63 (d, 1H, J = 6.3 Hz, NH); 7.39 (d, 2H, J = 8.3 Hz, CH_{arom}); 7.55 (d, 2H, J = 8.3 Hz, CH_{arom}). ^{13}C NMR (62.5 MHz, $CDCl_3$) δ (ppm): 20.8, 22.2 ($4CH_3$, isopropyl); 42.8, 50.3 (2CH, isopropyl); 128.1, 131.9 (4CH, arom); 125.0, 135.7 (2C, arom); 154.4, 171.1 (2C=O). MS, m/z(%): 327 (M^+), 326 (24), 241 (62), 183 (100), 157 (20), 75 (21), 57 (42). Analysis of $C_{14}H_{19}BrN_2O_2$ (327.22). (% calculation/ found): C: 51.39/51.35, H: 5.85/5.80, N: 8.56/8.61.

2.1c *N-(3,4-Dimethylbenzoyl)-N,N′-diisopropylurea (**9c**)*: White powder, (yield: 97%), M.p. 93-95°C. IR (KBr): ν = 3296 (NH), 3034, 2977, 1700, 1632, 1545, 1369, 800 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$) δ (ppm): 0.99 (d,6H, J = 6.5 Hz, CH_3 isopropyl); 1.41 (d,6H, J = 6.5 Hz, CH_3 isopropyl); 2.27 (s,6H, CH_3); 3.75-3.92 (m, 1H, CH isopropyl); 4.33-4.57 (m, 1H, CH isopropyl); 6.70 (d, 1H, J = 7.5 Hz, NH); 7.14-7.26 (m, 3H, CH_{arom}). ^{13}C NMR (62.5 MHz, $CDCl_3$) δ (ppm): 19.7, 19.8 ($2CH_3$); 20.9, 22.3 ($4CH_3$, isopropyl); 42.6, 50.5 (2CH, isopropyl); 123.9, 127.6, 129.7 (3CH, arom); 134.5, 137.1, 139.7 (3C, arom); 154.3, 163.6 (2C=O). MS, m/z (%): 276 (2), 133 (6), 105 (4), 58 (21), 42 (100). Analysis of $C_{16}H_{24}N_2O_2$ (276.37). (% calculation/ found): C: 69.53/69.49, H: 8.75/8.80, N: 10.14/10.18.

2.1d *N,N′-Diisopropyl-N-(4-methylbenzoyl)urea (**9d**)*: White powder, (yield: 96%), M.p. 85-87°C. IR (KBr):



Scheme 2. Two-component synthesis of *N*-acylurea derivatives **9**.



Scheme 3. Two-component synthesis of *N*-acylurea derivatives **12**.

v = 3327 (NH), 3078, 2974, 1700, 1638, 1551, 1377, 831 cm^{-1}. ^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 0.98 (d, 6H, J = 6.3 Hz, CH_3 isopropyl); 1.42 (d, 6H, J = 6.7 Hz, CH_3 isopropyl); 2.38 (s, 3H, CH_3); 3.75-3.87 (m, 1H, CH isopropyl); 4.31-4.45 (m, 1H, CH isopropyl); 6.78 (d, 1H, J = 6.3 Hz, NH); 7.21 (d, 2H, J = 7.5 Hz, CH_{arom}); 7.40 (d, 2H, J = 7.5 Hz, CH_{arom}). ^{13}C NMR (62.5 MHz, $CDCl_3$) δ (ppm): 20.9, 22.3 (4CH_3, isopropyl); 21.4 (CH_3); 42.6, 50.4 (2CH, isopropyl); 126.5, 129.2 (4CH, arom); 134.2, 141.1 (2C, arom); 154.3, 172.7 (2C=O). Analysis of $C_{15}H_{22}N_2O_2$ (262.35). (% calculation/ found): C: 68.67/68.72, H: 8.45/8.50, N: 10.68/10.63.

2.1e *N,N′-Diisopropyl-N-(4-methoxybenzoyl)urea (**9e**)*: White powder, (yield: 90%), M.p. 92-94°C. IR (KBr): v = 3313 (NH), 3082, 2984, 1700, 1655, 1513, 1253, 837 cm^{-1}. ^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 0.96 (d, 6H, J = 6.5 Hz, CH_3 isopropyl); 1.40 (d, 6H, J = 6.7 Hz, CH_3 isopropyl); 3.82 (s, 3H, OCH_3); 3.76-3.94 (m, 1H, CH isopropyl); 4.41-4.55 (m, 1H, CH isopropyl); 6.48 (d, 1H, J = 6.5 Hz, NH); 6.89 (d, 2H, J = 8.5 Hz, CH_{arom}); 7.50 (d, 2H, J = 8.5 Hz, CH_{arom}). ^{13}C NMR (62.5 MHz, $CDCl_3$) δ (ppm): 20.9, 22.3 (4CH_3, isopropyl); 42.7, 50.0 (2CH, isopropyl); 55.4 (OCH_3); 113.8, 128.9 (4CH, arom); 129.14, 161.7 (2C, arom); 154.5, 171.9 (2C=O). Analysis of $C_{15}H_{22}N_2O_3$ (278.35). (% calculation/ found): C: 64.73/64.78, H: 7.97/7.92, N: 10.06/10.11.

2.1f *N,N′-Diisopropyl-N-(3-phenoxybenzoyl)urea (**9f**)*: Yellow powder, (yield: 92%), M.p. 152-154°C. IR (KBr): v = 3351 (NH), 3073, 2979, 1685, 1638, 1582, 1248, 758 cm^{-1}. ^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 1.02 (d, 6H, J = 6.5 Hz, CH_3 isopropyl); 1.39 (d, 6H, J = 6.7 Hz, CH_3 isopropyl); 3.78-3.95 (m, 1H, CH isopropyl); 4.25-4.41 (m, 1H, CH isopropyl); 6.99 (broad doublet, 1H, NH); 7.02-7.47 (m, 9H, CH_{arom}). ^{13}C NMR (62.5 MHz, $CDCl_3$) δ (ppm): 20.8, 22.3 (4CH_3, isopropyl); 42.7, 50.6 (2CH, isopropyl); 116.0, 119.4, 120.4, 120.6, 124.1, 129.1, 130.2 (9CH, arom); 138.7, 153.8, 156.2 (3C, arom); 157.8, 171.8 (2C=O). Analysis of $C_{20}H_{24}N_2O_3$ (340.42). (% calculation/ found): C: 70.56/70.61, H: 7.11/7.17, N: 8.23/8.18.

2.1g *N,N′-Diisopropyl-N-(3-methylbenzoyl)urea (**9g**)*: Yellow powder, (yield: 95%), M.p. 72-74°C. IR (KBr): v = 3310 (NH), 3069, 2975, 1709, 1636, 1548, 1368, 741 cm^{-1}. ^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 0.98 (d, 6H, J = 6.5 Hz, CH_3 isopropyl); 1.41 (d, 6H, J = 6.7 Hz, CH_3 isopropyl); 2.36 (s, 3H, CH_3); 3.76-3.90 (m, 1H, CH isopropyl); 4.30-4.46 (m, 1H, CH isopropyl); 6.79 (broad doublet, 1H, NH); 7.20-7.28 (m, 4H, CH_{arom}). ^{13}C NMR (62.5 MHz, $CDCl_3$) δ (ppm): 20.8, 22.2 (4CH_3, isopropyl); 21.3 (CH_3); 42.6, 50.3 (2CH, isopropyl); 123.3, 126.8, 128.5, 131.3 (4CH, arom); 137.1, 138.6 (2C, arom); 154.1, 172.7 (2C=O). Analysis of $C_{15}H_{22}N_2O_2$ (262.35). (% calculation/ found): C: 68.67/68.62, H: 8.45/8.49, N: 10.68/10.63.

2.1h *N-[4-(Bromomethyl)benzoyl]-N,N′-diisopropylurea (**9h**)*: White powder, (yield: 90%), M.p. 119-121°C. IR (KBr): v = 3307 (NH), 3046, 2979, 1697, 1635, 1537, 1368, 800 cm^{-1}. ^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm): 0.97 (d, 6H, J = 6.5 Hz, CH_3 isopropyl); 1.41 (d,6H, J = 6.5 Hz, CH_3 isopropyl); 3.70-3.90 (m, 1H, CH isopropyl); 4.34-4.59 (m, 1H, CH isopropyl); 4.48 (s, 2H, CH_2); 6.63 (broad doublet, 1H, NH); 7.43 (d, 2H, J = 7.7 Hz, CH_{arom}), 7.48 (d, 2H, J =7.7 Hz, CH_{arom}). ^{13}C NMR (62.5

MHz, $CDCl_3$) δ (ppm): 20.8, 22.2 ($4CH_3$, isopropyl); 32.2 (CH_2); 42.8, 50.2 (2CH, isopropyl); 126.9, 129.3 (4CH, arom); 132.0, 140.5 (2C, arom); 163.5, 171.5 (2C=O). Analysis of $C_{15}H_{21}BrN_2O_2$ (341.24). (% calculation/ found): C: 52.80/52.85, H: 6.20/6.16, N: 8.21/8.26.

2.1i *N-(4-Cyanobenzoyl)-N,N′-diisopropylurea (**9i**)*: Yellow powder, (yield: 92%), M.p. 92-94°C. IR (KBr): ν = 3343 (NH), 3058, 2979, 2230, 1697, 1631, 1568, 1465, 1278, 868 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$) δ (ppm): 0.97 (d, 6H, J = 6.5 Hz, CH_3 isopropyl); 1.40 (d,6H, J = 6.5 Hz, CH_3 isopropyl); 3.70-3.91 (m, 1H, CH isopropyl); 4.31-4.42 (m,1H, CH isopropyl); 6.67 (broad doublet, 1H, NH); 7.61 (d, 2H, J = 7.7 Hz, CH_{arom}); 7.72 (d, 2H, J = 7.7 Hz, CH_{arom}). ^{13}C NMR (62.5 MHz, $CDCl_3$) δ (ppm): 20.8, 22.1 ($4CH_3$, isopropyl); 42.2, 50.1 (2CH, isopropyl); 108.0 (CN), 127.1, 132.5 (4CH, arom); 114.0, 141.1 (2C, arom); 156.1, 170.0 (2C=O). Analysis of $C_{15}H_{19}N_3O_2$ (273.33). (% calculation/ found): C: 65.91/ 65.86, H: 7.01/ 7.06, N: 15.37/ 15.42.

2.1j *N-(4-Chlorobenzoyl)-N,N′-diisopropylurea (**9j**)*: Yellow powder, (yield: 93%), M.p. 104-106°C. IR (KBr): ν = 3327 (NH), 3078, 2974, 1705, 1637, 1465, 1260, 834 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$) δ (ppm): 0.98 (d, 6H, J = 6.5 Hz, CH_3 isopropyl); 1.40 (d,6H, J = 6.7Hz, CH_3 isopropyl); 3.68-3.86 (m, 1H, CH isopropyl); 4.33-4.44 (m, 1H, CH isopropyl); 6.64 (d, 1H, J = 5.0 Hz, NH); 7.38 (d, 2H, J = 8.3 Hz, CH_{arom}); 7.46 (d, 2H, J = 8.3 Hz, CH_{arom}). ^{13}C NMR (62.5 MHz, $CDCl_3$) δ (ppm): 20.8, 22.2 ($4CH_3$, isopropyl); 42.2, 50.1 (2CH, isopropyl); 127.1, 128.9 (4CH, arom); 135.4, 137.1 (2C, arom); 153.6, 172.0 (2C=O). Analysis of $C_{14}H_{19}ClN_2O_2$ (282.77). (% calculation/ found): C: 59.47/ 59.52, H: 6.77/ 6.72, N: 9.91/ 9.96.

2.1k *N-(4-Fluorobenzoyl)-N,N′-diisopropylurea (**9k**)*: Yellow powder, (yield: 90%), M.p. 90-92°C. IR (KBr): ν = 3328 (NH), 3022, 2980, 1702, 1639, 1526, 1266, 846 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$) δ (ppm): 0.97 (d,6H, J = 6.5 Hz, CH_3 isopropyl); 1.41 (d,6H, J = 6.7 Hz, CH_3 isopropyl); 3.75-3.95 (m, 1H, CH isopropyl); 4.31-4.50 (m, 1H, CH isopropyl); 6.44 (broad doublet, 1H, NH); 7.06-7.57 (m, 4H, CH_{arom}). ^{13}C NMR (62.5 MHz, $CDCl_3$) δ (ppm): 20.5, 22.2 ($4CH_3$, isopropyl); 42.8, 50.0 (2CH, isopropyl); 115.7 (d,2CH, $^2J_{CF}$ = 21.7 Hz);128.1 (d, 2CH, $^3J_{CF}$ = 8.0Hz); 142.0 (C, arom); 150.5 (d, C, $^1J_{CF}$ = 310.0 Hz); 154.3, 177.0 (2C=O). Analysis of $C_{14}H_{19}FN_2O_2$ (266.31). (% calculation/ found): C: 63.14/ 63.10, H: 7.19/ 7.24, N: 10.52/ 10.57.

2.1l *N-(3,4-Dimethoxybenzoyl)-N,N′-diisopropylurea (**9l**)*: White powder, (yield: 92%), M.p. 66-68°C. IR (KBr): ν = 3325 (NH), 3017, 2981, 1699, 1651, 1465, 1368, 850 cm^{-1}. ^1H NMR ($CDCl_3$) (250 MHz, $CDCl_3$) δ (ppm): 1.04 (d, 6H, J = 6.5 Hz, CH_3 isopropyl); 1.42 (d,6H, J = 6.7 Hz, CH_3 isopropyl); 3.80 (s, 6H, OCH_3); 3.74-3.95 (m, 1H, CH isopropyl); 4.28-4.42 (m, 1H, CH isopropyl); 7.04 (broad doublet, ^1H, NH); 6.52-7.26 (m, 3H, CH_{arom}). ^{13}C NMR (62.5 MHz, $CDCl_3$) δ (ppm): 20.9, 22.3 ($4CH_3$, isopropyl); 42.7, 50.7 (2CH, isopropyl); 55.6 ($2OCH_3$); 102.6, 103.9 (3CH, arom); 138.8, 160.9 (3C, arom); 154.2, 171.0 (2C=O). Analysis of $C_{16}H_{24}N_2O_4$ (308.37). (% calculation/ found): C: 62.32/ 62.38, H: 7.84/ 7.80, N: 9.08/ 9.03.

2.1m *N-[4-(tert-Butyl)benzoyl]-N,N′-diisopropylurea (**9m**)*: White powder, (yield: 94%), M.p. 70-72°C. IR (KBr): ν = 3324 (NH), 3028, 2975, 1712, 1637, 1560, 1384, 846 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$) δ (ppm): 0.94 (d, 6H, J = 6.5 Hz, CH_3 isopropyl); 1.42 (d, 6H, J = 6.7Hz, CH_3 isopropyl); 1.31(s, 9H, CH_3); 3.75-3.90 (m, 1H,CH isopropyl); 4.35-4.51 (m, 1H, CH isopropyl); 6.65 (broad doublet, ^1H, NH); 7.32-7.50 (m, 4H, CH_{arom}). ^{13}C NMR (62.5 MHz, $CDCl_3$) δ (ppm): 20.9, 22.2 ($4CH_3$, isopropyl); 42.6, 50.2 (2CH, isopropyl); 31.1 ($3CH_3$); 34.89 (C); 125.5, 126.3 (4CH, arom); 135.5, 143.1 (2C, arom); 154.2, 173.1 (2C=O). Analysis of $C_{18}H_{28}N_2O_2$ (304.43). (% calculation/ found): C: 71.02/ 71.08, H: 9.27/ 9.32, N: 9.20/ 9.16.

2.1n *N-(3-Chlorobenzoyl)-N,N′-diisopropylurea (**9n**)*: Yellow powder, (yield: 96%), M.p. 80-82°C. IR (KBr): ν = 3307 (NH), 3028, 2974, 1712, 1631, 1463, 1371, 813 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$) δ (ppm): 0.99 (d, 6H, J = 6.5 Hz, CH_3 isopropyl); 1.41 (d, 6H, J =6.5Hz, CH_3 isopropyl); 3.78-3.91 (m, 1H, CH isopropyl); 4.33-4.48 (m, 1H, CH isopropyl); 6.63 (broad doublet, ^1H, NH); 7.31-7.49 (m, 4H, CH_{arom}). ^{13}C NMR (62.5 MHz, $CDCl_3$) δ (ppm): 20.8, 22.2 ($4CH_3$, isopropyl); 42.8, 50.1 (2CH, isopropyl); 124.4, 126.6, 130.0, 130.7 (4CH, arom); 134.7, 138.2 (2C, arom); 153.7, 170.4 (2C=O). Analysis of $C_{14}H_{19}ClN_2O_2$ (282.77). (% calculation/ found): C: 59.47/ 59.42, H: 6.77/ 6.82, N: 9.91/ 9.96.

2.1o *N,N′-Diisopropyl-N-(2-naphthylcarbonyl)urea (**9o**)*: Yellow powder, (yield: 95%), M.p. 65-67°C.

IR (KBr): v = 3377 (NH), 3059, 2934, 1698, 1625, 1540, 1385, 796 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$) δ (ppm): 1.13 (d, 6H, J = 6.5 Hz, CH_3 isopropyl); 1.40 (d, 6H, J = 6.5 Hz, CH_3 isopropyl); 3.76-3.92 (m, 1H, CH isopropyl); 4.08-4.20 (m, 1H, CH isopropyl); 7.42-7.96 (m, 8H, NH and CH_{arom}). ^{13}C NMR (62.5 MHz, $CDCl_3$) δ (ppm): 20.9, 22.3 ($4CH_3$, isopropyl); 42.5, 52.0 (2CH, isopropyl); 122.5, 124.4, 126.8, 127.4, 128.6, 129.0, 129.6 (7CH, arom); 125.1, 133.2, 135.1 (3C, arom); 153.5, 164.6 (2C=O). Analysis of $C_{18}H_{22}N_2O_2$ (298.38). (% calculation/ found): C: 72.46/ 72.52, H: 7.43/ 7.48, N: 9.39/ 9.34.

2.1p *N,N′-Diisopropyl-N-(2-thienylcarbonyl)urea (**9p**)*: Yellow powder, (yield: 93%), M.p. 45-47°C. IR (KBr): v = 3293 (NH), 3017, 2977, 1703, 1613, 1425, 1264, 800 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$) δ (ppm): 1.05 (d, 6H, J = 6.5 Hz, CH_3 isopropyl); 1.44 (d, 6H, J = 6.7Hz, CH_3 isopropyl); 3.79-3.96 (m, 1H, CH isopropyl); 4.58-4.70 (m, 1H, CH isopropyl); 6.48 (broad doublet, 1H, NH); 7.03-7.09 and 7.47-7.52 (m, 3H, CH_{arom}). ^{13}C NMR (62.5 MHz, $CDCl_3$) δ (ppm): 21.1, 22.2 ($4CH_3$, isopropyl); 43.0, 49.1 (2CH, isopropyl); 127.2, 129.7, 130.5 (3CH, arom); 138.6 (C, arom); 154.0, 177.0 (2C=O). Analysis of $C_{12}H_{18}N_2O_2S$ (254.35). (% calculation/ found): C: 56.67/ 56.62, H: 7.13/ 7.18, N: 11.01/ 11.04.

2.1q *N,N′-Dicyclohexyl-N-[(E)-2-methyl-3-phenyl-2-propenoyl]urea (**12a**)*: White powder, (yield: 92%), M.p. 127-129°C. IR (KBr): v = 3299 (NH), 3070, 2932, 1703, 1649, 1548, 1237, 753 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$) δ (ppm): 1.14-1.82 (m, 20H, CH_2 cyclohexane); 2.11 (s, 3H, CH_3); 3.55-3.75 (m, 1H, cyclohexane); 3.94-4.08 (m, 1H, cyclohexane); 6.73 (s, 1H, CH=C); 7.14 (d, 1H, J = 6.7 Hz, NH); 7.28-7.37 (m, 5H, CH_{arom}).^{13}C NMR (62.5 MHz, $CDCl_3$) δ (ppm): 15.8 (CH_3); 24.6, 25.3, 25.5, 26.5, 30.8, 32.8 ($10CH_2$, cyclohexane); 49.5, 58.4 (2CH, cyclohexane); 127.7 (CH); 128.4, 129.1, 130.1 (5CH, arom); 134.3, 135.6 (2C); 174.9, 154.2 (2C=O). MS, m/z (%): 368 (M^+), 130 (2), 58 (18), 43 (100). Analysis of $C_{23}H_{32}N_2O_2$ (368.51). (% calculation/ found): C: 74.96/ 74.92, H: 8.75/ 8.70, N: 7.60/ 7.54. C, H, N.

2.1r *N,N′-Diisopropyl-N-[(E)-3-(4-methylphenyl)-2-propenoyl]urea (**12b**)*: White powder, (yield: 89%), M.p. 115-117°C. IR (KBr): v = 3276 (NH), 3066, 2974, 1706, 1647, 1598, 1378, 808 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$) δ (ppm): 1.13 (d, 6H, J = 6.2 Hz, CH_3 isopropyl); 1.44 (d, 6H, J = 6.5Hz, CH_3 isopropyl); 2.36 (s, 3H, CH_3); 3.95-4.12 (m, 1H, CH isopropyl); 4.45-4.60 (m, 1H, CH isopropyl); 6.72 (d, 1H, J = 15.2 Hz, CH=CH); 7.17(d, 2H, J = 7.5 Hz, CH_{arom}); 7.38 (d, 2H, J = 7.5 Hz, CH_{arom}); 7.61 (broad doublet, 1H, NH); 7.69 (d, 1H, J = 15.2 Hz, CH=CH).^{13}C NMR (62.5 MHz, $CDCl_3$) δ (ppm): 21.5 (CH_3); 21.0, 22.6 ($4CH_3$, isopropyl); 42.8, 48.4 (2CH, isopropyl); 118.4, 143.9 (2CH); 127.1, 129.7 (4CH, arom); 131.8, 140.6 (2C, arom); 154.1, 168.0 (2C=O). MS, m/z(%): 288 (5), 161 (3), 145 (62), 117 (3), 105 (7), 57 (28), 43 (100). Analysis of $C_{17}H_{24}N_2O_2$ (288.38). (% calculation/ found): C: 70.80/ 70.76, H: 8.39/ 8.43, N: 9.71/ 9.76.

2.1s *N,N′-Dicyclohexyl-N-[(E)-3-phenyl-2-propenoyl] urea (**12c**)*: White powder, (yield: 86%), M.p. 140-142°C. IR (KBr): v = 3267 (NH), 3061, 2937, 1710, 1649, 1601, 1451, 1232, 764 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$) δ (ppm):1.12-2.01 (m, 20H, cyclohexane); 3.65-3.84 (m, 1H, cyclohexane); 4.05-4.20 (m, 1H, cyclohexane); 6.72 (d, 1H, J = 15.5 Hz, CH=CH); 7.14 (broad doublet, 1H, NH); 7.36-7.44 (m, 5H, CH_{arom}); 7.64 (d, 1H, J = 15.5 Hz, CH=CH). ^{13}C NMR (62.5 MHz, $CDCl_3$) δ (ppm): 24.7, 25.3, 25.4, 26.2, 30.9, 32.8 ($10CH_2$, cyclohexane); 49.9, 56.1 (2CH, cyclohexane); 127.9, 128.9, 130.1 (5CH, arom); 134.6 (C, arom); 119.3, 143.44 (2CH); 154.0, 166.7 (2C=O). Analysis of $C_{22}H_{30}N_2O_2$ (354.49). (% calculation/ found): C: 74.54/ 74.59, H: 8.53/ 8.59, N: 7.90/ 7.95.

2.1t *N,N′-Dicyclohexyl-N-[(E)-3-(4-methylphenyl)-2-propenoyl]urea (**12d**)*: White powder, (yield: 89%), M.p. 160-162°C. IR (KBr): v = 3273 (NH), 3048, 2936, 1712, 1645, 1598, 1453, 1232, 812 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$) δ (ppm): 1.25-1.99 (m, 20H, cyclohexane); 2.37 (s, 3H, CH_3); 3.68-3.85 (m, 1H, cyclohexane); 4.06-4.29 (m, 1H, cyclohexane); 7.09 (broad doublet, 1H, NH); 6.55 (d, 1H, J = 15.2 Hz, CH=CH); 7.18 (d, 2H, J = 7.5Hz, CH_{arom}); 7.38 (d, 2H, J = 7.5 Hz, CH_{arom}); 7.65 (d, 1H, J = 15.2 Hz, CH=CH).^{13}C NMR (62.5 MHz, $CDCl_3$) δ (ppm): 15.1 (CH_3); 24.7, 25.4, 25.5, 26.32, 30.1, 32.8 ($10CH_2$, cyclohexane); 49.9, 57.9 (2CH, cyclohexane); 118.2, 143.4 (2CH); 127.9, 129.6 (4CH, arom); 132.0, 140.5 (2C, arom); 166.2, 176.0 (2C=O). Analysis of $C_{23}H_{32}N_2O_2$ (368.51). (% calculation/ found): C: 74.96/ 74.92, H: 8.75/ 8.70, N: 7.60: 7.56.

2.1u *N-[(E)-3-(3-Chlorophenyl)-2- propenoyl]-N,N′-dicyclohexyl urea (**12e**)*: White powder, (yield: 89%), M.p. 119-121°C. IR (KBr): v = 3296 (NH), 3054, 2936,

1701, 1644, 1607, 1452, 1227, 992, 786 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$) δ (ppm): 0.94-2.01 (m, 20H, cyclohexane); 3.70-3.85 (m, 1H, cyclohexane); 4.05-4.19 (m, 1H, cyclohexane); 6.69 (d, 1H, J = 15.2 Hz, CH=CH); 6.95 (broad doublet, 1H, NH); 7.29-7.51 (m, 3H, CH_{arom}); 7.54 (d, 1H, J = 15.2 Hz, CH=CH).^{13}C NMR (62.5 MHz, $CDCl_3$) δ (ppm): 24.7, 25.3, 25.4, 26.2, 30.9, 32.8 ($10CH_2$, cyclohexane); 49.1, 55.9 (2CH, cyclohexane); 120.8, 134.9 (2CH); 126.0, 127.6, 129.9, 130.1 (4CH, arom); 136.5, 141.6 (2C, arom); 153.8, 166.6 (2C=O). Analysis of $C_{22}H_{29}ClN_2O_2$ (388.93). (% calculation/ found): C: 67.94/ 67.99, H: 7.52/ 7.49, N: 7.20/ 7.16.

2.1v *N-[(E)-3-(4-Chlorophenyl)-2- propenoyl]-N,N′-dicyclohexyl urea (**12f**)*: White powder, (yield: 87%), M.p. 175-177°C. IR (KBr): ν = 3261 (NH), 3017, 2920, 1703, 1643, 1527, 1370, 818 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$) δ (ppm): 1.10-1.94 (m, 20H, cyclohexane); 3.65-3.82 (m, 1H, cyclohexane); 4.05-4.18 (m, 1H, cyclohexane); 6.69 (d, 1H, J = 15.5 Hz, CH=CH); 6.84 (broad doublet, 1H, NH); 7.33 (d, 2H,J = 8.2 Hz, CH_{arom}); 7.39 (d, 2H, J = 8.2 Hz, CH_{arom}); 7.61 (d, 1H, J = 15.5 Hz, CH=CH).^{13}C NMR (62.5 MHz, $CDCl_3$) δ (ppm): 24.8, 25.3, 25.5, 26.2, 30.1, 33.7 ($10CH_2$, cyclohexane); 48.5, 56.9 (2CH, cyclohexane); 118.3, 139.1 (2CH), 129.1, 129.2 (4CH, arom); 134.2, 136.0 (2C, arom); 161.3, 169.1 (2C=O). Analysis of $C_{22}H_{29}ClN_2O_2$ (388.93). (% calculation/ found): C: 67.94/ 67.99, H: 7.52/ 7.49, N: 7.20/ 7.16.

2.1w *N,N′-Dicyclohexyl-N-[(E)-3-(3-methoxylphenyl)-2-propenoyl]urea (**12g**)*: White powder, (yield: 85%), M.p. 78-80°C. IR (KBr): ν = 3260 (NH), 3066, 2935, 1714, 1649, 1606, 1385, 844, 786 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$) δ (ppm): 1.31-1.98 (m, 20H, cyclohexane); 3.60-3.81 (m, 1H, cyclohexane); 3.78 (s, 3H, OCH_3); 4.02-4.20 (m, 1H, cyclohexane); 6.69 (d, 1H, J = 15.5 Hz, CH=CH); 6.88-7.25 (m, 5H, NH and CH_{arom}); 7.59 (d, 1H, J = 15.5 Hz, CH=CH).^{13}C NMR (62.5 MHz, $CDCl_3$) δ (ppm): 24.7, 25.4, 25.4, 26.2, 30.9, 32.8 ($10CH_2$, cyclohexane); 49.9, 55.8 (2CH, cyclohexane); 55.2 (OCH_3); 119.6, 143.2 (2CH), 112.8, 115.8, 120.6, 129.9 (4CH, arom); 135.1, 159.8 (2C, arom); 153.8, 166.3 (2C=O). Analysis of $C_{23}H_{32}N_2O_3$ (384.51). (% calculation/ found): C: 71.84/ 71.89, H: 8.39: 8.35, N: 7.29/ 7.34.

2.1x *N-[(E)-3-(4-Chlorophenyl)-2- propenoyl]-N,N′-diisopropylurea (**12h**)*: White powder, (yield: 86%), M.p. 151-153°C. IR (KBr): ν = 3280 (NH), 3072, 2975, 1705, 1651, 1609, 1466, 1378, 813 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$) δ (ppm): 1.23 (d, 6H, J = 6.7 Hz, CH_3 isopropyl); 1.43 (d, 6H, J = 6.7 Hz, CH_3 isopropyl); 3.97-4.20 (m, 1H, CH isopropyl); 4.47-4.61 (m, 1H, CH isopropyl); 6.72 (d, 1H, J = 15.5 Hz, CH=CH); 7.27 (broad doublet, 1H, NH); 7.32 (d, 2H, J = 8.5 Hz, CH_{arom}); 7.46 (d, 2H, J = 8.5 Hz, CH_{arom}); 7.58 (d, 1H, J = 15.5 Hz, CH=CH).^{13}C NMR (62.5 MHz, $CDCl_3$) δ (ppm): 21.0, 22.6 ($4CH_3$, isopropyl); 42.9, 48.3 (2CH, isopropyl); 120.0, 142.3 (2CH); 129.1, 129.2, (4CH, arom); 133.1, 136.0 (2C, arom); 153.9, 167.2 (2C=O). Analysis of $C_{16}H_{21}ClN_2O_2$ (308.80). (% calculation/ found): C: 62.23/ 62.27, H: 6.85/ 6.90, N: 9.07/ 9.02.

2.1y *N,N′-Diisopropyl-N-[(E)-3-(3-methoxylphenyl)-2-propenoyl]urea (**12i**)*: White powder, (yield: 86%), M.p. 73-75°C. IR (KBr): ν = 3343 (NH), 3064, 2976, 1695, 1647, 1364, 846, 795 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$) δ (ppm): 1.12 (d, 6H, J = 6.2 Hz, CH_3 isopropyl); 1.44 (d, 6H, J = 6.7 Hz, CH_3 isopropyl); 3.81(s, 3H, OCH_3); 3.96-4.10 (m, 1H, CH isopropyl); 4.47-4.58 (m, 1H, CH isopropyl); 6.74 (d, 1H, J = 15.2 Hz, CH=CH); 6.90-7.32 (m, 4H, CH_{arom}); 7.50 (broad doublet, 1H, NH); 7.62 (d, 1H, J = 15.2 Hz, CH=CH).^{13}C NMR (62.5 MHz, $CDCl_3$) δ (ppm): 21.0, 22.6 ($4CH_3$, isopropyl); 42.2, 48.4 (2CH, isopropyl);

Table 1. Experimental data for **12a**.

CCDC No.	1410529
Chemical formula	$C_{23}H_{32}N_2O_2$
M_r	368.50
Crystal system, space group	Orthorhombic, *Pbca*
Temperature (K)	100(2)
a, b, c (Å)	9.534(3), 18.823(4), 23.587(4)
V (Å^3)	4232.9(18)
Z	8
Radiation type	Mo $K\alpha$
μ (mm^{-1})	0.07
Crystal size (mm)	0.71 × 0.10 × 0.04
T_{min}, T_{max}	0.692, 1.000
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	13283, 5963, 3084
R_{int}	0.053
$(\sin\theta/\lambda)_{max}$ (Å^{-1})	0.703
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.047, 0.059, 1.00
No. of reflections	5963
No. of parameters	245
No. of restraints	1
H-atom treatment	H-atom parameters constrained
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.24, −0.23

Table 2. Synthesis of *N*-acylurea derivatives **9a-p** from *N*, *N′*-dialkylcarbodiimide **2** and benzoic acid derivatives **7** (see scheme 2).

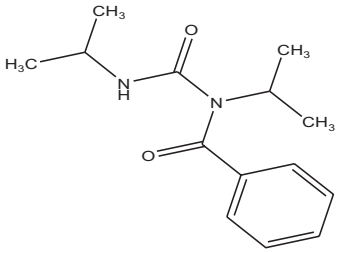
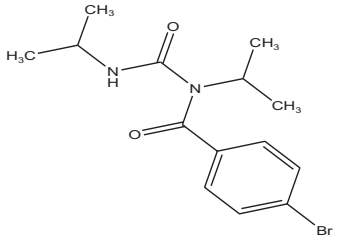
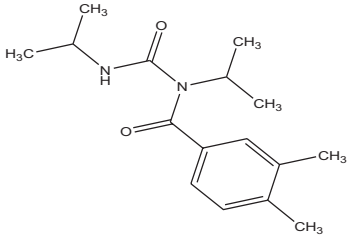
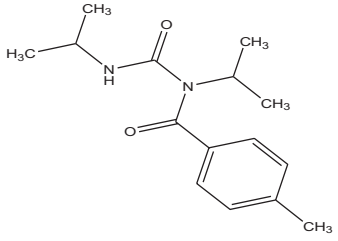
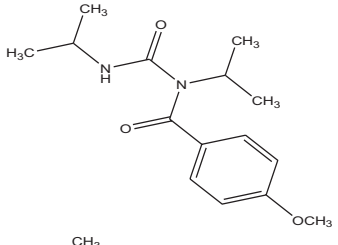
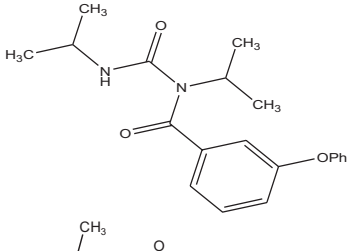
9	R′	Ar	Product	Yield (%)[a]
a	Isopropyl	Ph		95
b	Isopropyl	4-BrC_6H_4		94
c	Isopropyl	3,4-$Me_2C_6H_3$		97
d	Isopropyl	4-MeC_6H_4		96
e	Isopropyl	4-MeOC_6H_4		90
f	Isopropyl	3-PhOC_6H_4		92
g	Isopropyl	3-MeC_6H_4		95

Table 2. (continued)

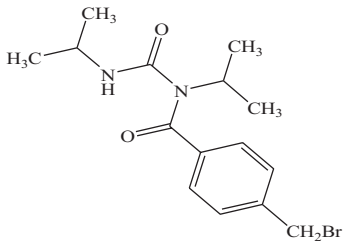
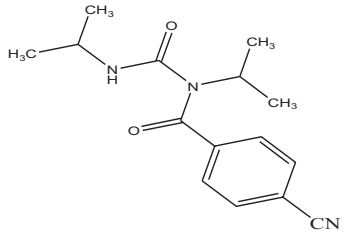
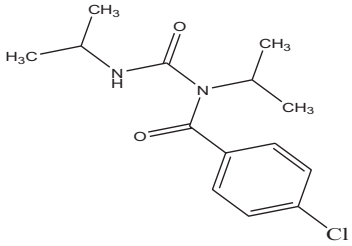
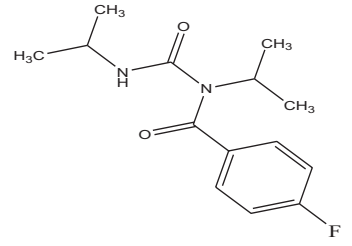
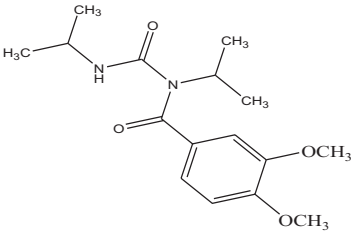
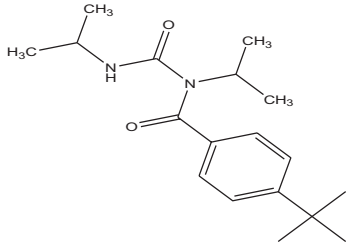
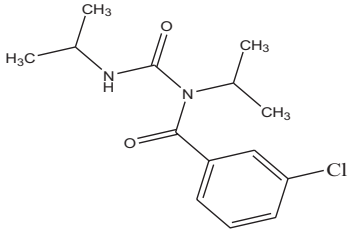
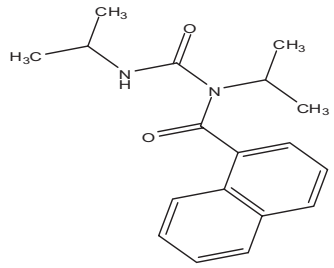
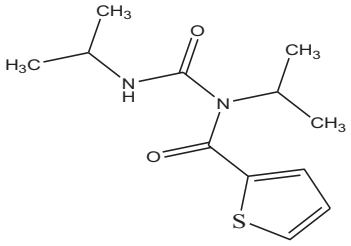
9	R′	Ar	Product	Yield (%)[a]
h	Isopropyl	4-$BrCH_2C_6H_4$		90
i	Isopropyl	4-NCC_6H_4		92
j	Isopropyl	4-ClC_6H_4		93
k	Isopropyl	4-FC_6H_4		90
l	Isopropyl	3,4-$MeO_2C_6H_3$		92
m	Isopropyl	4-t-BuC_6H_4		94
n	Isopropyl	3-ClC_6H_4		96

Table 2. (continued)

9	R′	Ar	Product	Yield (%)[a]
o	Isopropyl	$C_{11}H_8O_2$		95
p	Isopropyl	$C_5H_4SO_2$		93

[a]Yield of isolated **9**.

55.3 (OCH_3); 119.9, 143.7 (2CH); 113.2, 115.7, 120.5, 129.9 (4CH, arom); 135.9, 159.8 (2C, arom); 153.1, 166.5 (2C=O). Analysis of $C_{17}H_{24}N_2O_3$ (304.38). (% calculation/ found): C: 67.08/ 67.02, H: 7.95/ 7.90, N: 9.20/ 9.16.

2.1z *N-[(E)-3-(3-Chlorophenyl)-2- propenoyl]-N,N′-diisopropylurea (**12j**)*: White powder, (yield: 88%), M.p. 142-144°C. IR (KBr): $v = 3286$ (NH), 3073, 2979, 1706, 1651, 1611, 1465, 1374, 787 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$)2.1 δ (ppm): 1.23 (d, 6H, J = 6.5 Hz, CH_3 isopropyl); 1.44 (d, 6H, J = 6.7Hz, CH_3 isopropyl); 3.95-4.12 (m, 1H, CH isopropyl); 4.42-4.60 (m, 1H, CH isopropyl); 6.75 (d, 1H, J = 15.2 Hz, CH=CH); 7.32-7.44 (m, 5H, NH and CH_{arom}); 7.57 (d, 1H, J = 15.2 Hz, CH=CH).^{13}C NMR (62.5 MHz, $CDCl_3$) δ (ppm): 21.0, 22.6 ($4CH_3$, isopropyl); 42.9, 48.5 (2CH, isopropyl); 120.9, 142.1 (2CH); 126.2, 127.6, 130.0, 130.2 (4CH, arom); 134.9, 136.4 (2C, arom); 154.2, 167.4 (2C=O). Analysis of $C_{16}H_{21}ClN_2O_2$ (308.80). (% calculation/ found): C: 62.23/ 62.27, H: 6.85/ 6.90, N: 9.07: 9.02.

*2.1aa N,N′-Diisopropyl-N-[(E)-3-phenyl-2-propenoyl] urea (**12k**)* White powder, (yield: 86%), M.p. 94-96°C. IR (KBr): $v = 3284$ (NH), 3068, 2975, 1705, 1649, 1606, 1372, 759 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$) δ (ppm): 1.23 (d, 6H, J = 6.5 Hz, CH_3 isopropyl); 1.46 (d, 6H, J = 6.7Hz, CH_3 isopropyl); 3.92-4.13 (m, 1H, CH isopropyl); 4.45-4.62 (m, 1H, CH isopropyl); 6.76 (d, 1H, J = 15.5 Hz, CH=CH); 7.38-7.68 (m, 6H, NH and CH_{arom}); 7.78 (d, 1H, J = 15.5 Hz, CH=CH). ^{13}C NMR (62.5 MHz, $CDCl_3$) δ (ppm): 21.2, 22.6 ($4CH_3$, isopropyl); 42.8, 48.5 (2CH, isopropyl); 119.5, 143.9 (2CH); 127.1, 128.9, 130.2 (5CH, arom); 135.2 (C); 173.1, 154.5 (2C=O). Analysis of $C_{16}H_{22}N_2O_2$ (274.36). (% calculation/ found): C: 70.04/ 70.09, H: 8.08/ 8.13, N: 10.21/ 10.26.

*2.1ab N,N′-Diisopropyl-N-[(E)-2-methyl-3-phenyl-2-propenoyl]urea (**12l**)* White powder, (yield: 89%), M.p. 95-97°C. IR (KBr): $v = 3322$ (NH), 3066, 2970, 1695, 1650, 1531, 1262, 763 cm^{-1}. ^1H NMR (250 MHz, $CDCl_3$) δ (ppm): 1.17 (d, 6H, J = 6.2 Hz, CH_3 isopropyl); 1.46 (d, 6H, J = 6.7Hz, CH_3 isopropyl); 2.14 (s, 3H, CH_3); 3.90-4.02 (m, 1H, CH isopropyl); 4.34-4.44 (m, 1H, CH isopropyl); 6.71 (s, 1H, CH=C); 7.30-7.41(m, 5H, CH_{arom}); 7.52 (d, 1H, J = 5.7 Hz, NH).^{13}C NMR (62.5 MHz, $CDCl_3$) δ (ppm): 15.8 (CH_3); 21.0, 22.6 ($4CH_3$, isopropyl); 42.6, 50.6 (2CH, isopropyl); 127.8 (CH); 128.4, 129.1, 129.9 (5CH, arom); 134.2, 136.5 (2C); 154.5, 176.2 (2C=O). Analysis of $C_{17}H_{24}N_2O_2$ (288.38). (% calculation/ found): C: 70.80/ 70.76, H: 8.39/ 8.43, N: 9.71/ 9.76.

2.2 *X-Ray crystallography*

Crystals of **12a** for X-ray analysis were obtained by very slow evaporation of a CH_3OH/petroleum ether, 5:2 solution (20-25°C) in 48 h. The light yellow crystals

Table 3. Synthesis of *N*-acylurea derivatives **12a-l** from *N*, *N*'-dialkylcarbodiimide **2** and (*E*)-cinnamic acid **10** (see scheme 3).

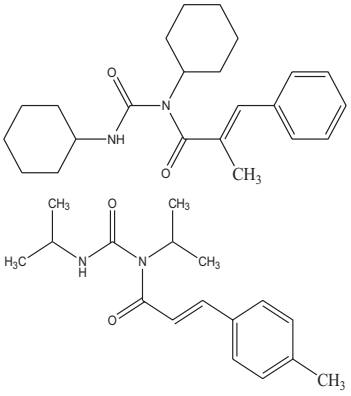
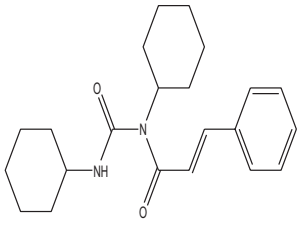
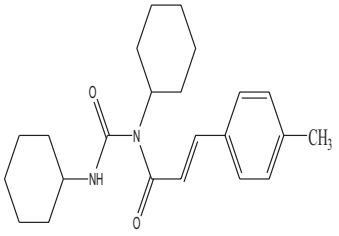
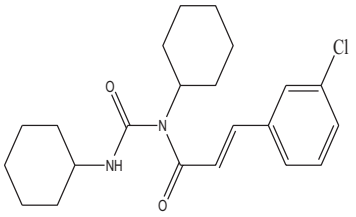
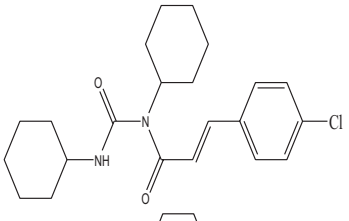
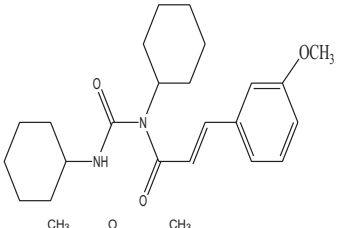
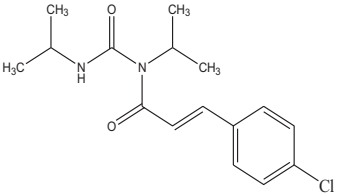
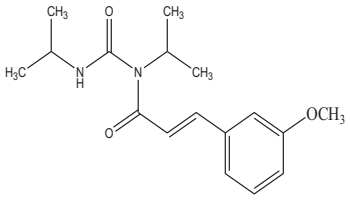
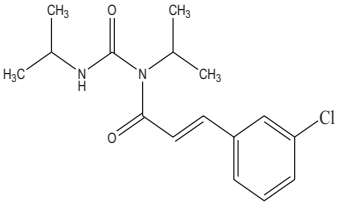
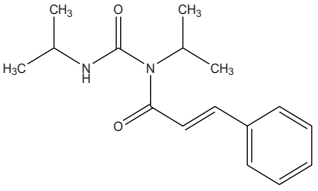
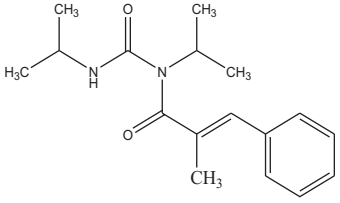
12	R′	R″	Ar	Product	Yield (%)[a]
a	Cyclohexyl	CH_3	Ph		92
b	Isopropyl	H	4-MeC_6H_4		89
c	Cyclohexyl	H	Ph		86
d	Cyclohexyl	H	4-MeC_6H_4		89
e	Cyclohexyl	H	3-ClC_6H_4		89
f	Cyclohexyl	H	4-ClC_6H_4		87
g	Cyclohexyl	H	3-MeOC_6H_4		85
h	Isopropyl	H	4-ClC_6H_4		86

Table 3. (continued)

12	R′	R″	Ar	Product	Yield (%)[a]
i	Isopropyl	H	3-MeOC_6H_4		86
j	Isopropyl	H	3-ClC_6H_4		88
k	Isopropyl	H	Ph		86
l	Isopropyl	CH_3	Ph		89

[a]Yield of isolated **12**.

were filtered off, washed with the cold solvent mixture, and dried at room temperature.

The crystallographic measurement of **12a** was performed on an Oxford Diffraction Xcalibur PX κ-geometry automated four-circle diffractometer with graphite-monochromatized Mo$K\alpha$ radiation (λ = 0.71073 Å). The data were collected at 100(2) K. Data were corrected for Lorentz and polarization effects. Data collection, cell refinement, data reduction, and analysis were carried out with CrysAlisCCD and CrysAlisRED, respectively.[33] The structures were solved by direct methods with the *SHELXS97* program,[34] and refined by a full-matrix least-squares technique with *SHELXL2014*[34] and anisotropic thermal

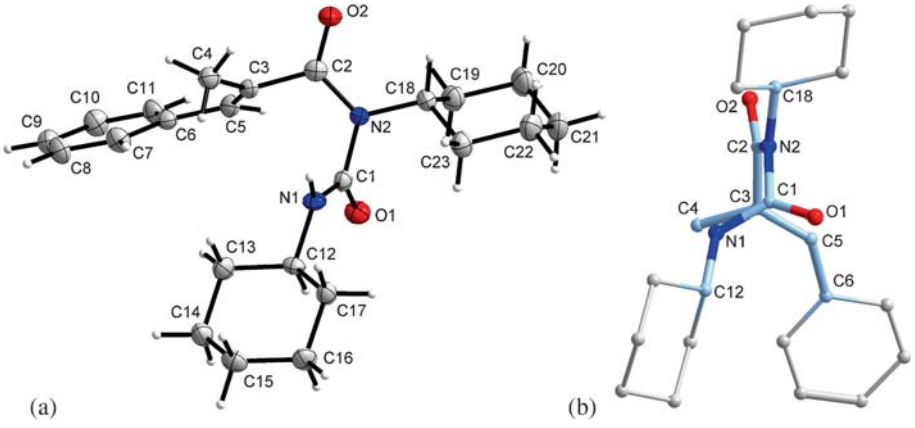


Figure 1. X-Ray structure of compound **12a**, showing the atom numbering scheme. (a) and the conformation of the main chain (b). Displacement ellipsoids in (a) are drawn at the 50% probability level.

Table 4. Selected geometric parameters (Å, °) for **12a**.

O(1)—C(1)	1.2240(14)	N(2)—C(1)	1.4356(14)
O(2)—C(2)	1.2251(13)	N(2)—C(18)	1.4827(13)
N(1)—C(1)	1.3266(14)	C(2)—C(3)	1.5036(15)
N(1)—C(12)	1.4602(13)	C(3)—C(5)	1.3291(17)
N(2)—C(2)	1.3670(14)		
C(1)—N(1)—C(12)	123.90(11)	C(2)—N(2)—C(18)	120.15(10)
C(2)—N(2)—C(1)	122.17(9)	C(1)—N(2)—C(18)	117.54(9)
C(12)—N(1)—C(1)—N(2)	−179.04	N(2)—C(2)—C(3)—C(5)	−68.12
C(2)—N(2)—C(1)—N(1)	−61.38	C(2)—C(3)—C(5)—C(6)	−172.65
C(1)—N(2)—C(2)—C(3)	−10.10		

parameters for non-H atoms. All H atoms were found in difference Fourier maps and were refined isotropically. In the final refinement cycles, the C-bonded H atoms were repositioned in their calculated positions and refined using a riding model, with C–H = 0.95–1.00 Å, and with U_{iso}(H) = 1.2U_{eq}(C) for CH and CH_2 or 1.5U_{eq}(C) for CH_3. N-bonded H atom was refined with N–H distance restrained to 0.880(2) Å, and with U_{iso}(H) = 1.2U_{eq}(N), and then it was constrained to ride on its parent atom (AFIX 3 instruction in *SHELXL2013*). Figures were made with the Diamond program.[35] Details of the conditions for the data collection and the structures refinements are given in table 1 and the crystallographic information file (CIF) deposited with The Cambridge Crystallographic Data Centre (www.ccdc.cam.ac.uk/; deposition number CCDC-1410529) and provided as Supplementary Information.

3. Results and Discussion

Carbodiimides such as dicyclohexylcarbodiimide (DCC) and diisopropylcarbodiimide (DIC) are very general reagents which are often used to activate carboxylic acid groups to nucleophilic substitution.[36–38] The following two general reactions have been found to take place. Firstly, it is the attachment of a proton, followed by the attack of the acid anion to form **3**. This can rearrange to make an acylurea **6**. Herein, we report the reaction of benzoic acid derivatives and (*E*)-cinnamic acid derivatives (**7**,**10**) with *N*, *N*′- dialkylcarbodiimide (**2**) in CH_2Cl_2 at room temperature to produce *N*-acylurea (**9**,**12**) (schemes 2 and 3, and tables 2 and 3). The reaction proceeded smoothly and cleanly under mild conditions and no side reactions were observed. In comparison with the previously reported methods, the important advantage of the reported method at ambient temperature is the use of water which is cheap, nontoxic and environmentally green solvent.

The structures of the products were deduced from their IR, Mass, ^{1}H NMR, ^{13}C NMR and elemental analyses. For example, the ^{1}H NMR spectrum of **9a** consisted of two doublets for the 4 CH_3 of isopropyl (δ = 0.98 and 1.42 ppm), two multiplets for 2 CH of isopropyl (δ = 3.75-3.87 and 4.31-4.45 ppm) and a doublet for NH (δ = 6.78 ppm, exchangeable by D_2O). The aryl groups exhibited characteristic signals in the aromatic region of the spectrum. The ^{1}H decoupled ^{13}C NMR spectrum of **9a** showed 10 distinct signals. Partial assignment of these signals is given in the experimental section. The ^{1}H and ^{13}C NMR spectra of compounds **9b–p** were similar to those of **9a**, except for the aromatic or heteroaromatic moieties, which exhibited characteristic signals with appropriate chemical shifts.

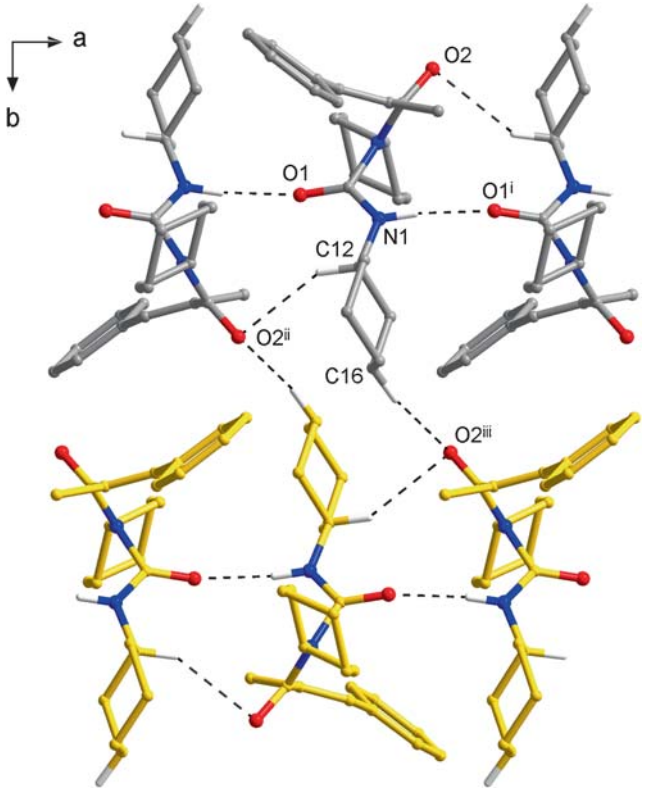


Figure 2. Arrangement of the molecules of **12a** within the layer parallel to (001) plane. Hydrogen bonds are shown as dashed lines. H atoms not involved in H-contacts are omitted for clarity. Symmetry codes are as in table 5.

Table 5. Hydrogen-bond geometry (Å, °) for **12a**.

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N(1)—H(1)···O(1)^{i}	0.88	1.97	2.8409(16)	171
C(12)—H(12)···O(2)^{ii}	1.00	2.59	3.4867(17)	149
C(16)—H(16*A*)···O(2)^{iii}	0.99	2.56	3.4737(15)	154

Symmetry codes: (i) $x+1/2, -y+3/2, -z+1$; (ii) $x-1/2, -y+3/2, -z+1$; (iii) $-x+3/2, y+1/2, z$.

We have also used electron-poor (*E*)-cinnamic acid **10** (scheme 3) instead of benzoic acid **7** in the reported reaction. The ^{1}H NMR spectrum of **12a** consisted of a multiplet for the 10 CH_2 of cyclohexyl ($\delta = 1.14$ - 1.82 ppm), two multiplets for 2 CH of cyclohexyl ($\delta = 3.55$-3.75 and 3.94-4.08 ppm), a singlet for CH_3 ($\delta = 2.11$ ppm), and a doublet for NH ($\delta = 7.14$ ppm, exchangeable by D_2O). The aryl groups exhibited characteristic signals in the aromatic region of the spectrum. The ^{1}H decoupled ^{13}C NMR spectrum of **12a** showed 17 distinct signals; partial assignment of these signals is given in the experimental section. The ^{1}H and ^{13}C NMR spectra of compounds **12b–l** were similar to those of **12a**, except for the aromatic moieties, and the alkyl groups exhibiting characteristic signals with appropriate chemical shifts. The structure of substituted *N*-acylurea **12a** was elucidated by X-ray single crystal analysis (figure 1).

As shown in table 4, the molecule of **12a** adopts bent conformation, with the main chain C(12)–N(1)–C(1)–N(2)–C(2)–C(3)–C(5)–C(6) arranged in a way shown in figure 1. Atoms C(1) and C(3) are in *synperiplanar* orientation (see the C1—N2—C2—C3 torsion angle), while the N(1), O(1) and C(4), C(5) are located on both sides of this four-atom planar fragment (in *sc* and *ac* conformation). As shown in figure 2 and table 5, screw rotation (2_1||[100]) and glide reflection (*b* glide plane) arrange molecules of **12a** into layers parallel to (001) plane *via* N–H···O and C–H···O hydrogen bonds.

4. Conclusions

In summary, we have described synthesis of *N*-acylurea derivatives (**9**,**12**) from carbodiimides **2** and carboxylic acids (**7**, **10**). The process is operationally very simple, fast and employs easily available reagents.

Supplementary Information

All additional information pertaining to characterization of the *N*-acylurea derivatives 9 and 12 are available in SI. IR spectra (Figures S3, S6, S9, S12, S15, S18, S21, S24, S27, S30, S33, S36, S39, S42, S45, S48, S51, S54, S57, S60, S63, S66, S69, S72, S75, S78, S81, S84), ^{1}H NMR spectra (Figures S4, S7, S10, S12, S16, S19, S22, S25, S28, S31, S34, S37, S40, S42, S46, S49, S52, S55, S58, S61, S64, S67, S70, S73, S76, S79, S82, S85), ^{13}C NMR spectra (Figures S5, S8, S11, S14, S17, S20, S22, S26, S29, S32, S35, S38, S41, S44, S47, S50, S53, S56, S59, S62, S65, S68, S71, S74, S77, S80, S83, S86). Supplementary Information is available at www.ias.ac.in/chemsci.

Acknowledgements

This work is funded by the grant NRF-2015-002423 of the National Research Foundation of Korea.

References

1. J Zhu and H Bienayme (eds.) 2005 *Multicomponent Reactions* (Weinheim: Wiley)
2. Shaabani A, Teimouri M B, Bazgir A and Bijanzadeh H R 2003 *Mol. Divers.* **6** 199
3. Yavari I, Mirzaei A, Hossaini Z and Souri S 2010 *Mol. Divers.* **14** 343
4. Ramazani A, Rezaei A, T Mahyari A, Rouhani M and Khoobi M 2010 *Helv. Chim. Acta.* **93** 2033
5. Yavari I, Sabbaghan M and Hossaini Z 2007 *Mol. Divers.* **11** 1
6. Domling A 2006 *Chem. Rev.* **106** 17
7. Ugi I, Werner B and Dömling A 2003 *Molecules* **8** 53
8. Williams A and Ibrahim I T 1981 *Chem. Rev.* **81** 589
9. Rebek J and Fitler D 1973*J. Am. Chem. Soc.* **95** 4052; (b) Rebek J and Feitler D 1974 *J. Am. Chem. Soc.* **96** 1606; (c) Rebek J and Feitler D 1975*J. Pept. Protein Res.* **7** 167
10. Klausner Y S and Bodansky M 1972 *Synthesis* **1** 453
11. Ramazani A and Mahyari A 2010 *Helv. Chim. Acta.* **93** 2203
12. Ramazani A and Bodaghi A 2000 *Tetrahedron Lett.* **41** 567
13. Pakravan P, Ramazani A, Noshiranzadeh N and Sedrpoushan A 2007 *Phosphorus, Sulfur Silicon Relat. Elem.* **182** 545
14. Ramazani A, Rahimifard M and Souldozi A 2007 *Phosphorus, Sulfur Silicon Relat. Elem.* **182** 1
15. Ramazani A, Rahimifard M, Noshiranzadeh N and Souldozi A 2007 *Phosphorus, Sulfur Silicon Relat. Elem.* **182** 413
16. Ramazani A, Ahmadi E, Kazemizadeh A. R, Dolatyari L, Noshiranzadeh N, Eskandari I and Souldozi A 2005 *Phosphorus, Sulphur, Silicon Relat. Elem.* **180** 2419

17. Ramazani A, Shajari N and Gouranlou F 2001 *Phosphorus, Sulfur Silicon Relat. Elem.* **174** 223
18. Ramazani A, Amini I and Massoudi A 2006 *Phosphorus, Sulfur Silicon Relat. Elem.* **181** 2225
19. Ramazani A, T Mahyari A, Rouhani M and Rezaei A 2009 *Tetrahedron Lett.* **50** 5625
20. Souldozi A, Ramazani A, Bouslimani N and Welter R 2007 *Tetrahedron Lett.* **48** 2617
21. Souldozi A and Ramazani A 2007 *Tetrahedron Lett.* **48** 1549
22. Souldozi A and Ramazani A 2009 *Phosphorus, Sulfur Silicon Relat. Elem.* **184** 3191
23. Souldozi A, Ślepokura K, Lis T and Ramazani A 2007 *Z. Naturforsch.* **62b** 835
24. Ramazani A and Rezaei A 2010 *Org. Lett.* **12** 2852
25. Ramazani A, Ahmadi Y, Rouhani M, Shajari N and Souldozi A 2010 *Heteroatom Chem.* **21** 368
26. Ramazani A, Ahmadi Y and Zeinali Nasrabadi F 2011 *Z. Naturforsch.* **66b** 184
27. Ramazani A, Zeinali Nasrabadi F, Mashhadi Malekzadeh A and Ahmadi Y 2011 *Monatsh. Chem.* **142** 625
28. Safaei-Ghomi J, Salimi F and Ramazani A 2013 *J. Chem. Sci.* **125** 1087
29. Ramazani A, Zeinali Nasrabadi F, Karimi Z and Rouhani M 2011 *Bull. Korean Chem. Soc.* **32** 2700
30. Massoudi A, Amini I, Ramazani A, Zeinali Nasrabadi F and Ahmadi Y 2012 *Bull. Korean Chem. Soc.* **33** 39
31. Ramazani A and Zeinali Nasrabadi F 2013 *Phosphorus, Sulfur, Silicon Relat. Elem.* **188** 1214
32. Ramazani A, Joo S W and Zeinali Nasrabadi F 2013 *Turk. J. Chem.* **37** 405
33. CrysAlisCCD and CrysAlisRED in KM4-CCD Software 2009 (Abingdon, England: Oxford Diffraction Ltd.)
34. Sheldrick G M 2008 *Acta Crystallogr. Sect. A* **64** 112
35. Brandenburg K 2005 *DIAMOND* Version 3.0 (Bonn, Germany: Crystal Impact GbR)
36. Sheehan J C and Hess G P 1955 *J. Am. Chem. Soc.* **77** 1067
37. Kohmoto S, Miyaji Y, Tsuruoka M, Kishikawa K, Yamamoto M and Yamada K 2001 *J. Chem. Soc. Perkin Trans.* 2082
38. Xi Z, Agback P, Sandström A and Chattopadhyaya J 1991 *Tetrahedron* **47** 9675