

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

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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

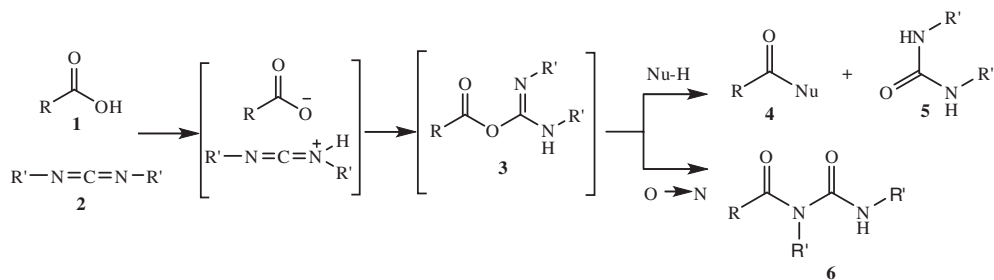
In recent years, there has been extreme interest on the applications of multicomponent reactions (MCRs) in modern synthetic organic chemistry.^{1–6} With respect to the simplicity of one-pot synthetic methods and high atom efficiency, MCRs have a highly significant position in comparison with other reactions.⁷ 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 known¹⁰ that in low dielectric constant solvents such as CH₂Cl₂, 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. ¹H and ¹³C NMR spectra (CDCl₃) 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 (F₂₅₄) powder.

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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 H₂O 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 (F₂₅₄) powder; petroleum ether–ethyl acetate (4:1)). The characterization data of the compounds are given below.

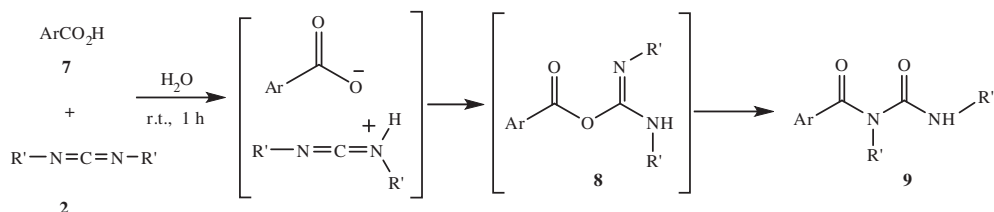
2.1a N-Benzoyl-N,N'-diisopropylurea (9a): White powder, (yield: 95%), M.p. 90–92°C. IR (KBr): $\nu = 3305$ (NH), 3072, 2977, 1678, 1646, 1550, 1459, 1315, 700 cm⁻¹. ¹H NMR (250 MHz, CDCl₃) δ (ppm): 0.97 (d, 6H, J = 6.3 Hz, CH₃ isopropyl); 1.42 (d, 6H, J = 6.3 Hz, CH₃ isopropyl); 3.72–3.90 (m, 1H, CH 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}). ¹³C NMR (62.5 MHz, CDCl₃) δ (ppm): 20.8, 22.2 (4CH₃, 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 C₁₄H₂₀N₂O₂ (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): $\nu = 3327$ (NH), 3077, 2973, 2855, 1708, 1639, 1550, 1376, 830 cm⁻¹. ¹H NMR (250 MHz, CDCl₃) δ

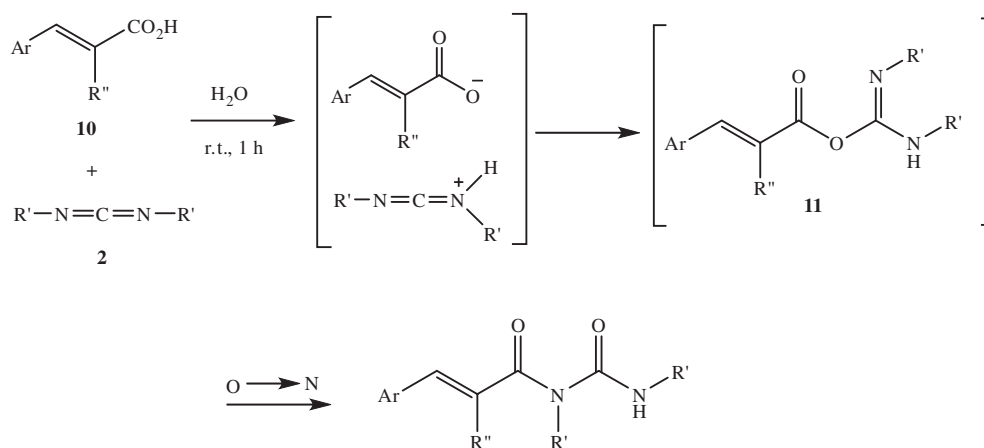
(ppm): 1.00 (d, 6H, J = 6.3 Hz, CH₃ isopropyl); 1.41 (d, 6H, J = 6.5 Hz, CH₃ isopropyl); 3.75–3.90 (m, 1H, CH isopropyl); 4.30–4.43 (m, 1H, CH isopropyl); 6.63 (d, 1H, J = 6.3 Hz, NH); 7.39 (d, 2H, J = 8.3 Hz, CH_{arom}); 7.55 (d, 2H, J = 8.3 Hz, CH_{arom}). ¹³C NMR (62.5 MHz, CDCl₃) δ (ppm): 20.8, 22.2 (4CH₃, 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 C₁₄H₁₉BrN₂O₂ (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): $\nu = 3296$ (NH), 3034, 2977, 1700, 1632, 1545, 1369, 800 cm⁻¹. ¹H NMR (250 MHz, CDCl₃) δ (ppm): 0.99 (d, 6H, J = 6.5 Hz, CH₃ isopropyl); 1.41 (d, 6H, J = 6.5 Hz, CH₃ isopropyl); 2.27 (s, 6H, CH₃); 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}). ¹³C NMR (62.5 MHz, CDCl₃) δ (ppm): 19.7, 19.8 (2CH₃); 20.9, 22.3 (4CH₃, 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 C₁₆H₂₄N₂O₂ (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**.

$\nu = 3327$ (NH), 3078, 2974, 1700, 1638, 1551, 1377, 831 cm^{-1} . ^1H 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 (4 CH_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 $\text{C}_{15}\text{H}_{22}\text{N}_2\text{O}_2$ (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): $\nu = 3313$ (NH), 3082, 2984, 1700, 1655, 1513, 1253, 837 cm^{-1} . ^1H 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 (4 CH_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 $\text{C}_{15}\text{H}_{22}\text{N}_2\text{O}_3$ (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): $\nu = 3351$ (NH), 3073, 2979, 1685, 1638, 1582, 1248, 758 cm^{-1} . ^1H 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 (4 CH_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 $\text{C}_{20}\text{H}_{24}\text{N}_2\text{O}_3$ (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): $\nu = 3310$ (NH), 3069, 2975, 1709, 1636, 1548, 1368, 741 cm^{-1} . ^1H 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 (4 CH_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 $\text{C}_{15}\text{H}_{22}\text{N}_2\text{O}_2$ (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): $\nu = 3307$ (NH), 3046, 2979, 1697, 1635, 1537, 1368, 800 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, $J = 6.5$ 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 (4 CH_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 $\text{C}_{15}\text{H}_{21}\text{BrN}_2\text{O}_2$ (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): $\nu = 3343$ (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 (4 CH_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 $\text{C}_{15}\text{H}_{19}\text{N}_3\text{O}_2$ (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): $\nu = 3327$ (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, $J = 6.7$ Hz, 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 (4 CH_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 $\text{C}_{14}\text{H}_{19}\text{ClN}_2\text{O}_2$ (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): $\nu = 3328$ (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 (4 CH_3 , isopropyl); 42.8, 50.0 (2CH, isopropyl); 115.7 (d, 2CH, $^2J_{\text{CF}} = 21.7$ Hz); 128.1 (d, 2CH, $^3J_{\text{CF}} = 8.0$ Hz); 142.0 (C, arom); 150.5 (d, C, $^1J_{\text{CF}} = 310.0$ Hz); 154.3, 177.0 (2C=O).

Analysis of $\text{C}_{14}\text{H}_{19}\text{FN}_2\text{O}_2$ (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): $\nu = 3325$ (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 (4 CH_3 , isopropyl); 42.7, 50.7 (2CH, isopropyl); 55.6 (2 OCH_3); 102.6, 103.9 (3CH, arom); 138.8, 160.9 (3C, arom); 154.2, 171.0 (2C=O). Analysis of $\text{C}_{16}\text{H}_{24}\text{N}_2\text{O}_4$ (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): $\nu = 3324$ (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, $J = 6.7$ Hz, 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 (4 CH_3 , isopropyl); 42.6, 50.2 (2CH, isopropyl); 31.1 (3 CH_3); 34.89 (C); 125.5, 126.3 (4CH, arom); 135.5, 143.1 (2C, arom); 154.2, 173.1 (2C=O). Analysis of $\text{C}_{18}\text{H}_{28}\text{N}_2\text{O}_2$ (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): $\nu = 3307$ (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, $J = 6.5$ Hz, 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 (4 CH_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 $\text{C}_{14}\text{H}_{19}\text{ClN}_2\text{O}_2$ (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): $\nu = 3377$ (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 (4 CH_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 $\text{C}_{18}\text{H}_{22}\text{N}_2\text{O}_2$ (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): $\nu = 3293$ (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, $J = 6.7$ Hz, 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 (4 CH_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 $\text{C}_{12}\text{H}_{18}\text{N}_2\text{O}_2\text{S}$ (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): $\nu = 3299$ (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 (10 CH_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 $\text{C}_{23}\text{H}_{32}\text{N}_2\text{O}_2$ (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): $\nu = 3276$ (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, $J = 6.5$ Hz, 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 (4 CH_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 $\text{C}_{17}\text{H}_{24}\text{N}_2\text{O}_2$ (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): $\nu = 3267$ (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 (10 CH_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 $\text{C}_{22}\text{H}_{30}\text{N}_2\text{O}_2$ (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): $\nu = 3273$ (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, $J = 7.5$ Hz, 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 (10 CH_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 $\text{C}_{23}\text{H}_{32}\text{N}_2\text{O}_2$ (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): $\nu = 3296$ (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, $\text{CH}=\text{CH}$); 6.95 (broad doublet, 1H, NH); 7.29-7.51 (m, 3H, CH_{arom}); 7.54 (d, 1H, $J = 15.2$ Hz, $\text{CH}=\text{CH}$). ^{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 $\text{C}_{22}\text{H}_{29}\text{ClN}_2\text{O}_2$ (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): $\nu = 3261$ (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, $\text{CH}=\text{CH}$); 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, $\text{CH}=\text{CH}$). ^{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 $\text{C}_{22}\text{H}_{29}\text{ClN}_2\text{O}_2$ (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-methoxyphenyl)-2-propenoyl]urea (**12g**): White powder, (yield: 85%), M.p. 78-80°C. IR (KBr): $\nu = 3260$ (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, $\text{CH}=\text{CH}$); 6.88-7.25 (m, 5H, NH and CH_{arom}); 7.59 (d, 1H, $J = 15.5$ Hz, $\text{CH}=\text{CH}$). ^{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 $\text{C}_{23}\text{H}_{32}\text{N}_2\text{O}_3$ (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): $\nu = 3280$ (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, $\text{CH}=\text{CH}$); 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, $\text{CH}=\text{CH}$). ^{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 $\text{C}_{16}\text{H}_{21}\text{ClN}_2\text{O}_2$ (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-methoxyphenyl)-2-propenoyl]urea (**12i**): White powder, (yield: 86%), M.p. 73-75°C. IR (KBr): $\nu = 3343$ (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, $\text{CH}=\text{CH}$); 6.90-7.32 (m, 4H, CH_{arom}); 7.50 (broad doublet, 1H, NH); 7.62 (d, 1H, $J = 15.2$ Hz, $\text{CH}=\text{CH}$). ^{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	$\text{C}_{23}\text{H}_{32}\text{N}_2\text{O}_2$
M_r	368.50
Crystal system, space group	Orthorhombic, <i>Pbca</i>
Temperature (K)	100(2)
<i>a</i> , <i>b</i> , <i>c</i> (Å)	9.534(3), 18.823(4), 23.587(4)
<i>V</i> (Å ³)	4232.9(18)
<i>Z</i>	8
Radiation type	Mo <i>K</i> α
μ (mm ⁻¹)	0.07
Crystal size (mm)	0.71 × 0.10 × 0.04
<i>T</i> _{min} , <i>T</i> _{max}	0.692, 1.000
No. of measured, independent and observed [<i>I</i> > 2σ(<i>I</i>)] reflections	13283, 5963, 3084
<i>R</i> _{int}	0.053
(sin θ/λ) _{max} (Å ⁻¹)	0.703
<i>R</i> [<i>F</i> ² > 2σ(<i>F</i> ²)], <i>wR</i> (<i>F</i> ²), <i>S</i>	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
$\Delta\rho_{\text{max}}$, $\Delta\rho_{\text{min}}$ (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).

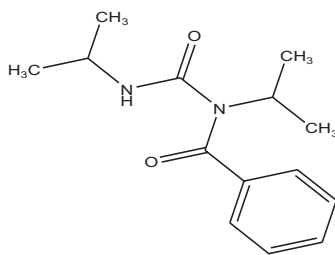
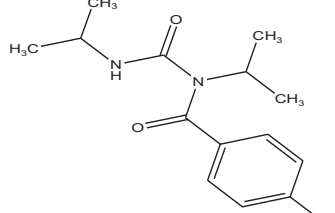
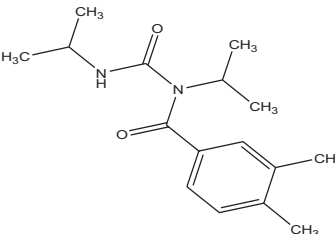
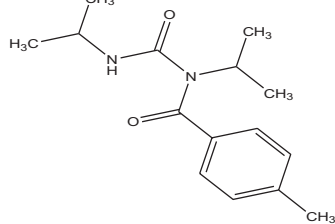
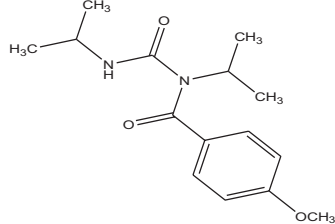
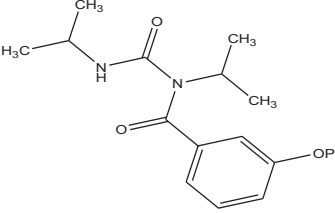
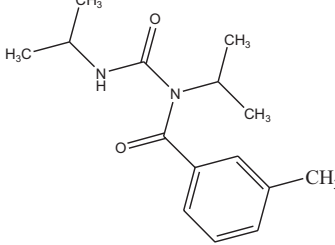
9	R'	Ar	Product	Yield (%)^a
a	Isopropyl	Ph		95
b	Isopropyl	4-BrC ₆ H ₄		94
c	Isopropyl	3,4-Me ₂ C ₆ H ₃		97
d	Isopropyl	4-MeC ₆ H ₄		96
e	Isopropyl	4-MeOC ₆ H ₄		90
f	Isopropyl	3-PhOC ₆ H ₄		92
g	Isopropyl	3-MeC ₆ H ₄		95

Table 2. (continued)

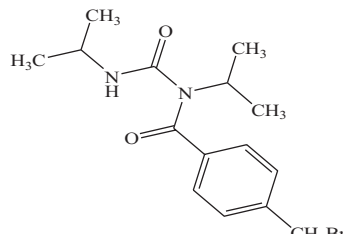
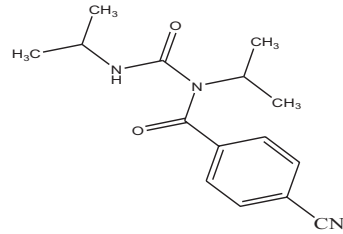
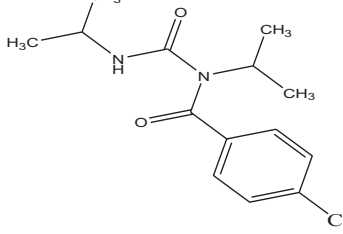
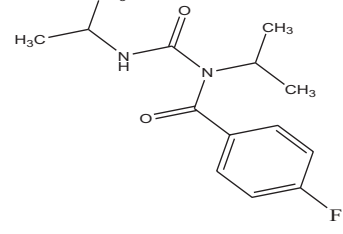
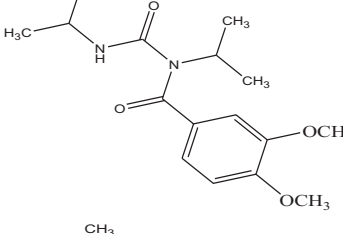
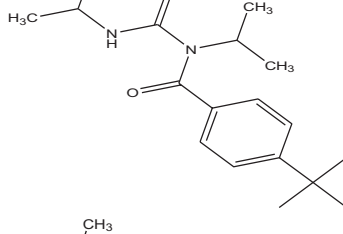
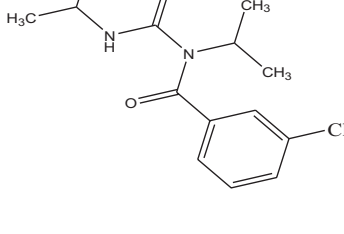
9	R'	Ar	Product	Yield (%) ^a
h	Isopropyl	4-BrCH ₂ C ₆ H ₄		90
i	Isopropyl	4-NCC ₆ H ₄		92
j	Isopropyl	4-ClC ₆ H ₄		93
k	Isopropyl	4-FC ₆ H ₄		90
l	Isopropyl	3,4-MeO ₂ C ₆ H ₃		92
m	Isopropyl	4-t-BuC ₆ H ₄		94
n	Isopropyl	3-ClC ₆ H ₄		96

Table 2. (continued)

9	R'	Ar	Product	Yield (%) ^a
o	Isopropyl	C ₁₁ H ₈ O ₂		95
p	Isopropyl	C ₅ H ₄ SO ₂		93

^aYield of isolated **9**.

55.3 (OCH₃); 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 C₁₇H₂₄N₂O₃ (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): $\nu = 3286$ (NH), 3073, 2979, 1706, 1651, 1611, 1465, 1374, 787 cm⁻¹. ¹H NMR (250 MHz, CDCl₃) δ (ppm): 1.23 (d, 6H, J = 6.5 Hz, CH₃ isopropyl); 1.44 (d, 6H, J = 6.7 Hz, CH₃ 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). ¹³C NMR (62.5 MHz, CDCl₃) δ (ppm): 21.0, 22.6 (4CH₃, 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 C₁₆H₂₁ClN₂O₂ (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): $\nu = 3284$ (NH), 3068, 2975, 1705, 1649, 1606, 1372, 759 cm⁻¹. ¹H NMR (250 MHz, CDCl₃) δ (ppm): 1.23 (d, 6H, J = 6.5 Hz, CH₃ isopropyl); 1.46 (d, 6H, J = 6.7 Hz, CH₃ 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). ¹³C NMR (62.5 MHz, CDCl₃) δ (ppm): 21.2, 22.6 (4CH₃, 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 C₁₆H₂₂N₂O₂ (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): $\nu = 3322$ (NH), 3066, 2970, 1695, 1650, 1531, 1262, 763 cm⁻¹. ¹H NMR (250 MHz, CDCl₃) δ (ppm): 1.17 (d, 6H, J = 6.2 Hz, CH₃ isopropyl); 1.46 (d, 6H, J = 6.7 Hz, CH₃ isopropyl); 2.14 (s, 3H, CH₃); 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). ¹³C NMR (62.5 MHz, CDCl₃) δ (ppm): 15.8 (CH₃); 21.0, 22.6 (4CH₃, 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 C₁₇H₂₄N₂O₂ (288.38). (% calculation/ found): C: 70.80/ 70.76, H: 8.39/ 8.43, N: 9.71/ 9.76.

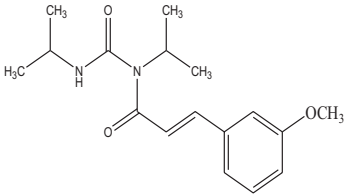
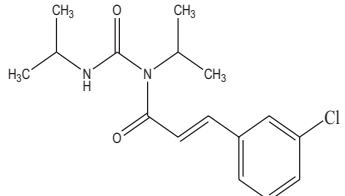
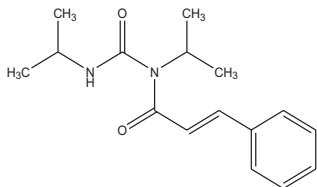
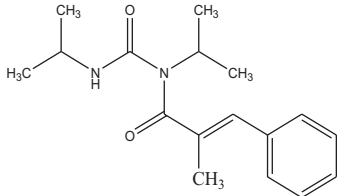
2.2 X-Ray crystallography

Crystals of **12a** for X-ray analysis were obtained by very slow evaporation of a CH₃OH/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 ₆ H ₄		89
c	Cyclohexyl	H	Ph		86
d	Cyclohexyl	H	4-MeC ₆ H ₄		89
e	Cyclohexyl	H	3-ClC ₆ H ₄		89
f	Cyclohexyl	H	4-ClC ₆ H ₄		87
g	Cyclohexyl	H	3-MeOC ₆ H ₄		85
h	Isopropyl	H	4-ClC ₆ H ₄		86

Table 3. (continued)

12	R'	R''	Ar	Product	Yield (%) ^a
i	Isopropyl	H	3-MeOC ₆ H ₄		86
j	Isopropyl	H	3-ClC ₆ H ₄		88
k	Isopropyl	H	Ph		86
l	Isopropyl	CH ₃	Ph		89

^aYield 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 MoK α radiation ($\lambda = 0.71073$ 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 CrysAlis-CCD 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

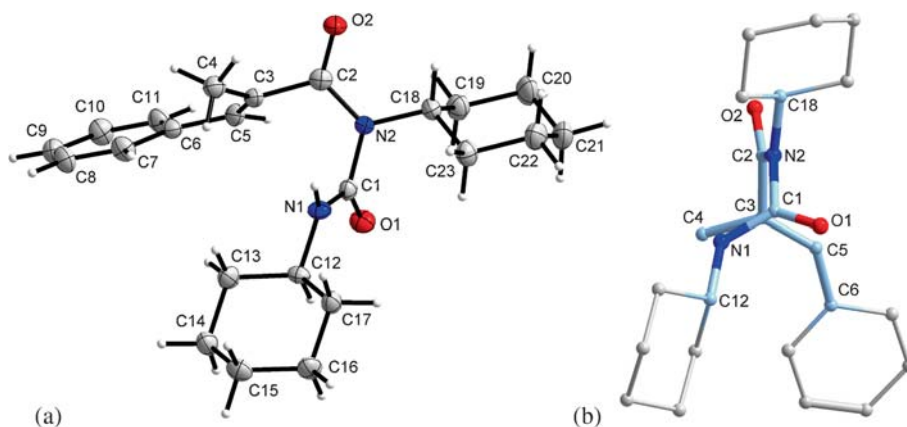


Figure 1. X-Ray structure of compound **12a**, showing the atom numbering scheme. (a) and the conformation of the main chain (b). Displacement ellipsoids in (a) are drawn at the 50% probability level.

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 $U_{\text{iso}}(\text{H}) = 1.2U_{\text{eq}}(\text{C})$ for CH and CH₂ or $1.5U_{\text{eq}}(\text{C})$ for CH₃. N-bonded H atom was refined with N—H distance restrained to 0.880(2) Å, and with $U_{\text{iso}}(\text{H}) = 1.2U_{\text{eq}}(\text{N})$, 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 CH₂Cl₂ 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, ¹H NMR, ¹³C NMR and elemental analyses. For example, the ¹H NMR spectrum of **9a**

consisted of two doublets for the 4 CH₃ of isopropyl ($\delta = 0.98$ and 1.42 ppm), two multiplets for 2 CH of isopropyl ($\delta = 3.75$ –3.87 and 4.31–4.45 ppm) and a doublet for NH ($\delta = 6.78$ ppm, exchangeable by D₂O). The aryl groups exhibited characteristic signals in the aromatic region of the spectrum. The ¹H decoupled ¹³C NMR spectrum of **9a** showed 10 distinct signals. Partial assignment of these signals is given in the experimental section. The ¹H and ¹³C 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.

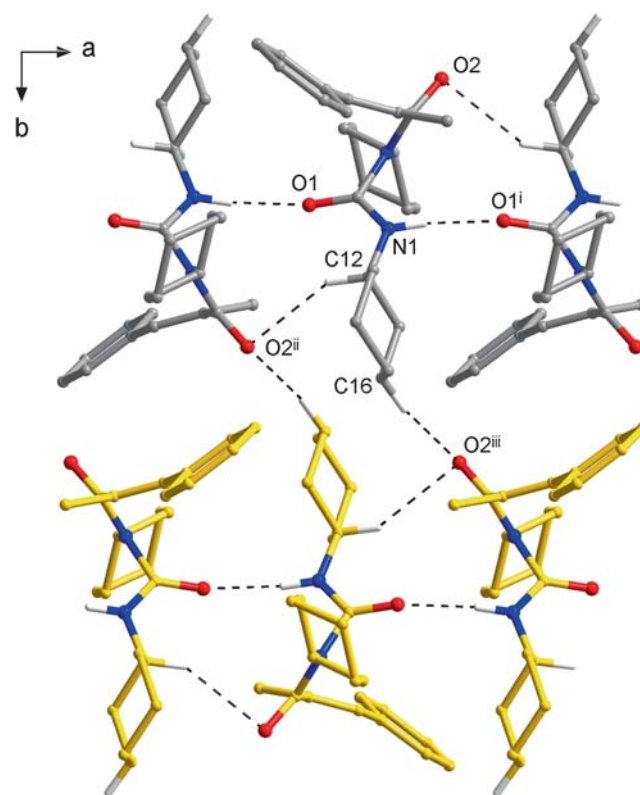


Figure 2. Arrangement of the molecules of **12a** within the layer parallel to (001) plane. Hydrogen bonds are shown as dashed lines. H atoms not involved in H-contacts are omitted for clarity. Symmetry codes are as in table 5.

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

<i>D</i> —H... <i>A</i>	<i>D</i> —H	H... <i>A</i>	<i>D</i> ... <i>A</i>	<i>D</i> —H... <i>A</i>
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(16A)...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 ¹H NMR spectrum of **12a** consisted of a multiplet for the 10 CH₂ 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 CH₃ ($\delta = 2.11$ ppm), and a doublet for NH ($\delta = 7.14$ ppm, exchangeable by D₂O). The aryl groups exhibited characteristic signals in the aromatic region of the spectrum. The ¹H decoupled ¹³C NMR spectrum of **12a** showed 17 distinct signals; partial assignment of these signals is given in the experimental section. The ¹H and ¹³C 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), ¹H 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), ¹³C 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.

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