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DIRECT AMIDATION OF (2-BENZAZOLYLTHIO)ACETIC ACIDS BY STERICALLY HINDERED CARBODIIMIDES

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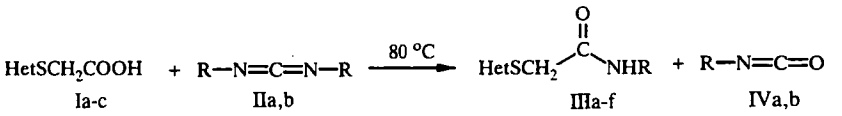
Carbon acids react with carbodiimides to form acid anhydrides and N,N'-disubstituted ureas and/or N-acyl-N,N'-disubstituted ureas [1, 2]. As a rule in this reaction only the simplest aliphatic and aromatic acids and carbodiimides have been investigated [3, 4].

There is only one report of the reaction of (2-heterylthio)acetic acids with carbodiimides. Specifically, it was shown [5] that (2-pyridylthio)acetic acid reacts with dicyclohexylcarbodiimides to give thiazolo[3,2-a]pyridine-3-oxide.

Our previous report [6] of the anomalous reaction of aliphatic and aromatic carbon acids with sterically hindered carbodiimides served as an important reason for investigation of (2-benzazolylthio)acetic acids Ia-c. It was found that acids Ia-c react with the sterically hindered carbodiimides (IIa, b) when heated in benzene to give high yields of the (2-benzazolylthio)acetic acid amides (IIIa-f) and isocyanates (IVa, b), i.e., achieving direct amidation of acids of type I.



I a Het = benzoxazol-2-yl; b Het = benzothiazol-2-yl, c Het = benzimidazol-2-yl;
II, IV a R = 2,4,6-$(CH_3)_3C_6H_2$, b R = 2,6-$(C_3H_7$-*i*$)C_6H_3$; III a R = 2,4,6-$(CH_3)_3C_6H_2$,
Het = benzoxazol-2-yl; b R = 2,6-$(C_3H_7$-*i*$)$, Het = benzothiazol-2-yl; c R = 2,4,6-$(CH_3)_3C_6H_2$,
Het = benzimidazol-2-yl; d R = 2,6-$(C_3H_7$-*i*$)C_6H_3$, Het = benzoxazol-2-yl;
e R = 2,6-$(C_3H_7$-*i*$)C_6H_3$, Het = benzothiazol-2-yl; f R = 2,6-$(C_3H_7$-*i*$)C_6H_3$, Het = benzimidazol-2-yl

Bearing in mind that the basic compounds needed for the synthesis of amides of (2-benzazolylthio)acetic acids (the acid chlorides) are not known but that the carbodiimides IIa, b are relatively available compounds [7, 8], the reported reaction can serve as a suitable method for the synthesis of sterically hindered (2-benzazolylthio)acetic acid amides.

A mixture of the acid (Ia-c, 0.01 mole) and the carbodiimide (IIa, b, 0.01 mole) in benzene (25 ml) was refluxed for 5-18 h (the completion of the reaction was monitored by IR spectroscopy by following the disappearance of the carbodiimide group absorption band at 2170 cm^{-1}). Solvent was evaporated and the residue was treated with hexane (10 ml) and held at 0-5°C for 12 h. The amide precipitate (IIIa-f) was filtered off and the isocyanates (IVa, b [9, 10]) were obtained by distillation of the filtrate in 60-63% yields. IR spectra were recorded in compressed KBr and PMR spectra in DMSO-D_6.

(Benzoxazolyl-2-thio)acetic Acid N-mesitylamide (IIIa). mp 154-155°C (ethanol). IR spectrum: 1665 (C=O), 3275 cm^{-1} (N–H). PMR spectrum: 2.10 (6H, s, two CH_3 groups); 2.20 (3H, s, CH_3); 4.36 (2H, s, CH_2); 6.84 (2H, s, C_6H_2); 7.24-7.87 (4H, m, C_6H_4); 9.60 ppm (1H, br.s, NH). Yield 95%. Found, %: N 8.73; S 10.14. $C_{18}H_{18}N_2O_2S$. Calculated, %: N 8.85; S 9.82.

(Benzothiazolyl-2-thio)acetic Acid N-mesitylamide (IIIb), mp 138-140°C (benzene–hexane, 1:2). IR spectrum: 1665 (C=O), 3275 cm^{-1} (N–H). PMR spectrum: 2.13 (6H, s, two CH_3 groups); 2.22 (3H, s, CH_3); 4.35 (2H, s, CH_2); 6.84 (2H, s, C_6H_2); 7.43-7.92 (4H, m, C_6H_4); 8.74 ppm (1H, br.s, NH). Yield 77%. Found, %: N 8.01; S 18.44. $C_{18}H_{18}N_2OS_2$. Calculated, %: N 8.18; S 18.72.

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(Benzimidazolyl-2-thio)acetic Acid N-mesitylamide (IIIc), mp 165-166°C (benzene–hexane, 1:1). IR spectrum: 1670 (C=O), 3260 cm^{-1} (N–H). PMR spectrum: 2.10 (6H, s, two CH_3 groups); 2.19 (3H, s, CH_3); 4.60 (2H, s, CH_2); 5.74 (1H, br.s, NH); 6.82 (2H, s, C_6H_2); 7.11-7.96 (4H, m, C_6H_4); 8.70 ppm (1H, br.s, NH). Yield 64%. Found, %: N 13.12; S 10.07. $C_{18}H_{19}N_3OS$. Calculated, %: N 12.91; S 9.85.

(Benzoxazolyl-2-thio)acetic Acid N-(2,6-diisopropyl)phenylamide (IIId), mp 150-151°C (benzene–hexane, 1:1). IR spectrum: 1675 (C=O), 3280 cm^{-1} (N–H). PMR spectrum; 1.06 (12H, d, J = 7 Hz, four CH_3 groups); 3.28 (2H, heptet, J = 7 Hz, two CH groups); 4.36 (2H, s, CH_2); 7.17-7.61 (7H, m, C_6H_4, C_6H_3); 8.95 ppm (1H, br.s, NH). Yield 80%. Found, %: N 7.80; S 9.14. $C_{20}H_{24}N_2O_2S$. Calculated, %: N 7.86; S 8.91.

(Benzothiazolyl-2-thio)acetic Acid N-(2,6-diisopropyl)phenylamide (IIIe), mp 122-124°C (benzene–hexane, 1:1); IR spectrum: 1680 (C=O), 3290 cm^{-1} (N–H). PMR spectrum: 1.02 (12H, d, J = 7 Hz, four CH_3 groups); 3.15 (2H, heptet, J = 7 Hz, two CH groups); 4.36 (2H, s, CH_2); 7.17-7.61 (7H, m, C_6H_4, C_6H_3); 8.95 ppm (1H, br.s, NH). Yield 76%. Found, %: N 7.32; S 17.07. $C_{20}H_{24}N_2OS_2$. Calculated, %: N 7.52; S 17.21.

(Benzimidazolyl-2-thio)acetic Acid N-(2,6-diisopropyl)phenylamide (IIIf), mp 180-182°C (benzene–hexane, 1:1). IR spectrum: 1675 (C=O), 3310 cm^{-1} (N–H). PMR spectrum: 1.18 (12H, m, J = 7 Hz, four CH_3 groups); 3.32 (2H, heptet, J = 7 Hz, two CH groups); 4.22 (2H, s, CH_2); 7.21-7.92 ppm (8H, m, C_6H_4, C_6H_3). Yield 72%. Found, %: N 11.53; S 9.31. $C_{20}H_{25}N_3OS_2$. Calculated, %: N 11.82; S 9.02.

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