PREPARATION OF 2,4-DICHLOROBENZOYL SUBSTITUTED ISOXAZOLIDINES

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A characteristic feature of some commercial agrochemicals and drugs is the 2,4-dichlorobenzoyl building block[1 – 3]. Within the scope of our research aimed at utilization of 1,3-dipolar cycloaddition reactions to heterocycles as well to pesticide programme we report the 1,3-dipolar cycloaddition of C-(2,4-dichlorobenzoyl)-N-phenylnitrone (*I*) to some alkenes and partially saturated heterocycles.

EXPERIMENTAL

The melting points are uncorrected, the ^{1}H and ^{13}C NMR spectra of deuteriochloroform solutions containing tetramethylsilane as an internal reference were measured with a Varian VXR 300 spectrometer. The IR spectra were taken with Philips analytical PU 9800 FTIR spectrometer.

Isoxazolidines *II – XII*

C-(2,4-Dichlorobenzoyl)-N-phenylnitrone *I* (ref.[4]) (2.9 g, 10 mmol) and the appropriate dipolarophile (10 – 50 mmol) in benzene (50 ml) or chloroform (50 ml) was warmed to 40 – 50 °C within 10 min and then stirred at room temperature for 4 – 24 h (TLC monitoring). The solvent was evaporated under reduced pressure, the residue was purified on silica gel (chloroform) to give isooxazolidines *II – XII*. In some cases the cycloadduct was precipitated in pure state from the reaction mixture. Compounds *VI* and *VII* were obtained as viscose oils. Characteristic data for compounds *II – XII* are presented in Table I and NMR data are following:

2-Phenyl-3-(2,4-dichlorobenzoyl)-5-butylisoxazolidine (II). ^{1}H NMR spectrum: 0.84 t, 3 H (CH_3); 1.25 – 1.37 m, 4 H (2 × CH_2); 1.54 – 1.63 m, 2 H (CH_2); 2.31 – 2.53 m, 2 H (H-4); 4.05 m, 1 H (H-5); 5.02 dd, 1 H (H-3, J(3,4) = 8.7 and 8.4 Hz); 6.87 – 7.33m, 8 H (H-arom). ^{13}C NMR spectrum: 13.99 q (CH_3); 22.68 t (CH_2); 28.62 t (CH_2); 32.80 t (CH_2); 35.50 t (C-4); 73.09 d (C-5); 78.45 d (C-3), 114.09, 122.14, 127.24, 129.18, 129.61, 130.23, 130.90, 136.71, 136.88, 150.19 (C-arom); 201.48 s (C=O).

2,5-Diphenyl-3-(2,4-dichlorobenzoyl)isoxazolidine (III). ^{1}H NMR spectrum: 2.74 – 3.06 m, 2 H (H-4); 5.09 dd, 1 H (H-5, J(5,4A) = J(5,4B) = 8.4 Hz); 5.21 dd, 1 H (H-3), J(3,4A) = 8.4 Hz, J(3,4B) = 3.6 Hz); 7.00 – 7.48 m, 13 H (H-arom). ^{13}C NMR spectrum: 37.83 t (C-4); 73.35 d (C-3); 80.18 d (C-5); 114.22,

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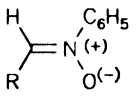
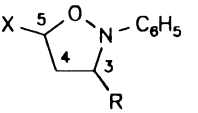
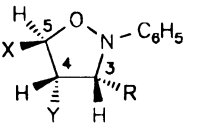


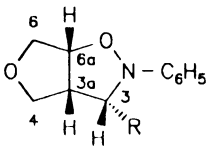
I



II, X = $CH_3(CH_2)_3$–
III, X = C_6H_5



IV, X = C_6H_5, Y = COOH
V, X = 2-furyl, Y = $COOC_2H_5$



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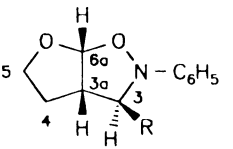
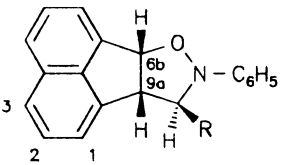


VII



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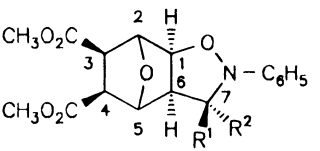
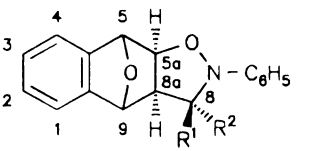
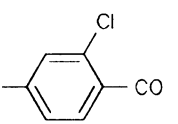


IX, R^1 = H, R^2 = R
X, R^1 = R, R^2 = H



XI, R^1 = H, R^2 = R
XII, R^1 = R, R^2 = H

In formulae *I*–*XII* : R = 

122.47, 127.27, 127.35, 128.07, 128.90, 129.24, 129.70, 130.39, 130.99, 136.83, 136.88, 137.36, 149.89 (C-arom); 200.93 s (C=O).

4-[2,5-Diphenyl-3-(2,4-dichlorobenzoyl)]isoxazolidinylcarboxylic acid (IV). ^{1}H NMR spectrum: 4.49 dd, 1 H (H-4), $J(4,5)$ = 3.0 Hz, $J(3,4)$ = 7.8 Hz); 5.28 d, 1 H (H-3); 5.78 d, 1 H (H-5); 6.99 – 7.48 m, 13 H (H-arom). ^{13}C NMR spectrum: 55.87 d (C-4); 74.80 d (C-3); 82.63 d (C-5); 114.56, 123.03, 127.45, 127.48, 128.83, 129.18, 129.41, 129.92, 130.52, 131.22, 135.91, 136.14, 137.35, 148.30 (C-arom); 170.33 s (C=O); 198.51 s (C=O).

Ethyl 4-[2-phenyl-3-(2,4-dichlorobenzoyl)-5-(2-furyl)]isoxazolidinylcarboxylate (V). ^{1}H NMR spectrum: 1.07 t, 3 H (CH_3); 4.02 q, 2 H (CH_2); 4.60 dd, 1 H (H-4, $J(3,4)$ = 6.9 Hz, $J(4,5)$ = 2.1 Hz); 5.50 d, 1 H (H-3); 5.76 d, 1 H (H-5); 6.41 dd, 1 H (H-furan, $J(3,4)$ = 3.1 Hz); 6.56 d, 1 H (H-furan); 6.99 dd, 1 H (H-furan); 7.09 – 7.49 m, 8 H (H-arom). ^{13}C NMR spectrum 13.93 q (CH_3); 53.57 d (C-4); 61.85 t (CH_2); 75.43 d (C-5); 76.28 d (C-3); 110.76, 110.85, 114.68, 123.02, 127.39, 129.23, 129.43, 130.39, 130.92, 136.51, 136.93, 143.79, 148.14, 148.73 (C-arom, C-furan); 170.24 s (C=O); 200.03 s (C=O).

2-Phenyl-3-(2,4-dichlorobenzoyl)-2,3,3a,4,6,6a-hexahydrofuro[3,4-d]isoxazole (VI). ^{1}H NMR spectrum: 3.48 – 3.57 m, 3 H (H-3a, H-4A, H-6A); 4.09 d, 1 H (H-4B, $J(4B,3a)$ = 10.8 Hz); 4.40 d, 1 H (H-6B), $J(6B,6a)$ = 9.3 Hz); 4.81 d, 1 H (H-3, $J(3,3a)$ = 9 Hz); 4.98 dd, 1 H (H-6a, $J(3a,6a)$ = 7.2 Hz), $J(6,6a)$ = 6.9 Hz); 6.97 – 7.44 m, 8 H (H-arom). ^{13}C NMR spectrum: 53.50 d (C-3a); 68.17 t (C-4); 71.98 d (C-3); 75.65 t (C-6); 83.44 d (C-6a); 114.27, 122.65, 126.77, 128.71, 128.92, 129.21, 131.16, 135.71, 138.15, 148.88 (C-arom); 204.12 s (C=O).

2-Phenyl-3-(2,4-dichlorobenzoyl)-2,3,3a,4,6,6a-hexahydrofuro[2,3-d]isoxazole (VII). ^{1}H NMR spectrum: 1.83 – 1.90 m, 1 H (H-4A); 2.11 – 2.25 m, 1 H (H-4B); 3.30 – 3.39 m, 1 H (H-3a); 3.76 – 3.90 m, 2 H (H-5), 4.99 s, 1 H (H-3); 5.99 d, 1 H (H-6a, $J(3a,6a)$ = 5.4 Hz); 6.87 – 7.41 m, 8 H (H-arom). ^{13}C NMR spectrum: 30.72 t (C-4); 48.57 d (C-3a); 68.41 t (C-5); 76.72 d (C-3); 109.61 d (C-6a); 114.10, 121.82, 127.46, 128.79, 129.63, 130.23, 130.57, 136.66, 137.06, 149.41 (C-arom); 198.48 s (C=O).

8-Phenyl-9-(2,4-dichlorobenzoyl)-9,9a-dihydro-6bH,8H-acenaphtho[1,2-d]isoxazole (VIII). ^{1}H NMR spectrum: 5.32 d, 1 H (H-9a), $J(6b, 9a)$ = 6.6 Hz); 5.61 s, 1 H (H-9); 6.15 d, 1 H (H-6b); 6.45 – 7.63 m, 14 H (H-arom). ^{13}C NMR spectrum: 54.31 d (C-9a); 75.85 d (C-9); 86.65 d (C-6b); 113.65, 119.80, 121.41, 122.17, 123.82, 125.37, 127.38, 127.42, 127.97, 128.17, 129.65, 130.36, 130.48, 130.99, 136.77, 137.05, 138.50, 141.15, 141.84, 148.54 (C-arom); 200.34 s (C=O).

3,4-Dimethoxycarbonyl-7-(2,4-dichlorobenzoyl)-8-phenyl-9-10-dioxa-8-azatricyclo[4,3,0,0^{2,5}]decane (IX-*anti*). ^{1}H NMR spectrum: 2.92 d, 1 H (H-4), $J(3,4)$ = 9.3 Hz); 2.97 d, 1 H (H-3); 3.46 dd, 1 H (H-6, $J(6,7)$ = 3.0 Hz, $J(1,6)$ 7.0 Hz); 3.64 s, 3 H ($COOCH_3$), 3.66 s, 3 H ($COOCH_3$); 4.54 d, 1 H (H-1); 4.84 s, 1 H (H-5); 4.88 d, 1 H (H-7); 4.93 s, 1 H (H-2); 6.86 – 7.44 m (H-arom). ^{13}C NMR spectrum: 46.70 d (C-4); 50.03 d (C-3); 52.35 q (CH_3); 52.43 q (CH_3); 54.86 d (C-6); 74.98 d (C-7); 80.37 d (C-5); 81.60 d (C-2); 84.74 d (C-1); 115.14, 122.73, 127.41, 128.91, 130.02, 130.29, 131.11, 135.97, 137.46, 149.29 (C-arom); 170.33 s (C=O); 170.36 s (C=O); 198.37 s (C=O).

3,4-Dimethoxycarbonyl-7-(2,4-dichlorobenzoyl)-8-phenyl-9,10-dioxa-8azatricyclo[4,3,0,0^{2,5}]decane (X-*syn*). ^{1}H NMR spectrum: 2.90 s, 2 H (H-3,H-4); 3.05 dd, 1 H (H-6, $J(1,6)$ = 6.3 Hz, $J(6,7)$ = 9.0 Hz); 3.72 s, 6 H (2 × $COOCH_3$); 4.49 d, 1 H (H-1); 4.83 d, 1 H (H-7); 4.99 s, 1 H (H-2); 5.27 s, 1 H (H-5); 7.00 – 7.56 m, 8 H (H-arom). ^{13}C NMR spectrum: 47.40 d (C-4); 49.55 d (C-3); 52.53 q (CH_3); 57.15 d (C-6); 74.35 d (C-7); 78.11 d (C-5); 80.06 d (C-2); 83.96 d (C-1); 114.33, 122.87, 126.82, 128.20, 129.33, 129.57, 130.73, 135.45, 138.31, 148.53 (C-arom); 170.31 s (C=O); 170.58 s (C=O); 205.03 (C=O).

7-Phenyl-8-(2,4-dichlorobenzoyl)-8,8a-dihydro-5aH,7H-5-9-epoxynaphthaleno[2,3-d]isoxazole (XI-*anti*). ^{1}H NMR spectrum: 3.48 dd, 1 H (H-8a, $J(5a,8a)$ = 6.3 Hz, $J(8,8a)$ = 3.3 Hz); 4.62 d, 1 H (H-5a); 4.94 d, 1 H (H-8); 5.26 s, 1 H (H-9); 5.37 s, 1 H (H-5); 6.84 – 7.45 m, 12 H (H-arom). ^{13}C NMR spectrum: 55.09 d (C-8a); 75.14 d (C-8); 81.45 d (C-9); 82.81 d (C-5); 85.25 d (C-5a); 115.04, 119.91, 120.88, 122.46, 127.29, 127.47, 127.71, 128.79, 130.00, 130.19, 131.19, 136.15, 137.29, 141.54, 145.09, 149.81 (C-arom); 191.10 s (C=O).

7-Phenyl-8-(2,4-dichlorobenzoyl)-8,8a-dihydro-5aH,7H-5,9-epoxynaphthaleno[2,3-d]isoxazole (XII-*syn*). ^{1}H NMR spectrum: 3.20 dd, 1 H (H-8a, J(5a,8a) = 6.3 Hz, J(8,8a) = 9.3 Hz); 4.68 d, 1 H (H-5a); 4.77 d, 1 H (H-8); 5.37 s, 1 H (H-5); 5.76 s, 1 H (H-9); 6.91 – 7.62 m (H-arom). ^{13}C NMR spectrum: 57.40 d (C-8a); 73.77 d (C-8); 78.95 d (C-9), 81.47 d (C-5); 86.14 d (C-5a); 114.25, 120.28, 120.71, 122.59, 126.82, 127.43, 127.80, 128.36, 129.16, 129.43, 130.84, 135.38, 138.73, 142.21, 144.61, 148.98 (C-arom); 205.95 s (C=O).

TABLE I
Characteristic data for compounds *II* – *XII*

Compound	Formula (M. w.)	M. p., °C (Yield, %)[a]	Calculated/Found			ν(C=O), cm^{-1}
			% C	% H	% N	
II	$C_{20}H_{21}Cl_2NO_2$ (378.3)	55 – 57 (42)	63.50 63.36	5.60 5.54	3.70 3.66	1 712
III	$C_{22}H_{17}Cl_2NO_2$ (398.3)	118 – 121 (81)	66.34 66.59	4.30 4.30	3.52 3.63	1 711
IV	$C_{23}H_{17}Cl_2NO_4$ (442.3)	121 – 123 (58)	62.45 62.17	3.87 4.05	3.17 3.20	1 713
V	$C_{23}H_{19}Cl_2NO_5$ (460.3)	87 – 88 (26)	60.01 59.79	4.16 4.20	3.04 3.06	1 732
VIII	$C_{26}H_{17}Cl_2NO_2$ (446.32)	125 – 128 (50)	69.94 69.96	3.84 3.88	3.14 3.12	1 706
IX	$C_{21}H_{21}Cl_2NO_7$ (506.3)	189 – 192 (24)	56.93 56.63	4.18 4.18	2.77 2.75	1 710
X	$C_{24}H_{21}Cl_2NO_7$ (506.3)	162 – 164 (23)	56.93 57.03	4.18 4.24	2.77 2.94	1 709
XI	$C_{24}H_{17}Cl_2NO_3$ (438.3)	140 – 142 (36)	65.75 65.59	3.91 4.10	3.16 3.23	1 709
XII	$C_{24}H_{17}Cl_2NO_3$ (438.3)	157 – 159 (23)	65.75 65.63	3.91 4.07	3.19 3.24	1 705

[a] Yields are calculated for compounds purified by chromatography.

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