Synthesis of (2*S*)-2-(Benzoylamino)-3-(heteroaryl)propyl Benzoates

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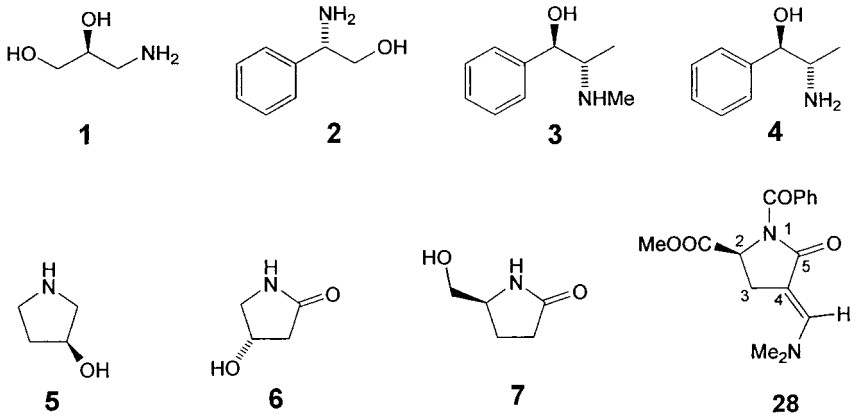
(3*E*,5*S*)-1-Benzoyl-5-[(benzoyloxy)methyl]-3-[(dimethylamino)methylidene]pyrrolidin-2-one (**9**) was prepared in two steps from commercially available (*S*)-5-(hydroxymethyl)pyrrolidin-2-one (**7**) (*Scheme 1*). Compound **9** gave, in one step, upon treatment with various C,N- and C,O-1,3-dinucleophiles **10**–**18**, the corresponding 3-(quinolizin-3-yl)- and 3-(2-oxo-2*H*-pyran-3-yl)-substituted (2*S*)-2-(benzoylamino)propyl benzoates **19**–**27** (*Schemes 1* and *2*).

Introduction. – Chiral β-amino alcohols and their derivatives found a wide application in the synthesis of optically active compounds, especially as chiral building blocks, chiral auxiliaries, and resolving agents (for an illustration, see [1]; for the synthesis of some β-amino alcohols, see [2]). As a consequence, numerous chiral synthons of this type, *e.g.,* (2*S*)-3-aminopropane-1,2-diol (**1**), (2*S*)-2-phenylglycinol (**2**), (1*R*,2*S*)-ephedrine (**3**), (1*R*,2*S*)-norephedrine (**4**), (3*S*)-pyrrolidin-3-ol (**5**), (4*S*)-4-hydroxypyrrolidin-2-one (**6**), and (5*S*)-5-(hydroxymethyl)pyrrolidin-2-one (**7**), are commercially available, usually in both enantiomeric forms. Previously, we have shown that 3-(dimethylamino)prop-2-enoates can serve as useful and versatile synthetic tools for the preparation of a variety of heterocyclic systems; for short reviews, see [3]; for recent publications, see [4]. In this connection, we have recently used chiral 3-(dimethylamino)prop-2-enoate analogs derived from L-glutamic and L-pyroglutamic acid for the preparation of (*S*)-3-(heteroaryl)alanine and (*S*)-3-(heteroaryl)lactic acid derivatives, as well as for the preparation of heterocyclic systems with an α-amino acid structural element partially incorporated into the cyclic system [5–11]. In continuation of our work in this field, we now report a novel, one-step synthesis of 3-(heteroaryl)-substituted (2*S*)-2-(benzoylamino)propyl benzoates **19**–**27** from easily available (3*E*,5*S*)-1-benzoyl-5-[(benzoyloxy)methyl]-3-[(dimethylamino)methylidene]pyrrolidin-2-one (**9**).

Results and Discussion. – The starting pyrrolidinone **9** was prepared in two steps from commercially available (*S*)-5-(hydroxymethyl)pyrrolidin-2-one (**7**) (*Scheme 1*). This was first fully protected by benzoylation of the OH and NH groups to give (*S*)-1-benzoyl-5-[(benzoyloxy)methyl]pyrrolidin-2-one (**8**), which, upon treatment with *tert*-butyl bis(dimethylamino)methyl ether (*Bredereck*'s reagent) and according to the procedure described previously for the preparation of analogous 5-substituted (3*E*,5*S*)-3-(dimethylamino)methylidene]pyrrolidin-2-ones and (3*E*,5*S*)-3-(dimethylamino)methylidene]tetrahydrofuran-2-ones [5][6], afforded the desired pyrrolidinone **9**. The orientation around the exocyclic C=C bond of **9** was determined by NMR.

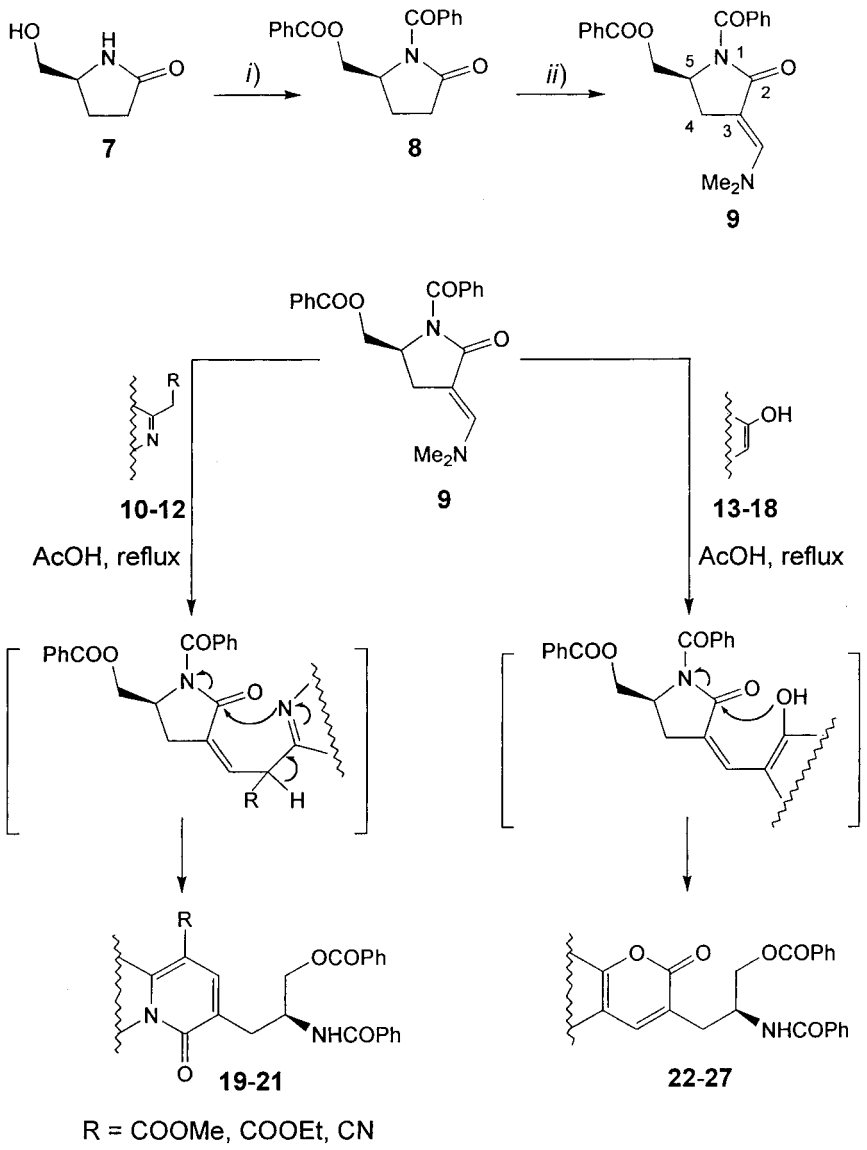


No NOE effect was observed between $Me_2N-CH=C$ and H–C(4) of **9**, thus indicating the (*E*)-configuration. Additionally, the chemical shift δ for $Me_2N-CH=C$ of **9** (7.08 ppm) is in agreement with that for $Me_2N-CH=C$ in structurally closely related methyl (2*S*,4*E*)-1-benzoyl-4-[(dimethylamino)methylidene]-5-oxopyrrolidine-2-carboxylate (**28**) (7.02 ppm) [5]. The (*E*)-configuration in **9** is also in agreement with the configuration of acyclic alkyl 3-(dimethylamino)prop-2-enoates, where the dimethylamino group is always *trans*-oriented with respect to the ester group [3][4].

Pyrrolidinone **9** was then treated in refluxing AcOH with two types of 1,3-dinucleophiles: pyridine-2-acetic acid and quinoline-2-acetic acid derivatives **10**–**12** and carbocyclic and heterocyclic 1,3-dicarbonyl compounds and their analogs **13**–**18** (*Schemes 1* and *2*). Treatment of **9** with C,N-dinucleophiles **10**–**12** afforded substituted (2*S*)-2-(benzoylamino)-3-(quinolizin-3-yl)propyl benzoates **19**–**21**, while, with C,O-dinucleophiles **13**–**18**, (2*S*)-2-(benzoylamino)-3-(2-oxo-2*H*-pyran-3-yl)propyl benzoates **22**–**27** were formed. Presumably, the transformation of **9** with 1,3-dinucleophiles **10**–**18** into 3-(heteroaryl)alaninol derivatives **19**–**27** proceeds *via* the 'ring switching' mechanism (*Scheme 1*). Thus, first the substitution of the dimethylamino group takes place, followed by the second attack of a dinucleophile at the ring carbonyl group, which results in simultaneous cleavage of the pyrrolidinone ring and formation of the 3-(heteroaryl)-substituted (2*S*)-2-(benzoylamino)-3-(heteroaryl)propyl benzoate. The proposed mechanism is supported by our previous results from the cyclic and acyclic 3-(dimethylamino)prop-2-enoate series [3][4][7–11], and by the results of *Young* and co-workers on the transformations of closely related (*S*)-3-(formyl)pyroglutamic-acid derivatives [12].

The structures of compounds **19**–**27** were confirmed by ^{1}H- and ^{13}C-NMR spectroscopy and by elemental analysis for C, H, and N. ^{1}H- and ^{13}C-NMR Spectra of compounds **19**–**27** are in agreement with NMR spectra of closely related 3-(heteroaryl)alanine and 3-(heteroaryl)lactic acid derivatives [7–10]. So far, the optical purity of the isolated products was not studied in detail; however, it might be presumed that, under the reaction conditions employed, a pronounced racemization of the β-amino alcohol structural element would be unlikely. The yields were not optimized and were generally relatively poor, especially when compared with the yields of related 3-(heteroaryl)alanine derivatives [7]. Nevertheless, since the precursor **9** is easily available and only one step is required for further transformation into amino

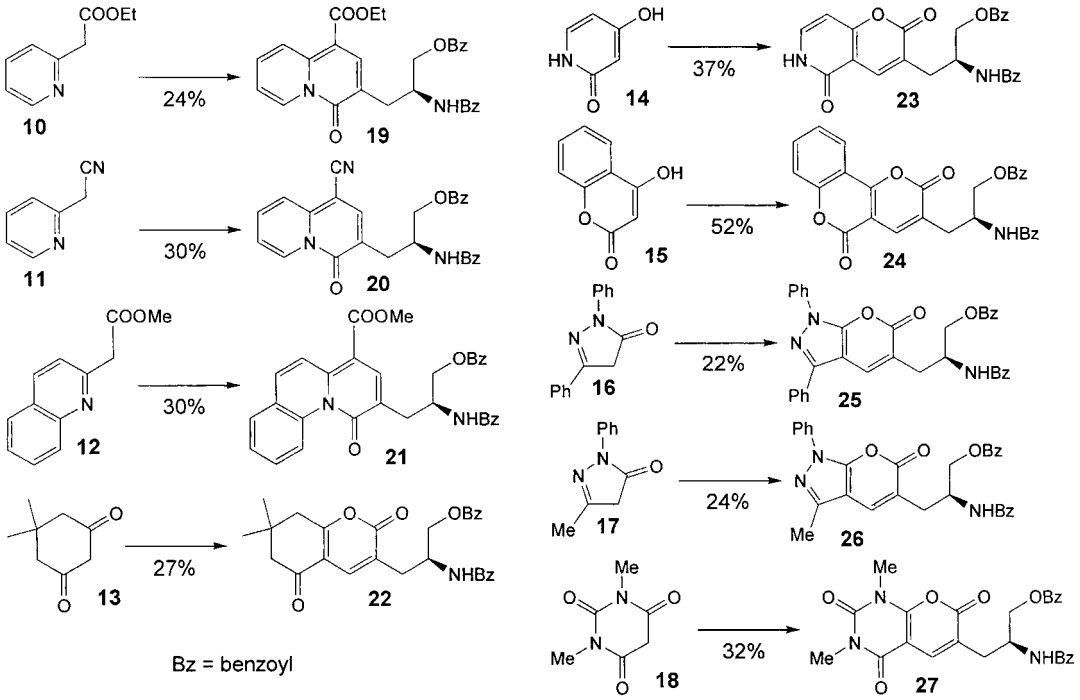
Scheme 1



i) PhCOCl, pyridine, r.t. *ii*) $(Me_2N)_2CHO^tBu$, toluene, 100°.

alcohols **19**–**27**, this method could be conveniently employed for a simple preparation of 3-(heteroaryl)alaninols.

Scheme 2



Experimental Part

General. All starting materials were commercially available (in most cases from *Fluka*) and purified by standard techniques. TLC: *Merck*, Al foils, silica gel *60 F 254*, 0.2 mm. M.p.: *Kofler* micro hot stage. Optical rotations: *Perkin-Elmer-241-MC* polarimeter. ^{1}H- and ^{13}C-NMR: *Bruker-Advance-DPX-300* spectrometer. Elemental analyses: *Perkin-Elmer* CHN analyser *2400*.

*(5*S*)-1-Benzoyl-5-[(benzoyloxy)methyl]pyrrolidin-2-one* (**8**). Benzoyl chloride (12.8 ml, 110 mmol) was added to a soln. of (5*S*)-5-(hydroxymethyl)pyrrolidin-2-one (**7**; 5.750 g, 50 mmol) in pyridine (50 ml), and the mixture was stirred at r.t. for 2 h. Volatile components were evaporated; $CHCl_3$ (150 ml) was added to the residue, the resulting soln. washed with 4% HCl soln. (100 ml) and aq. $NaHCO_3$ soln. (50 ml), dried (Na_2SO_4), and evaporated. The residue was triturated with Et_2O/petroleum ether 1:1 (60 ml), cooled (0°), and filtered off: **8** (13.25 g, 82%). M.p. 69–72° (Et_2O/petroleum ether). $[\alpha]_D^{23} = -153.2$ ($c = 0.85$, CH_2Cl_2). ^{1}H-NMR (300 MHz, $CDCl_3$): 2.10–2.20 (*m*, H–C(4)); 2.29–2.43 (*m*, H–C(4)); 2.56 (*ddd*, *J* = 4.2, 9.8, 18.1, H–C(3)); 2.79 (*ddd*, *J* = 9.0, 9.8, 17.7, H–C(3)); 4.57 (*dd*, *J* = 3.0, 11.7, 1 H, PhCOOCH_2); 4.78 (*dd*, *J* = 4.1, 11.7, 1 H, PhCOOCH_2); 4.87–4.93 (*m*, H–C(5)); 7.35–7.61 (*m*, 8 arom. H); 7.97–8.01 (*m*, 2 arom. H). ^{13}C-NMR (75.5 MHz, $CDCl_3$): 20.4; 31.4; 55.5; 64.7; 127.6; 128.5; 128.7; 129.1; 129.9; 131.6; 133.4; 134.8; 165.5; 170.1; 174.8. Anal. calc. for $C_{19}H_{17}NO_4$ (323.35): C 70.85, H 5.30, N 4.33; found: C 71.05, H 5.36, N 4.30.

*(3*E*,5*S*)-1-Benzoyl-5-[(benzoyloxy)methyl]-3-[(dimethylamino)methylidene]pyrrolidin-2-one* (**9**). A mixture of **8** (3.231 g, 10 mmol), toluene (20 ml), and *tert*-butyl bis(dimethylamino)methyl ether (2.610 g, 15 mmol) was heated at 90–100° for 2 h. The volatile components were evaporated and the solid residue crystallized from Et_2O: **9** (2.690 g, 71%). M.p. 116–118° (AcOEt/hexane). $[\alpha]_D^{23} = -29.9$ ($c = 0.95$, CH_2Cl_2). ^{1}H-NMR (300 MHz, $CDCl_3$): 2.98 (*ddd*, *J* = 1.5, 3.4, 14.3, H–C(4)); 2.98 (*s*, Me_2N); 3.20 (*ddd*, *J* = 1.5, 9.4, 14.3, H–C(4)); 4.63 (*dd*, *J* = 3.8, 11.3, 1 H, PhCOOCH_2); 4.68 (*dd*, *J* = 3.8, 11.3, 1 H, PhCOOCH_2); 4.70–4.77 (*m*, H–C(5)); 7.08 (br. *t*, *J* = 1.5, Me_2N–C*H*=C); 7.33–7.47 (*m*, 5 arom. H); 7.52–7.58 (*m*, 3 arom. H); 8.00–8.03 (*m*, 2 arom. H). ^{13}C-NMR (75.5 MHz, (D_6)DMSO): 26.4; 42.4; 53.6; 65.3; 92.6; 127.9; 128.8; 128.9; 130.1; 130.3; 131.3; 133.5; 136.4; 147.5; 166.9; 170.7; 171.4. Anal. calc. for $C_{22}H_{22}N_2O_4$ (378.43): C 69.83, H 5.86, N 7.40; found: C 69.98, H 5.90, N 7.52.

(2S)-2-(Benzoylamino)-3-(heteroaryl)propyl Benzoates **19**–**27**: *General Procedure.* A mixture of **9** (0.379 g, 1 mmol), 1,3-dinucleophile **10**–**18** (1 mmol), and glacial AcOH (4 ml) was heated under reflux for 2–3 h. Volatile components were evaporated, and the solid residue was crystallized from the appropriate solvent: (2*S*)-2-(benzoylamino)-3-(heteroaryl)propyl benzoates **19**–**27**.

*(2S)-2-(Benzoylamino)-3-[1-(ethoxycarbonyl)-4-oxo-4*H*-quinolizin-3-yl]propyl Benzoate* (**19**). From ethyl pyridine-2-acetate (**10**) (3 h): 0.122 g (24%) of **19**. M.p. 205–207° (AcOEt). $[\alpha]_D^{23} = -75.1$ ($c = 0.57$, DMF). ^{1}H-NMR (300 MHz, (D_6)DMSO): 1.22 (*t*, *J* = 7.2, $COOCH_2$*Me*); 2.95 (*dd*, *J* = 9.0, 13.6, H–C(3)); 3.18 (*dd*, *J* = 5.1, 13.4, H–C(3)); 4.22 (*q*, *J* = 7.2, $COOCH_2$Me); 4.37 (*dd*, *J* = 6.6, 11.1, H–C(1)); 4.57 (*dd*, *J* = 5.3, 10.9, H–C(1)); 4.64–4.75 (*m*, H–C(2)); 7.37–7.52 (*m*, 5 arom. H, H–C(7′)); 7.61–7.66 (*m*, 1 H of Ph); 7.72–7.75 (*m*, 2 H of Ph); 7.82–7.87 (*m*, H–C(8′)); 7.94–7.96 (*m*, 2 H of Ph); 8.37 (*s*, H–C(2′)); 8.52 (*d*, *J* = 8.3, NH); 9.05 (*d*, *J* = 9.0, H–C(9)); 9.20 (*d*, *J* = 7.2, H–C(6′)). ^{13}C-NMR (75.5 MHz, (D_6)DMSO): 15.0; 33.2; 48.7; 61.1; 66.9; 101.3; 116.3; 117.7; 123.9; 128.0; 128.9; 129.0, 129.5; 130.0; 130.5; 132.0; 134.2; 134.8; 135.6; 140.5; 144.1; 158.8; 165.4; 166.4; 167.4. Anal. calc. for $C_{29}H_{26}N_2O_6$ (498.54): C 69.87, H 5.26, N 5.62; found: C 69.69, H 5.07, N 5.70.

*(2S)-2-(Benzoylamino)-3-(1-cyano-4-oxo-4*H*-quinolizin-3-yl)propyl Benzoate* (**20**). From pyridine-2-acetonitrile (**11**) (3 h): 0.135 g (30%) of **20**. M.p. 194–196° (AcOEt). $[\alpha]_D^{23} = -92.3$ ($c = 0.62$, MeCOOH). ^{1}H-NMR (300 MHz, (D_6)DMSO): 2.94 (*dd*, *J* = 8.7, 13.6, H–C(3)); 3.13 (*dd*, *J* = 5.7, 13.6, H–C(3)); 4.38 (*dd*, *J* = 6.8, 10.9, H–C(1)); 4.47 (*dd*, *J* = 5.3, 10.9, H–C(1)); 4.69–4.81 (*m*, H–C(2)); 7.40–7.54 (*m*, 5 H of Ph, H–C(7)); 7.60–7.66 (*m*, 1 H of Ph); 7.72–7.75 (*m*, 2 H of Ph); 7.83–7.94 (*m*, H–C(8′), H–C(9′), 2 H of Ph); 8.06 (*s*, H–C(2′)); 8.46 (*d*, *J* = 8.7, NH)); 9.12–9.15 (*m*, H–C(6′)). ^{13}C-NMR (75.5 MHz, (D_6)DMSO): 32.5; 47.5; 66.0; 82.7; 114.0; 117.2; 117.3; 117.4; 122.5; 127.0; 128.1; 128.5; 128.9; 129.0; 131.1; 133.2; 134.5; 134.9; 139.3; 144.3; 157.2; 165.4; 166.5. Anal. calc. for $C_{27}H_{21}N_3O_4$ (451.48): C 71.83, H 4.69, N 9.31; found: C 71.55, H 4.68, N 9.54.

*(2S)-2-(Benzoylamino)-3-[4-(methoxycarbonyl)-1-oxo-1*H*-benzo[*c*]quinolizin-2-yl]propyl Benzoate* (**21**). From methyl quinoline-2-acetate (**12**) (3 h): 0.162 g (30%) of **21**. M.p. 217–219° (AcOEt). $[\alpha]_D^{23} = -8.4$ ($c = 0.56$, CH_2Cl_2). ^{1}H-NMR (300 MHz, (D_6)DMSO): 2.92 (*dd*, *J* = 9.9, 14.1, H–C(3)); 3.17 (*dd*, *J* = 4.5, 13.2, H–C(3)); 3.76 (*s*, MeO); 4.41 (*dd*, *J* = 6.8, 10.9, H–C(1)); 4.51 (*dd*, *J* = 5.1, 11.1, H–C(1)); 4.75–4.83 (*m*, H–C(2)); 7.39–7.52 (*m*, 5 H of Ph); 7.57–7.65 (*m*, 1 H of Ph, 2 H of Het); 7.71–7.74 (*m*, 2 H of Ph); 7.82–7.86 (*m*, 1 H of Het); 7.88 (*d*, *J* = 9.4, H–C(6′)); 7.94–7.97 (*m*, 2 H of Ph); 8.14 (*s*, H–C(3′)); 8.49 (*d*, *J* = 8.7, NH); 8.62 (*d*, *J* = 9.4, H–C(5′)); 9.33–9.36 (*m*, 1 H of Het). ^{13}C-NMR (75.5 MHz, (D_6)DMSO): 33.8; 48.4; 52.9; 67.1; 104.3; 120.9; 122.7; 124.8; 126.4; 127.9; 128.0; 128.8; 129.0; 129.3; 129.5; 130.0; 130.5; 132.0; 133.8; 134.2; 135.3; 135.6; 138.4; 144.5; 164.3; 166.2; 166.5; 167.5. Anal. calc. for $C_{32}H_{26}N_2O_6$ (534.57): C 71.90, H 4.90, N 5.24, found: C 71.74, H 4.54, N 4.95.

*(2S)-2-(Benzoylamino)-3-(5,6,7,8-tetrahydro-7,7-dimethyl-2,5-dioxo-2*H*-[1]benzopyran-3-yl)propyl Benzoate* (**22**). From 5,5-dimethylcyclohexane-1,3-dione (**13**) (3 h): 0.126 g (27%) of **22**. M.p. 140–142° (AcOEt). $[\alpha]_D^{23} = -72.1$ ($c = 0.68$, CH_2Cl_2). ^{1}H-NMR (300 MHz, (D_6)DMSO): 0.97 (*s*, Me); 1.02 (*s*, Me); 2.33 (*s*, CH_2(8′)); 2.70 (*dd*, *J* = 9.4, 13.6, H–C(3)); 2.73 (*s*, CH_2(6′)); 2.89 (*dd*, *J* = 4.3, 13.4, H–C(3)); 4.35 (*dd*, *J* = 5.8, 11.1, H–C(1)); 4.46 (*dd*, *J* = 5.3, 10.9, H–C(1)); 4.60–4.68 (*m*, H–C(2)); 7.39–7.55 (*m*, 5 H of Ph); 7.63–7.70 (*m*, 3 H of Ph, H–C(4′)); 7.96–7.99 (*m*, 2 H of Ph); 8.40 (*d*, *J* = 8.7, NH). ^{13}C-NMR (75.5 MHz, (D_6)DMSO): 28.2; 28.5; 33.2; 33.0; 47.7; 50.5; 66.9; 113.7; 123.4; 127.9; 129.1; 129.6; 130.1; 130.4; 132.1; 134.3; 135.4; 137.2; 162.0; 166.4; 167.6; 172.7; 194.8. Anal. calc. for $C_{28}H_{27}NO_6$(473.54): C 71.02, H 5.75, N 2.96; found: C 70.86, H 5.66, N 3.26.

*(2S)-2-(Benzoylamino)-3-(5,6-dihydro-2,5-dioxo-2*H*-pyrano[3,2-*c*]pyridin-3-yl)propyl Benzoate* (**23**). From pyridine-2,4-diol (**14**) (2 h): 0.166 g (37%) of **23**. M.p. 229–232° (AcOEt). $[\alpha]_D^{23} = -153.6$ ($c = 0.50$, DMF). ^{1}H-NMR (300 MHz, (D_6)DMSO): 2.77 (*dd*, *J* = 9.6, 13.8, H–C(3)); 2.94 (*dd*, *J* = 4.5, 13.6, H–C(3)); 4.37 (*dd*, *J* = 6.8, 10.9, H–C(1)); 4.46 (*dd*, *J* = 5.3, 10.9, H–C(1)); 4.61–4.73 (*m*, H–C(2)); 6.31 (*d*, *J* = 6.8, H–C(8′)); 7.39-7.56 (*m*, 5 H of Ph, H–C(7′)); 7.62–7.72 (*m*, 3 H of Ph); 7.78 (*s*, H–C(4′)); 7.96–7.98 (*m*, 2 H of Ph); 8.44 (*d*, *J* = 8.7, N*H*Bz); 11.90 (*s*, H–N(6′)). ^{13}C-NMR (75.5 MHz, (D_6)DMSO): 33.2; 48.0; 66.9; 98.3; 109.0; 123.1; 128.0; 129.1; 129.5; 130.1; 130.5; 132.0; 134.2; 135.5; 138.4; 138.8; 159.8; 161.4; 163.3; 166.4; 167.6. Anal. calc. for $C_{25}H_{20}N_2O_6$ (444.44): C 67.65, H 4.54, N 6.30; found: C 67.79, H 4.40, N 6.49.

*(2S)-2-(Benzoylamino)-3-(2,5-dioxo-2*H*,5*H*-pyrano[3,2-*c*][1]benzopyran-3-yl)propyl Benzoate* (**24**). From 4-hydroxy-2*H*-1-benzopyran-2-one (**15**) (2 h): 0.256 g (52%) of **24**. M.p. 231–233° (AcOEt). $[\alpha]_D^{23} = -311.1$ ($c = 0.44$, DMF). ^{1}H-NMR (300 MHz, (D_6)DMSO): 2.87 (*dd*, *J* = 9.4, 13.9, H–C(3)); 3.02 (*dd*, *J* = 4.7, 13.8, H–C(3)); 4.40 (*dd*, *J* = 6.4, 10.9, H–C(1)); 4.51 (*dd*, *J* = 5.3, 10.9, H–C(1)); 4.70–4.79 (*m*, H–C(2)); 7.39–7.52 (*m*, 5 H of Ph, 2 H of Het); 7.58–7.63 (*m*, 1 H of Ph); 7.70–7.80 (*m*, 2 H of Ph, 1 H of Het); 7.90 (*s*, H–C(4′)); 7.96–8.00 (*m*, 2 H of Ph, 1 H of Het); 8.49 (*d*, *J* = 8.7, NH). ^{13}C-NMR (75.5 MHz, (D_6)DMSO): 33.3; 47.8; 66.8; 104.3; 113.7; 117.9; 123.7; 126.2; 126.3; 128.0; 129.1; 129.5; 130.1; 130.4; 132.1; 134.2; 135.1; 135.4; 138.3; 153.5;

159.3; 160.2; 160.5; 166.4; 167.7. Anal. calc. for $C_{29}H_{21}NO_7$(495.49): C 70.30, H 4.27, N 2.83; found: C 70.15, H 4.37, N 2.93.

*(2*S*)-2-(Benzoylamino)-3-(1,6-dihydro-6-oxo-1,3-diphenylpyrano[2,3-*c*]pyrazol-3-yl)propyl Benzoate* (**25**). From 2,5-diphenyl-3*H*-pyrazol-3-one (**16**) (3 h): 0.128 g (22%) of **25**. M.p. 209–212° (AcOEt). $[\alpha]_D^{23} = -43.7$ ($c = 0.81$, CH_2Cl_2). ^{1}H-NMR (300 MHz, (D_6)DMSO): 2.84 (*dd*, *J* = 9.2, 13.8, H–C(3)); 3.00 (*dd*, *J* = 4.5, 13.9, H–C(3)); 4.43 (*dd*, *J* = 6.7, 10.9, H–C(1)); 4.52 (*dd*, *J* = 4.9, 10.9, H–C(1)); 4.67–4.77 (*m*, H–C(2)); 7.36–7.41 (*m*, 2 H of Ph); 7.43–7.52 (*m*, 7 H of Ph); 7.59–7.65 (*m*, 3 H of Ph); 7.73–7.81 (*m*, 4 H of Ph); 7.86–7.88 (*m*, 2 H of Ph); 7.96–7.98 (*m*, 2 H of Ph); 8.22 (*s*, H–C(4′)); 8.50 (*d*, *J* = 8.7, NH). ^{13}C-NMR (75.5 MHz, (D_6)DMSO): 33.5; 48.1; 66.9; 100.5; 117.9; 121.8; 127.6; 128.0; 128.5; 128.9; 129.1; 129.5; 129.9; 130.0; 130.4; 130.5; 132.1; 132.2; 134.2; 135.3; 137.3; 138.0; 145.8; 150.8; 160.3; 166.4; 167.6. Anal. calc. for $C_{35}H_{27}N_3O_5$ (495.49): C 73.78, H 4.78, N 7.38; found: C 73.87, H 4.65, N 7.45.

*(2*S*)-2-(Benzoylamino)-3-(1,6-dihydro-3-methyl-6-oxo-1-phenylpyrano[2,3-*c*]pyrazol-3-yl)propyl Benzoate* (**26**). From 5-methyl-2-phenyl-3 H-pyrazol-3-one (**17**) (3 h): 0.120 g (24%) of **26**. M.p. 160–162° (AcOEt). $[\alpha]_D^{23} = -26.3$ ($c = 0.65$, CH_2Cl_2). ^{1}H-NMR (300 MHz, (D_6)DMSO): 2.29 (*s*, Me); 2.77 (*dd*, *J* = 8.5, 13.8, H–C(3)); 2.94 (*dd*, *J* = 5.7, 13.9, H–C(3)); 4.39 (*dd*, *J* = 7.0, 11.1, H–C(1)); 4.49 (*dd*, *J* = 5.1, 11.1, H–C(1)); 4.63–4.75 (*m*, H–C(2)); 7.37-7.64 (*m*, 9 H of Ph); 7.72–7.78 (*m*, 4 H of Ph); 7.96–7.98 (*m*, 2 H of Ph, H–C(4′)); 8.45 (*d*, *J* = 8.7, NH). ^{13}C-NMR (75.5 MHz, (D_6)DMSO): 12.8; 33.8; 48.2; 66.7; 102.1; 116.4; 121.1; 127.9; 128.0; 128.0; 129.1; 129.5; 130.0; 130.4; 132.0; 134.2; 135.5; 137.4; 137.9; 144.8; 150.2; 160.7; 166.4; 167.6. Anal. calc. for $C_{30}H_{25}N_3O_5$ (507.55): C 70.99, H 4.96, N 8.28; found: C 71.24, H 4.83, N 8.18.

*(2*S*)-2-(Benzoylamino)-3-(2,3,4,7-tetrahydro-1,3-dimethyl-2,4,7-trioxo-2*H*-pyrano[2,3-*d*]pyrimidin-6-yl)-propyl Benzoate* (**27**). From 1,3-dimethylbarbituric acid (**18**) (3 h): 0.155 g (32%) of **27**. M.p. 189–191° (AcOEt). $[\alpha]_D^{23} = -148.2$ ($c = 0.51$, MeCOOH). ^{1}H-NMR (300 MHz, (D_6)DMSO): 2.79 (*dd*, *J* = 9.4, 14.3, H–C(3)); 2.89 (*dd*, *J* = 4.7, 13.8, H–C(3)); 3.20 (*s*, Me); 3.35 (*s*, Me); 4.34 (*dd*, *J* = 6.4, 10.9, H–C(1)); 4.47 (*dd*, *J* = 5.1, 11.1, H–C(1)); 4.59–4.70 (*m*, H–C(2)); 7.40–7.54 (*m*, 5 H of Ph); 7.61–7.68 (*m*, 1 H of Ph); 7.73–7.76 (*m*, 2 H of Ph); 7.91 (*s*, H–C(4′)); 7.96–7.99 (*m*, 2 H of Ph); 8.43 (*d*, *J* = 8.7, NH). ^{13}C-NMR (75.5 MHz, (D_6)DMSO): 28.8; 29.6; 32.3; 47.9; 66.9; 92.9; 116.0; 128.0; 129.1; 129.5; 130.1; 130.4; 132.1; 134.2; 135.4; 140.6; 150.2; 158.2; 159.5; 159.6; 166.4; 167.5. Anal. calc. for $C_{26}H_{23}N_3O_7$ (489.48): C 63.80, H 4.74, N 8.58; found: C 63.55, H 4.59, N 8.58.

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