The Synthesis of Pyrazolo[1,2-*a*]pyrazoles. Regio- and Stereo-Selective 1,3-Dipolar Cycloadditions of (1*Z*)-*rel*-(4*R*,5*R*)-1-Arylmethylene-4-benzoylamino-5-phenyl-3-pyrazolidinon-1-azomethinimines

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Reaction of *rel*-(4*R*,5*R*)-4-benzoylamino-5-phenyl-3-pyrazolidinone (**4**) with aromatic aldehydes **5a-f** gave the corresponding (1*Z*)-*rel*-(4*R*,5*R*)-1-arylmethylene-4-benzoylamino-5-phenyl-3-pyrazolidinon-1-azomethinimines **6a-f**. 1,3-Dipolar cycloadditions of azomethinimines **6a-f** to various dipolarophiles, which were found to proceed regio- and stereo-selectively, afforded the corresponding pyrazolo[1,2-*a*]-pyrazoles **8a-f**, **10**, and **13-16**. Reaction of azomethinimine **6a** with hydrogen cyanide gave *rel*-(5*R*,6*R*)-6-benzoylamino-5,6-dihydro-3,5-diphenyl-1-oxo-1*H*,7*H*-pyrazolo[1,2-*a*][1,2,3]triazole (**18**) as a representative of a new ring system.

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Recently, much attention has been payed to the synthesis of 2-amino-2,3-dihydro-1-oxo-1*H*,5*H*-pyrazolo[1,2-*a*]-pyrazole derivatives, since they were the first non-β-lactam containing compounds exhibiting inhibition of penicillin-binding proteins [1]. Especially, LY 186826, **1**, showed very strong activity which is even larger than that of several penicillins and cephalosporins [2] (Figure 1).

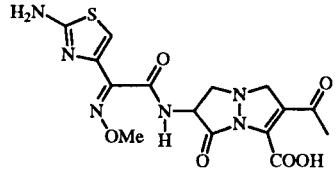
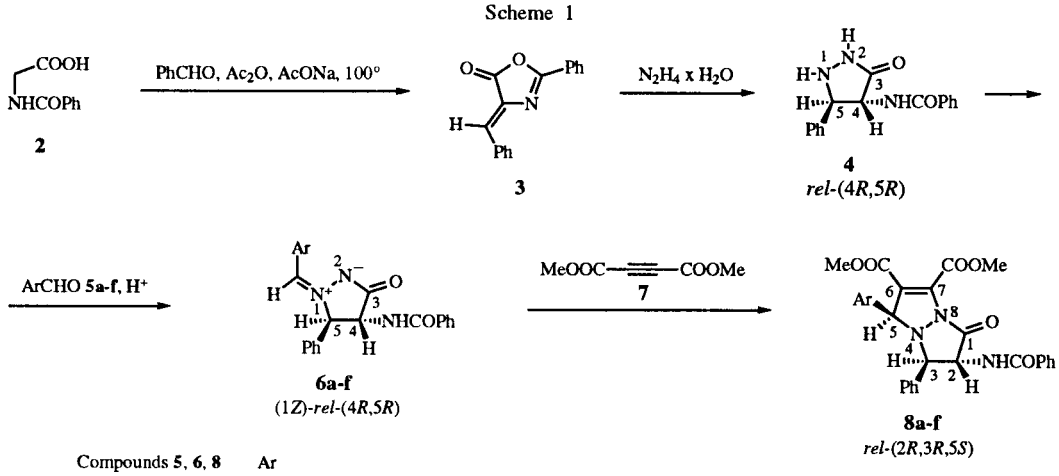


Figure 1. LY 186826 (**1**)

1,3-Dipolar cycloaddition of various acetylenes to 1-alkylidene-3-pyrazolidinon-1-azomethinimines is the most common reaction for the preparation of 2,3-dihydro-1-oxo-1*H*,5*H*-pyrazolo[1,2-*a*]pyrazoles [3-7]. However, much less work has been done on the transformations of 4-benzoylamino-5-phenyl-3-pyrazolidinone **4** [8]. In continuation of our work on the chemistry of azomethinimines [9-11], we now report some stereo-selective 1,3-dipolar cycloaddition reactions of (1*Z*)-*rel*-(4*R*,5*R*)-1-arylmethylene-4-benzoylamino-5-phenyl-3-pyrazolidinon-1-azomethinimines **6a-g**. We have chosen 4-benzoylamino-5-phenyl-3-pyrazolidinone (**4**), accessible in two steps from hippuric acid (**2**) *via* 4-benzylidene-2-phenyl-5(4*H*)-oxazolone **3** [8,12], as starting material. First, we examined

Scheme 1

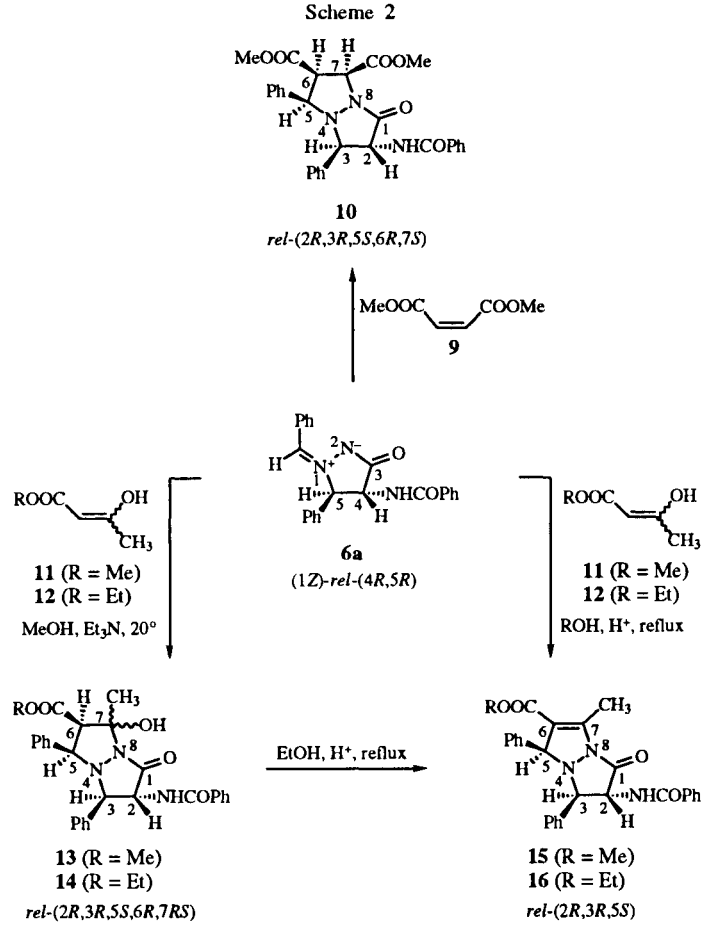


Compounds **5**, **6**, **8**	Ar
a	phenyl
b	4-methoxyphenyl
c	4-dimethylaminophenyl
d	4-nitrophenyl
e	3-nitrophenyl
f	2,6-dichlorophenyl

the relative configuration of the pyrazolidinone **4** by ^{1}H nmr, since no such assignments were given in the literature [8]. A large coupling constant, J_{H4H5} = 11.0 Hz, indicated *rel*-(4*R*,5*R*)-configuration of 4-benzoylamino-5-phenyl-3-pyrazolidinone (**4**). Pyrazolidinone **4** is therefore a racemate (α_D = 0.0°) with *trans*-configuration. Acid-catalysed reaction of *rel*-(4*R*,5*R*)-4-benzoylamino-5-phenyl-3-pyrazolidinone (**4**) with the following substituted benzaldehydes **5a-f**: benzaldehyde (**5a**), 4-methoxybenzaldehyde (**5b**), 4-dimethylaminobenzaldehyde (**5c**), 4-nitrobenzaldehyde (**5d**), 3-nitrobenzaldehyde (**5e**), and 2,6-dichlorobenzaldehyde (**5f**), gave the corresponding (1*Z*)-*rel*-(4*R*,5*R*)-1-arylmethylene-4-benzoylamino-5-phenyl-3-pyrazolidinon-1-azomethinimines **6a-f**. (*Z*)-Orientation around the exocyclic C=N double bond was determined by nmr (NOESY), which showed that the distance between H_5 and C*H*=N in azomethinimine **6a** is 0.25 nm. This observation is in contrast to our previous experiences with the structures of stable azomethinimines [9-11]. Cycloadditions of ylides **6a-f** to dimethyl acetylenedicarboxylate (**7**) afforded the corresponding diastereoisomerically pure *rel*-(2*R*,3*R*,5*S*)-5-aryl-2-benzoylamino-6,7-bis(methoxycarbonyl)-2,3-dihydro-1-oxo-3-phenyl-1*H*,5*H*-pyrazolo-[1,2-*a*]pyrazoles **8a-f**. The relative configuration of cycloadduct **8a** was determined by nmr (NOESY, d_{H3H5} = 0.24 nm). The distance between H_3 and H_5 in cycloadduct **8a** clearly indicates the *cis*-relationship. Consequently, cycloaddition of an azomethinimine **6** to dimethyl acetylenedicarboxylate (**7**) must take place almost exclusively at the less hindered face of azomethinimine **6**, in order to give the racemic cycloadduct **8** with *rel*-(2*R*,3*R*,5*S*)-configuration [13] (Scheme 1).

Next, we decided to examine this unexpected stereoselectivity in more detail. For this purpose, (1*Z*)-*rel*-(4*R*,5R)-1-benzylidene-4-benzoylamino-5-phenyl-3-pyrazolidinon-1-azomethinimine (**6a**), as the model azomethinimine, was treated with some other dipolarophiles such as dimethyl maleinate (**9**), methyl acetoacetate (**11**), ethyl acetoacetate (**12**), and hydrogen cyanide. It turned out that not only stereoselectivity but, with unsymmetrically substituted dipolarophiles **11** and **12**, also regioselectivity accompanied the cycloaddition reactions. Thus, treatment of (1*Z*)-*rel*-(4*R*,5*R*)-1-benzylidene-4-benzoylamino-5-phenyl-3-pyrazolidinon-1-azomethinimine (**6a**) with dimethyl maleinate (**9**) gave *rel*-(2*R*,3*R*,5*S*,6*R*,7*S*)-2-benzoylamino-6,7-bis(methoxycarbonyl)-3,5-diphenyl-1-oxoperhydropyrazolo[1,2-*a*]pyrazole (**10**) as the only diastereoisomer. The *cis*-orientation between the protons H_3 and H_5 was determined by nmr (NOESY, d_{H3H5} = 0.23 nm). Taking into account, that protons attached to the positions 5 and 6 are also *cis*-oriented (J_{H5H6} = 11.0 Hz), we concluded, that *exo*-approach of dimethyl maleinate (**9**) to the less hindered face of azomethinimine **6a** took place. Reaction of (1*Z*)-*rel*-(4*R*,5*R*)-1-benzylidene-4-benzoylamino-5-phenyl-3-pyrazolidinon-1-azomethinimine (**6a**) with methyl acetoacetate (**11**) and ethyl acetoacetate (**12**), performed in the presence of a base at room temperature, resulted in the formation of diastereoisomeric mixtures, *rel*-(2*R*,3*R*,5*S*,6*R*,7*RS*)-2-benzoylamino-3,5-diphenyl-7-hydroxy-6-methoxycarbonyl-7-methyl-1-oxoperhydropyrazolo[1,2-*a*]pyrazole (**13**) and *rel*-(2*R*,3*R*,5*S*,6*R*,7*RS*)-2-benzoylamino-3,5-diphenyl-6-ethoxycarbonyl-7-hydroxy-7-methylperhydropyrazolo[1,2-*a*]pyrazole (**14**), respectively. We distinguished between the diastereoisomers in the mixtures of **13** and **14** by ^{1}H nmr, since two sets of signals appear in the corresponding spectra. However, we were so far unable to separate these two diastereoisomers in a preparative manner. Fortunately, treatment of diastereoisomeric mixtures **13** and **14** with acid resulted in elimination of water and formation of diastereoisomerically pure products, *rel*-(2*R*,3*R*,5*S*)-2-benzoylamino-2,3-dihydro-3,5-diphenyl-6-methoxycarbonyl-7-methyl-1-oxo-1*H*,5*H*-pyrazolo-[1,2-*a*]pyrazole (**15**) and *rel*-(2*R*,3*R*,5*S*)-2-benzoylamino-2,3-dihydro-3,5-diphenyl-6-ethoxycarbonyl-7-methyl-1-oxo-1*H*,5*H*-pyrazolo[1,2-*a*]pyrazole (**16**), respectively. These transformations, however, proved the diastereoisomeric nature of mixtures **13** and **14**. *rel*-(2*R*,3*R*,5*S*)-2-

Scheme 2



Benzoylamino-2,3-dihydro-3,5-diphenyl-6-methoxycarbonyl-7-methyl-1-oxo-1*H*,5*H*-pyrazolo[1,2-*a*]pyrazole (**15**) and *rel*-(2*R*,3*R*,5*S*)-2-benzoylamino-2,3-dihydro-3,5-phenyl-6-ethoxycarbonyl-7-methyl-1-oxo-1*H*,5*H*-pyrazolo[1,2-*a*]pyrazole (**16**) have also been prepared directly by acid-catalysed reaction of (1*Z*)-*rel*-(4*R*,5*R*)-1-benzylidene-4-benzoylamino-5-phenyl-3-pyrazolidinone-1-azomethinimine (**6a**) with methyl acetoacetate (**11**) and ethyl acetoacetate (**12**), respectively. Both, a large coupling constant (J_{H5H6} = 10.9-11.2 Hz), which was

Table 1
Experimental and Analytical Data

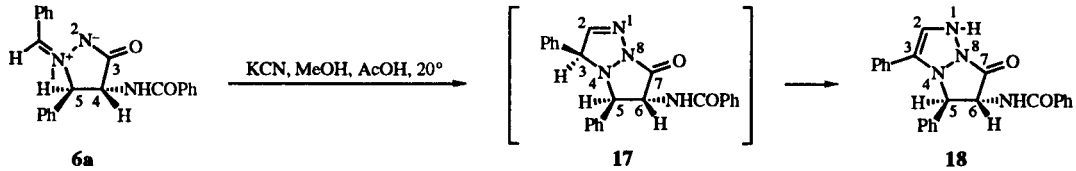
Compound	yield (%)	mp °C	M+ (m/e)	Molecular Formula Analyses
6a	89	240-241 (from ethanol)		$C_{23}H_{19}N_3O_2$ Calcd: C, 74.77; H, 5.19; N, 11.38 Found: C, 74.51; H, 5.14; N, 11.65
6b	78	228-230 (from ethanol)	399	$C_{24}H_{21}N_3O_3$ Calcd: C, 72.15; H, 5.30; N, 10.52 Found: C, 72.06; H, 5.06; N, 10.58
6c	93	252-254 (from ethanol)	412	$C_{25}H_{24}N_4O_2$ Calcd: C, 72.78; H, 5.87; N, 13.59 Found: C, 72.50; H, 5.60; N, 14.06
6d	76	169-171 (from ethanol)	414	$C_{23}H_{18}N_4O_4$ Calcd: C, 66.65; H, 4.38; N, 13.53 Found: C, 66.99; H, 4.31; N, 13.47
6e	90	207-209 (from ethanol)	414	$C_{23}H_{18}N_4O_4$ Calcd: C, 66.65; H, 4.38; N, 13.53 Found: C, 66.23; H, 4.04; N, 13.41
6f	88	214-216 (from ethanol)		$C_{23}H_{17}Cl_2N_3O_2$ Calcd: C, 63.15; H, 3.92; N, 9.61 Found: C, 63.07; H, 3.63; N, 9.94
8a	86	205-206 (from methanol)	511	$C_{29}H_{25}N_3O_6$ Calcd: C, 68.08; H, 4.93; N, 8.22 Found: C, 68.08; H, 4.88; N, 8.10
8b	75	197-198 (from methanol)		$C_{30}H_{27}N_3O_7$ Calcd: C, 66.52; H, 5.03; N, 7.76 Found: C, 66.63; H, 4.82; N, 8.07
8c	81	208-209 (from methanol)		$C_{31}H_{30}N_4O_6$ Calcd: C, 67.12; H, 5.46; N, 10.11 Found: C, 66.83; H, 5.24; N, 10.42
8d	80	174-175 (from methanol)		$C_{29}H_{24}N_4O_8$ Calcd: C, 62.57; H, 4.35; N, 10.07 Found: C, 62.35; H, 4.08; N, 10.23
8e	89	208-209 (from methanol)		$C_{29}H_{24}N_4O_8$ Calcd: C, 62.57; H, 4.35; N, 10.07 Found: C, 62.56; H, 4.10; N, 10.36
8f	77	227-229 (from methanol)		$C_{29}H_{23}Cl_2N_3O_6$ Calcd: C, 60.09; H, 4.00; N, 7.25 Found: C, 60.11; H, 3.83; N, 7.32
10	64	188-190 (from toluene)		$C_{29}H_{27}N_3O_6$ Calcd: C, 67.81; H, 5.30; N, 8.19 Found: C, 68.02; H, 5.06; N, 7.90
13	40	179-180 (washed with ether)		$C_{28}H_{27}N_3O_5$ Calcd: C, 69.25; H, 5.61; N, 8.66 Found: C, 69.46; H, 5.77; N, 8.70
14	63	173 (from methanol)		$C_{29}H_{29}N_3O_5$ Calcd: C, 69.71; H, 5.85; N, 8.42 Found: C, 69.42; H, 5.75; N, 8.74
15	66	216-218 dec (from methanol)		$C_{28}H_{25}N_3O_4$ Calcd: C, 71.92; H, 5.39; N, 8.99 Found: C, 71.60; H, 5.56; N, 9.12
16	62	200-201 (from methanol)		$C_{29}H_{27}N_3O_4$ Calcd: C, 72.32; H, 5.65; N, 8.73 Found: C, 72.06; H, 5.45; N, 8.71
18	81	254-255 dec (from ethanol/DMF)		$C_{24}H_{20}N_4O_2$ Calcd: C, 72.70; H, 5.09; N, 14.14 Found: C, 72.50; H, 5.00; N, 14.32

Table 2

^{1}H NMR Data

Compound	MHz Solvent	^{1}H NMR (δ - TMS)
4	300 DMSO-d_6	4.60 (1H, d, H_5), 4.99 (1H, dd, H_4), 5.49 (1H, br s, H_1), 7.28-7.37 (3H, m, 3H-Ph), 7.45-7.54 (5H, m, Ph), 7.84-7.87 (2H, m, 2H-Ph), 8.80 (1H, d, N*H*COPh), 9.56 (1H, s, H_2), J_{H4H5} = 11.0 Hz, J_{NHCH} = 9.0 Hz
6a	300 DMSO-d_6	4.65 (1H, dd, H_4), 5.80 (1H, dd, H_5), 7.40 (1H, br s, C*H*=N$^+$-N$^-$), 7.45-7.56 (11H, m, 11H-Ph), 7.87-7.90 (2H, m, 2H-Ph), 8.34-8.37 (2H, m, 2H-Ph), 9.23 (1H, d, N*H*COPh), J_{H4H5} = 5.2 Hz, J_{NHCH} = 7.8 Hz, $J_{H5\text{-}CH=N^+}$ = 0.8 Hz
6b	60 $CDCl_3$	3.84 (3H, s, CH_3), 5.07 (1H, t, H_4), 5.74 (1H, d, H_5), 6.67 (1H, s, C*H*=N$^+$-N$^-$), 6.82 (2H, d, 2H-Ar), 7.30-7.50 (8H, m, Ph and 3H-PhCO), 7.81-8.00 (2H, m, 2H-PhCO), 8.12 (2H, d, 2H-Ar), 8.50 (1H, d, N*H*COPh), J_{H4H5} = J_{NHCH} = 6.0 Hz, $J_{H5\text{-}CHN+}$ = 0.5 Hz, J_{Ar} = 9.0 Hz
6c	60 DMSO-d_6	3.00 (6H, s, NMe_2), 4.65 (1H, dd, H_4), 5.75 (1H, d, H_5), 6.80 (2H, d, 2H-Ar), 7.20 (1H, s, C*H*=N$^+$-N$^-$), 7.46-7.62 (8H, m, Ph and 3H-PhCO), 7.90-8.05 (2H, m, 2H-PhCO), 8.22 (2H, d, 2H-Ar), 9.20 (1H, d, N*H*COPh), J_{H4H5} = 5.0 Hz, J_{NHCH} = 8.0 Hz, J_{Ar} = 9.0 Hz
6d	60 DMSO-d_6	4.70 (1H, dd, H_4), 5.96 (1H, d, H_5), 7.50-7.62 (9H, m, Ph, 3H-PhCO, and C*H*=N$^+$-N$^-$), 7.87-8.02 (2H, m, 2H-PhCO), 8.35 (2H, d, 2H-Ar), 8.65 (2H, d, 2H-Ar), 9.33 (1H, d, N*H*COPh), J_{H4H5} = 5.4 Hz, J_{NHCH} = 7.6 Hz, J_{Ar} = 9.0 Hz
6e	60 DMSO-d_6	4.66 (1H, dd, H_4), 5.86 (1H, d, H_5), 7.35-7.65 (9H, m, Ph, 3H-PhCO, and C*H*=N$^+$-N$^-$), 7.80-8.00 (3H, m, 2H-PhCO and 1H-Ar), 8.28-8.68 (2H, m, 2H-Ar), 9.27 (1H, d, N*H*COPh), 9.48 (1H, m, 1H-Ar), J_{H4H5} = 5.0 Hz, J_{NHCH} = 8.2 Hz
6f	60 DMSO-d_6	4.81 (1H, dd, H_4), 5.86 (1H, d, H_5), 7.40-7.63 (12H, m, Ph, 3H-PhCO, 3H-Ar, and C*H*=N$^+$-N$^-$), 7.81-7.98 (2H, m, 2H-PhCO), 9.20 (1H, d, N*H*COPh), J_{H4H5} = 6.8 Hz, J_{NHCH} = 8.2 Hz, $J_{H5\text{-}CHN^+}$ = 0.8 Hz
8a	60 $CDCl_3$	3.54 (3H, s, OMe), 4.06 (3H, s, OMe), 4.71 (1H, d, H_3), 5.40 (1H, dd, H_2), 5.58 (1H, s, H_5), 7.19-7.78 (16H, m, 5H-Ar, 5H-Ph, 5H-PhCO, and N*H*COPh), J_{H2H3} = 11.0 Hz, J_{NHCH} = 8.6 Hz
8b	60 $CDCl_3$	3.59 (3H, s, OMe), 3.78 (3H, s, OMe), 4.05 (3H, s, OMe), 4.69 (1H, d, H_3), 5.34 (1H, dd, H_2), 5.53 (1H, s, H_5), 6.74 (2H, d, Ar), 7.02-7.76 (13H, m, 2H-Ar, 10H-Ph, and N*H*COPh), J_{H2H3} = 11.0 Hz, J_{NHCH} = 9.0 Hz, J_{Ar} = 9.2 Hz
8c	60 $CDCl_3$	2.86 (6H, s, NMe_2), 3.55 (3H, s, OMe), 4.02 (3H, s, OMe), 4.63 (1H, d, H_3), 5.30 (1H, dd, H_2), 5.43 (1H, s, H_5), 6.51 (2H, d, 2H-Ar), 7.00-7.74 (13H, m, 2H-Ar, 10H-Ph, and N*H*COPh), J_{H2H3} = 11.0 Hz, J_{NHCH} = 9.0 Hz, J_{Ar} = 8.8 Hz
8d	60 $CDCl_3$	3.58 (3H, s, OMe), 4.10 (3H, s, OMe), 4.76 (1H, d, H_3), 5.45 (1H, dd, H_2), 5.71 (1H, s, H_5), 7.12-7.73 (13H, m, 2H-Ar, 10H-Ph, and N*H*COPh), 8.10 (2H, d, 2H-Ar), J_{H2H3} = 11.0 Hz, J_{NHCH} = 8.2 Hz, J_{Ar} = 9.0 Hz
8e	60 DMSO-d_6	3.59 (3H, s, OMe), 3.98 (3H, s, OMe), 4.78 (2H, m, H_2 and H_3), 5.92 (1H, s, H_5), 7.07-8.15 (14H, m, 4H-Ar, and 10H-Ph), 9.18 (1H, d, N*H*COPh), J_{NHCH} = 9.0 Hz
8f	60 $CDCl_3$	3.60 (3H, s, OMe), 4.00 (3H, s, OMe), 4.32 (1H, d, H_3), 5.38 (1H, dd, H_2), 6.46 (1H, s, H_5), 6.50 (1H, d, N*H*COPh), 7.00-7.80 (13H, m, 3H-Ar, 10H-Ph), J_{H2H3} = 10.4 Hz, J_{NHCH} = 8.2 Hz
10	300 $CDCl_3$	3.58 (3H, s, OMe), 3.85 (3H, s, OMe), 3.86 (1H, dd, H_6), 4.37 (1H, d, H_3), 4.38 (1H, d, H_7), 4.82 (1H, dd, H_5), 5.57 (1H, dd, H_2), 6.76 (1H, d, N*H*COPh), 6.95-7.05 (6H, m, 6H-Ph), 7.11-7.21 (4H, m, 4H-Ph), 7.32-7.38 (2H, m, 2H-Ph), 7.42-7.48 (1H, m, 1H-Ph), 7.68-7.71 (2H, m, 2H-Ph), J_{H2H3} = 12.0 Hz, J_{H5H6} = 8.8 Hz, J_{H6H7} = 11.0 Hz, J_{H3H5} = 0.7 Hz, J_{NHCH} = 8.6 Hz
13	300 DMSO	major isomer **A** 1.96 (3H, s, 7-Me), 3.55 (3H, s, OMe), 3.57 (1H, d, H_6), 4.28 (1H, d, H_5), 4.38 (1H, d, H_3), 5.09 (1H, dd, H_2), 6.94-7.03 (6H, m, 6H-Ph), 7.10-7.14 (2H, m, 2H-Ph), 7.19 (1H, br s, OH), 7.21-7.25 (2H, m, 2H-Ph), 7.42-7.57 (3H, m, 3H-Ph), 7.79-7.83 (2H, m, 2H-Ph), 8.93 (1H, d, N*H*COPh), J_{H2H3} = 12.4 Hz, J_{H5H6} = 11.2 Hz, J_{NHCH} = 9.1 Hz minor isomer **B** 1.78 (3H, s, 7-Me), 3.61 (3H, s, OMe), 3.66 (1H, d, H_6), 4.12 (1H, d, H_5), 4.24 (1H, d, H_3), 4.88 (1H, dd, H_2), 6.94-7.03 (6H, m, 6H-Ph), 7.10-7.14 (2H, m, 2H-Ph), 7.15 (1H, s, OH), 7.21-7.25 (2H, m, 2H-Ph), 7.42-7.57 (3H, m, 3H-Ph), 7.79-7.83 (2H, m, 2H-Ph), 8.93 (1H, d, N*H*COPh), J_{H2H3} = 11.8 Hz, J_{H5H6} = 11.0 Hz, J_{NHCH} = 8.8 Hz **A**:**B** = 4:3
14	300 DMSO-d_6	major isomer **A** 1.12 (3H, t, C*H*$_3$CH$_2$); 1.97 (3H, s, 7-Me), 3.52 (1H, d, H_6), 3.90-4.17 (2H, m, C*H*$_2$CH$_3$), 4.28 (1H, d, H_5), 4.38 (1H, d, H_3), 5.09 (1H, dd, H_2), 6.94-7.03 (6H, m, 6H-Ph), 7.11-7.13 (2H, m, 2H-Ph), 7.18 (1H, s, OH), 7.20-7.25 (2H, m, 2H-Ph), 7.45-7.57 (3H, m, 3H-Ph), 7.80-7.83 (2H, m, 2H-Ph), 8.92 (1H, d, N*H*COPh), J_{CH3CH2} = 7.1 Hz, J_{H2H3} = 12.4 Hz, J_{H5H6} = 11.2 Hz, J_{NHCH} = 9.1 Hz minor isomer **B** 1.13 (3H, t, C*H*$_3$CH$_2$), 1.79 (3H, s, 7-Me), 3.62 (1H, d, H_6), 3.90-4.17 (2H, m, C*H*$_2$CH$_3$), 4.12 (1H, d, H_5), 4.23 (1H, d, H_3), 4.88 (1H, dd, H_2), 6.94-7.03 (6H, m, 6H-Ph), 7.11-7.15 (2H, m, 2H-Ph), 7.13 (1H, s, OH), 7.20-7.25 (2H, m, 2H-Ph), 7.45-7.57 (3H, m, 3H-Ph), 7.80-7.83 (2H, m, 2H-Ph), 8.92 (1H, d, N*H*COPh), J_{CH2CH2} = 7.1 Hz, J_{H2H3} = 11.9 Hz, J_{H5H6} = 10.9 Hz, J_{NHCH} = 8.8 Hz **A**:**B** = 3:2
15	300 DMSO-d_6	2.64 (3H, d, 7-Me), 3.48 (3H, s, OMe), 4.71 (1H, d, H_3), 4.85 (1H, dd, H_2), 5.22 (1H, d, H_5), 7.04-7.22 (10H, m, 10H-Ph), 7.48-7.56 (3H, m, 3H-Ph), 7.81-7.83 (2H, m, 2H-Ph), 9.067 (1H, d, N*H*COPh), J_{H2H3} = 11.3 Hz, J_{H5CH3} = 1.3 Hz, J_{NHCH} = 8.1 Hz
16	300 $CDCl_3$	0.98 (3H, t, C*H*$_3$CH$_2$), 2.75 (3H, d, 7-CH_3), 3.93 (1H, dq, C*H*$_a$H$_b$CH$_3$), 4.02 (1H, dq, CH$_a$*H*$_b$CH$_3$), 4.67 (1H, d, H_3), 4.74 (1H, dd, H_2), 5.15 (1H, d, H_5), 6.83 (1H, d, N*H*COPh), 7.05-7.17 (10H, m, 10H-Ph), 7.34-7.39 (2H, m, 2H-Ph), 7.45-7.51 (1H, m, 1H-Ph), 7.69-7.72 (2H, m, 2H-Ph), J_{H2H3} = 11.2 Hz, J_{NHCH} = 7.2 Hz, J_{H5CH3} = 1.5 Hz, J_{CH3CH2} = 7.1 Hz, J_{CH2} (gem) = 11.2 Hz
18	300 DMSO-d_6	5.25 (1H, t, H_6), 5.50 (1H, d, H_5), 7.14 (1H, s, H_1), 7.21-7.74 (14H, m, 13H-Ph and H_2), 7.99-8.02 (2H, m, 2H-Ph), 8.80 (1H, d, N*H*COPh), J_{H2H3} = 9.7 Hz, J_{NHCH} = 9.2 Hz

Scheme 3



6a (1*Z*)-*rel*-(4*R*,5*R*) **17** *rel*-(3*S*,5*R*,6*R*) **18** *rel*-(5*R*,6*R*)

observed in ^{1}H nmr spectra of mixtures **13** and **14**, and *cis*-orientation between H_3 and H_5 in compound **15** (NOESY, d_{H3H5} = 0.23 nm), indicates the *exo*-approach of acetoacetates **11** and **12** to the less hindered face of azomethinimine **6a** [13] (Scheme 2).

Treatment of (1*Z*)-*rel*-(4*R*,5*R*)-1-benzylidene-4-benzoylamino-5-phenyl-3-pyrazolidinon-1-azomethinimine (**6a**) with potassium cyanide and acetic acid in methanol gave *rel*-(5*R*,6*R*)-6-benzoylamino-5,6-dihydro-3,5-diphenyl-1-oxo-1*H*,7*H*-pyrazolo[1,2-*a*][1,2,3]triazole (**18**). Compound **18** is a representative of a novel ring system, since only the preparation of 1*H*-pyrazolo-[1,2-*a*][1,2,3]triazol-4-ium salts have been previously reported in the literature [14]. Presumably, this cycloaddition proceeds *via* the formation of 3*H*,7*H*-isomer **17**, which tautomerizes into a more stable 1*H*,7*H*-isomer **18** (Scheme 3).

EXPERIMENTAL

Melting points were taken on a Kofler micro hot stage and on a Büchi 535 melting point apparatus. The ^{1}H nmr spectra were obtained on a Varian E-360 (60 MHz) and on a Bruker Avance DPX 300 (300 MHz) spectrometer with DMSO-d_6 or deuteriochloroform as solvents and TMS as internal standard. NOESY experiments were performed on a Bruker Avance DPX 300 (300 MHz) spectrometer. The microanalyses for C, H, and N were obtained on a Perkin-Elmer CHN Analyser 2400. Mass spectra were obtained on a Autospeck Q spectrometer (VG - Analytical).

4-Benzylidene-2-phenyl-5(4*H*)-oxazolone (**3**) was prepared according to the procedure described in the literature [12].

rel-(4*S*,5*R*)-4-Benzoylamino-5-phenyl-3-pyrazolidinone (**4**).

This compound was prepared by a slightly modified procedure described in the literature [8]. A mixture of 4-benzylidene-2-phenyl-5(4*H*)-oxazolone (**3**, 24.9 g, 0.1 mole), ethanol (100 ml), and hydrazine hydrate (80%, 15 ml) was heated under reflux for 5 hours, cooled, and the precipitate collected by filtration to give **4** in 53% yield, mp 229-231° (from ethanol), lit [8] mp 225-227°.

(1*Z*)-*rel*-(4*R*,5*R*)-1-Arylmethylene-4-benzoylamino-5-phenyl-3-pyrazolidinon-1-azomethinimines **6a-f**. General Procedure.

A mixture of *rel*-(4*R*,5*R*)-4-benzoylamino-5-phenyl-3-pyrazolidinone (**4**, 2.81 g, 0.01 mole), substituted benzaldehyde **5a-f** (0.012 mole) and anhydrous ethanol (30 ml) was heated at the reflux temperature for 5 minutes. Trifluoroacetic acid (10 drops, approximately 0.05 ml) was added through a reflux condenser, and the mixture was refluxed for 1 hour, cooled, and the precipitate collected by filtration to give azomethinimines **6a-f**. Experimental and analytical data for azomethinimines **6a-f** are given in Tables 1 and 2.

rel-(2*R*,3*R*,5*S*)-5-Aryl-2-benzoylamino-6,7-bis(methoxycarbonyl)-2,3-dihydro-1-oxo-3-phenyl-1*H*,5*H*-pyrazolo[1,2-*a*]pyrazoles **8a-f**. General Procedure.

A mixture of (1*Z*)-*rel*-(4*R*,5*R*)-1-arylmethylene-4-benzoylamino-5-phenyl-3-pyrazolidinon-1-azomethinimine **6a-f** (0.005 mole), dimethyl acetylenedicarboxylate (**7**, 0.71 g, 0.005 mole), and anisole (30 ml) was heated at the reflux temperature until complete dissolution of azomethinimine **6a-f** (approximately 1-2 hours). Volatile components were evaporated *in vacuo*. Methanol (3 ml) was added to the residue, and the mixture was left in a refrigerator for 2 hours. The precipitate was collected by filtration to give cycloadducts **8a-f**. Experimental and analytical data for *rel*-(2*R*,3*R*,5*S*)-5-aryl-2-benzoylamino-6,7-bis(methoxycarbonyl)-2,3-dihydro-1-oxo-3-phenyl-1*H*,5*H*-pyrazolo[1,2-*a*]pyrazoles **8a-f** are given in Tables 1 and 2.

rel-(2*R*,3*R*,5*S*,6*R*,7*S*)-2-Benzoylamino-6,7-bis(methoxycarbonyl)-3,5-diphenyl-1-oxoperhydropyrazolo[1,2-*a*]pyrazole (**10**).

A mixture of (1*Z*)-*rel*-(4*R*,5*R*)-1-arylmethylene-4-benzoylamino-5-phenyl-3-pyrazolidinon-1-azomethinimine (**6a**, 0.369 g, 0.001 mole), dimethyl maleinate (**9**, 0.150 g, 0.00104 mole) and anisole (5 ml) was heated at the reflux temperature for 3 hours, cooled, and volatile components evaporated *in vacuo*. Toluene (5 ml) was added to the residue and the precipitate collected by filtration to give **10**. Experimental and analytical data for *rel*-(2*R*,3*R*,5*S*,6*R*,7*S*)-2-benzoylamino-6,7-bis(methoxycarbonyl)-3,5-diphenyl-1-oxoperhydropyrazolo[1,2-*a*]pyrazole (**10**) are given in Tables 1 and 2.

rel-(2*R*,3*R*,5*S*,6*R*,7*RS*)-2-Benzoylamino-3,5-diphenyl-7-hydroxy-6-methoxycarbonyl-7-methyl-1-oxoperhydropyrazolo[1,2-*a*]pyrazole (**13**) and *rel*-(2*R*,3*R*,5*S*,6*R*,7*RS*)-2-Benzoylamino-3,5-diphenyl-6-ethoxycarbonyl-7-hydroxy-7-methyl-1-oxoperhydro-pyrazolo[1,2-*a*]pyrazole (**14**). General Procedure.

A mixture of (1*Z*)-*rel*-(4*R*,5*R*)-1-arylmethylene-4-benzoylamino-5-phenyl-3-pyrazolidinon-1-azomethinimine (**6a**, 0.738 g, 0.002 mole), acetoacetic ester **11,12** (0.0022 mole), methanol (8 ml), and triethylamine (0.28 ml, 0.002 mole) was stirred at room temperature for 5 hours, left at 4° for 2 days, and the precipitate collected by filtration to give **13** or **14**, respectively. Experimental and analytical data for mixtures **13** and **14** are given in Tables 1 and 2.

rel-(2*R*,3*R*,5*S*)-2-Benzoylamino-2,3-dihydro-3,5-diphenyl-6-methoxycarbonyl-7-methyl-1-oxo-1*H*,5*H*-pyrazolo[1,2-*a*]pyrazole (**15**).

Procedure A.

A mixture of (1*Z*)-*rel*-(4*R*,5*R*)-1-arylmethylene-4-benzoylamino-5-phenyl-3-pyrazolidinon-1-azomethinimine (**6a**, 0.369 g, 0.001 mole), methyl acetoacetate (**11**, 0.125 g, 0.00108 mole), and anhydrous methanol (4 ml) was heated at the reflux temperature for 5 minutes, then trifluoroacetic acid (4 drops, catalytic amount) was added, and the mixture was refluxed for 5 hours, cooled in a refrigerator, and the precipitate collected by filtration to give **15**.

Procedure B.

A mixture of **13** (0.485 g, 0.001 mole) and anhydrous methanol (4 ml) was heated at the reflux temperature for 5 minutes, then trifluoroacetic acid (4 drops, catalytic amount) was added and the whole mixture was refluxed for 5 hours, cooled in a refrigerator, and the precipitate collected by filtration to give **15**. Experimental and analytical data for compound **15** are given in Tables 1 and 2.

rel-(2*R*,3*R*,5*S*)-2-Benzoylamino-2,3-dihydro-3,5-diphenyl-6-ethoxycarbonyl-7-methyl-1-oxo-1*H*,5*H*-pyrazolo[1,2-*a*]pyrazole (**16**).

Procedure A.

A mixture of (1*Z*)-*rel*-(4*R*,5*R*)-1-arylmethylene-4-benzoylamino-5-phenyl-3-pyrazolidinon-1-azomethinimine (**6a**, 0.369 g, 0.001 mole), ethyl acetoacetate (**12**, 0.140 g, 0.00108 mole), and anhydrous ethanol (4 ml) was heated at reflux temperature for 5 minutes. Trifluoroacetic acid (4 drops, catalytic amount) was added, and the mixture was refluxed for 5 hours, cooled in a refrigerator, and the precipitate collected by filtration to give **16**.

Procedure B.

A mixture of **14** (0.499 g, 0.001 mole) and anhydrous ethanol (4 ml) was heated at the reflux temperature for 5 minutes. Trifluoroacetic acid (4 drops, catalytic amount) was added and the mixture was refluxed for 5 hours, cooled in a refrigerator, and the precipitate collected by filtration to give **16**. Experimental and analytical data for compound **16** are given in Tables 1 and 2.

rel-(5*R*,6*R*)-6-Benzoylamino-5,6-dihydro-3,5-diphenyl-7-oxo-1*H*,7*H*-pyrazolo[1,2-*a*][1,2,3]triazole (**18**).

A mixture of (1*Z*)-*rel*-(4*R*,5*R*)-1-arylmethylene-4-benzoylamino-5-phenyl-3-pyrazolidinon-1-azomethinimine (**6a**, 0.369 g, 0.001 mole), potassium cyanide (0.100 g, 0.0015 mole), and methanol (4 ml) was stirred at room temperature for 5 minutes, then acetic acid (0.07 ml, 0.0012 mole) was added, and the mixture was stirred at room temperature for 3 hours. The precipitate was collected by filtration to give **18**. Experimental and analytical data for compound **18** are given in Tables 1 and 2.

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