Synthesis of Spiro-1-pyrazolines by the 1,3-Dipolar Cycloaddition of Exocyclic α,β-Unsaturated Ketones with Diazomethane

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Dedicated to Professor Dr. Mihály T. Beck on the occasion of his 70th birthday.

1,3-Dipolar cycloadditions of exocyclic α,β-unsaturated ketones **1-22** with diazomethane afforded spiro-1-pyrazolines **23-44** in a diastereospecific reaction. The structure and stereochemistry of each compound synthesised has been elucidated by nmr spectroscopic measurements and other analytical techniques. It has been proven that the stereochemistry of the starting α,β-enones was retained in the course of these cycloadditions.

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Introduction.

Because of their diverse bioactivities, pyrazolines are important nitrogen-containing five-membered heterocyclic compounds widely used in drug research [1-4]. As a result, numerous pyrazolines have hitherto been published in the literature and several procedures have been developed for their syntheses [5]. One of the most popular synthetic methods is based on the cycloaddition of diazoalkanes to carbon-carbon double bonds.

1,3-Dipolar cycloadditions of chalcones and related α,β-unsaturated ketones with diazomethane have been investigated in detail [6-14]. It has been concluded that the sole isolable product of this type of reaction is the thermodynamically more stable 2-pyrazoline [15] originating from the spontaneous isomerization of the initially formed 1-pyrazoline. On the other hand, the reaction of exocyclic α,β-unsaturated ketones with diazomethane has provided spiro-1-pyrazolines as stable products [16-21].

In our previous studies [17-19,22] 1,3-dipolar cycloadditions of both (*E*)- and (*Z*)-isomers of various exocyclic α,β-enones with diazomethane have been investigated [23]. The reactions were found to be diastereospecific providing spiro-1-pyrazolines in which the stereochemistry of the starting α,β-enones has been retained. It has also turned out that the substitution pattern of the arylidene moiety has no influence either on the stereochemical outcome or on the rate of each reaction.

In this paper we report on the 1,3-dipolar cycloadditions of exocyclic α,β-unsaturated ketones bearing a bulky arylidene moiety (compounds **1-8**) and 2-arylidene-1-benzosuberones **9-22** with diazomethane.

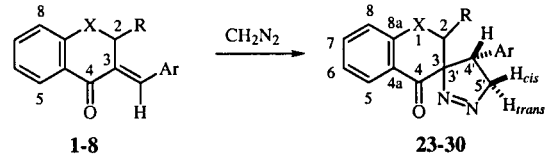
Results and Discussion.

Chemistry.

Following our previous studies on the 1,3-dipolar cycloadditions of 2-arylidene-1-tetralones, 3-arylidenechromanones, -1-thiochromanones and -flavanones [17-19] with diazomethane, we have performed other experiments with new representatives of these α,β-enones. A major aim of our present work was to obtain information on the influence of the space demand of the aryl group in the arylmethylene moiety of the starting materials.

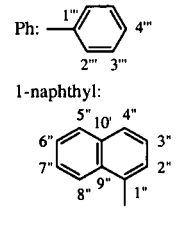
Compounds **1-8** were allowed to react with diazomethane in a mixture of anhydrous ether and methylene chloride (*cf.* Experimental), leading to the formation of *trans*-spiro-1-pyrazolines **23-30** in good yields. The nmr spectroscopic measurements (*vide infra*) unambiguously revealed that this cycloaddition was regio- and completely stereoselective providing stereohomogeneous *trans*-spiro-1-pyrazolines [24]. In the case of (*E*)-3-naphthylidene-1-tetralones **1,2**, (*E*)-3-naphthylidenechromanones **3,4** and (*E*)-3-naphthylidene-1-thiochromanones **5,6** (Scheme 1) no difference was observed in this reaction as a result of the presence of either a 1-naphthyl or a 2-naphthyl group and this may result from the free rotation of the naphthyl group.

Scheme 1



1-8 **23-30**

	X	R	Ar
1, 23	CH_2	H	1-naphthyl
2, 24	CH_2	H	2-naphthyl
3, 25	O	H	1-naphthyl
4, 26	O	H	2-naphthyl
5, 27	S	H	1-naphthyl
6, 28	S	H	2-naphthyl
7, 29	O	Ph	2-naphthyl
8, 30	S	Ph	2-naphthyl

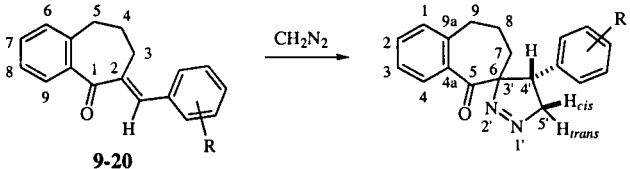


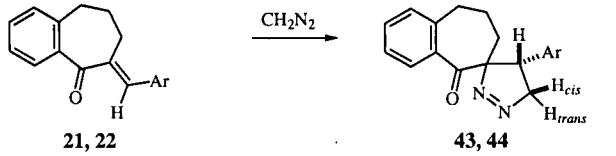
However, if a phenyl group is at position 2 as in the 3-arylideneflavanones or in their 1-thio analogues, pyrazolines could be prepared only from the 3-(2-naphthylidene)flavanone **7** and 3-(2-naphthylidene)-1-thioflavanone **8**. Neither the 3-(1-naphthylidene)flavanone nor its 1-thio analogue afforded any pyrazoline-type compound on treatment with diazomethane under similar reaction conditions. In these cases the lack of the pyrazoline formation may be a consequence of a strong

steric hindrance originating from the very hindered rotation of the 1-naphthyl group in these compounds. Spiro-1-pyrazolines **23-30** are stable compounds, no isomerization into their corresponding 2-pyrazoline isomers or decomposition by denitrogenation were observed on standing at room temperature for several months.

As far as the 2-arylidene-1-benzosuberones are concerned, only the reaction of the unsubstituted 2-benzylidene-1-benzosuberone and diazomethane has hitherto been performed to obtain spiro-1-pyrazoline [19]. Since this 1,3-dipolar cycloaddition of the homologous 2-arylidene-1-indanones [22] and 2-arylidene-1-tetralones [17,18] was thoroughly investigated, it seemed expedient to study the similar reaction of 2-arylidene-1-benzosuberones with various substituents in their benzylidene moiety and bearing a 1-naphthylidene or a 2-naphthylidene moiety. For this reason, (*E*)-2-arylidene-1-benzosuberones **9-22** were allowed to react with diazomethane under the above-mentioned reaction conditions, leading to the formation of *trans*-spiro-1-pyrazolines **31-44** in good yields [24] (Scheme 2).

Scheme 2





9, 31 R = 2-Me
10, 32 R = 4-Me
11, 33 R = 4-*i*-Pr
12, 34 R = 2-OMe
13, 35 R = 3-OMe
14, 36 R = 4-OMe
15, 37 R = 4-F

16, 28 R = 2-Cl
17, 39 R = 3-Cl
18, 40 R = 4-Cl
19, 41 R = 4-Br
20, 42 R = 4-CN
21, 43 Ar = 1-napthyl
22, 44 Ar = 2-napthyl

infra). On this basis it can be concluded that the cycloaddition reported here is regio- and completely stereoselective in the case of these α,β-enones with a seven-membered ring as well. The stereochemistry of the starting α,β-enones is retained in the course of the reaction. Thus, (*E*)-2-arylidene-1-benzosuberones **9-22** afforded *trans*-spiro-1-pyrazolines **31-44** as the sole products. Neither the substitution pattern of the arylidene moiety (compounds **9-20**) nor the presence of a bulky group like 1-naphthyl (**21**) or 2-naphthyl (**22**) moiety influenced the rate and the stereochemical outcome of the reaction. Spiro-1-pyrazolines **30-44** are stable substances. It can also be stated that the size of the benzocycloalkanone ring bearing the arylidene moiety has no influence either on the course of this 1,3-dipolar cycloaddition or on the stability of spiro-1-pyrazolines obtained in this way.

Nuclear Magnetic Resonance Spectroscopy.

A detailed analysis of the ^1H, ^{13}C, COSY, HETCOR and HMBC nmr spectra of pyrazolines **23-44** has revealed the presence of a spiro-1-pyrazoline ring. This conclusion was based on the presence of three protons coupled with each other, two methylenic and one methynic, and also on the presence of one carbon shared by two rings, one of which is the pyrazolinic one (Table 1).

The assignments of these protons and of the stereochemistry of these spiro-1-pyrazolines **23-44** were mainly based on 2D NOESY experiments (Table 2). The close proximity between both H-2 and those of the naphthyl or aryl groups of 4'-position allowed us to conclude that in all cases the stereochemistry of the starting materials was retained [23], the carbonyl and naphthyl groups are in a *trans* configuration. The NOE cross peaks observed between H-2_{ax} and H-8", H-2_{eq} and H-2", H-4' and H-8" and also between H-5'*trans* and H-2" in the 2D NOESY spectra of *trans*-4'-(1-naphthyl)spiro-1-pyrazolines **23**, **25** and **27**, is indicative that the 1-naphthyl group has no free rotation. This fact is due to the steric interaction with H-2 protons. However, in the case of *trans*-4'-(2-naphthyl)spiro-1-pyrazolines **24**, **26** and **28** there is a free rotation of the 2-naphthyl group, which can be seen from the close proximity of H-1", H-3" and H-4', H-2_{ax} and H-2_{eq}. In the case of spiro-1-pyrazolines **29**

Table 1

^1H and ^{13}C nmr Chemical Shifts of the Pyrazoline Ring of Compounds **23-44**.

Compounds	H-4'	H-5'*cis*	H-5'*trans*	C-3'	C-4'	C-5'
23,25,27	4.81-4.93	5.06-5.11	5.42-5.48	98.7-102.4	35.8-37.6	86.3-87.1
43	4.95	4.65	5.21	106.9	38.5	83.7
24,26,28-30	3.93-4.22	4.91-5.07	5.18-5.37	98.2-103.4	42.4-44.7	85.0-89.6
44	4.10	4.79	5.03	105.5	45.0	83.5
32,33,35-37	3.86-4.04	4.70-4.75	4.85-4.91	105.0-105.9	44.0-44.5	83.2-84.1
39-42						
31,34,38	4.17-4.47	4.57-4.75	4.98-5.06	104.4-106.6	39.6-41.4	84.1-83.2

The spiro-1-pyrazoline structure of compounds synthesised in this way was unambiguously proven by ir and nmr spectroscopic measurements (*cf.* Experimental and *vide*

Table 2

Results Obtained From 2D NOESY Spectra of Spiro-1-pyrazolines **23-42**

Compounds	Protons	NOE cross peaks with	Compounds	Protons	NOE cross peaks with
	H-4'	H-5'*cis*, H-8"		H-4'	H-5'*cis*, H-1", H-3"
	H-5'*cis*	H-5'*trans*, H-4'		H-5'*cis*	H-5'*trans*, H-4'
23, 25, 27	H-5'*trans*	H-5'*cis*, H-2"	**24, 26, 28**	H-5'*trans*	H-5'*cis*, H-1", H-3"
	$H\text{-}2_{ax}$	$H\text{-}2_{eq}$, H-8"		$H\text{-}2_{ax}$	$H\text{-}2_{eq}$, H-1", H-3"
	$H\text{-}2_{eq}$	$H\text{-}2_{ax}$, H-2"		$H\text{-}2_{eq}$	$H\text{-}2_{ax}$, H-1", H-3"
	H-4'	H-5'*cis*, H-1", H-3", H-2"',6"'		H-4'	H-5'*cis*, H-2", H-6"
				H-5'*cis*	H-5'*trans*, H-4'
29, 30	H-5'*cis*	H-5'*trans*, H-4'	**32, 33, 35-37, 39-42**	H-5'*trans*	H-5'*cis*, H-2", H-6"
	H-5'*trans*	H-5'*cis*, H-1", H-3"		$H\text{-}7_{ax}$	$H\text{-}7_{eq}$, H-2", H-6"
	$H\text{-}2_{ax}$	H-1", H-3" H-2"',6"'		$H\text{-}7_{eq}$	$H\text{-}7_{ax}$, H-2", H-6"

and **30**, prepared from (*E*)-3-(2-naphthylidene)flavanone **7** and thioflavanone **8**, besides the proximities described for compounds **24**, **26** and **28**, there is also a close proximity between H-4', $H\text{-}2_{ax}$ and the *ortho*-protons H-2"',6"' of the 2-phenyl ring.

The results obtained from the 2D NOESY spectra of spiro-1-pyrazolines **43** and **44** are similar to those of, respectively, **23**, **25**, **27** and **24**, **26**, **28**. In such way the naphthyl group in **44** has free rotation but not in **43**.

The results obtained for spiro-1-pyrazolines **33-42** seem to indicate that the 4'-aryl rings have free rotation in all these compounds, and, as a consequence, NOE cross peaks where observed between H-2" (except for compounds **31**, **34** and **38** which have 2-substituted-4'-aryl groups), H-6" and H-5'*trans*, H-4' and both H-7.

Table 3

Connectivities Found in the HMBC spectra of Spiro-1-pyrazolines **23-42**

Compounds	Protons	Long-range Correlated Carbons
23-30	H-5	C-4, C-7 and C-8a
	H-6 and H-8	C-4a
	H-2eq and H-4'	C-4 and C-3'
23, 25, 27	H-4', H-5' and H-3"	C-1"
	H-2" and H-4"	C-9"
24, 26, 28-30	H-4', H-5' and H-4"	C-2"
	H-1" and H-5"	C-10"
29, 30	H-4"	C-9"
	H-3"',5"'	C-1"'
	H-4	C-2, C-5 and C-9a
31-44	2 x H-7 and H-4'	C-3', C-5
	H-1 and H-3	C-4a
31-43	H-4', H-5', H-3" and H-5"	C-1"
43	H-2" and H-5"	C-9"
44	H-4', H-5' and H-4"	C-2"
	H-1" and H-4"	C-9"
31	2"-CH_3	C-1", C-2" and C-3"
32	4"-CH_3	C-3",5" and C-4"
33	4"-$CH(CH_3)_2$	2 x CH_3 and C-4"
34	2"-OCH_3	C-2"
35	3"-OCH_3	C-3"
36	4"-OCH_3	C-4"

In the case of spiro-1-pyrazolines **31**, **34** and **38**, which have 2-substituents in the 4'-aryl groups, there are shifts to higher frequencies in the resonances of all H-4' when compared with the corresponding protons of compounds **32**, **33**, **35-37**, **39-42**, which have no substituents at such positions (Table 1). This effect can be explained by the steric interaction between H-4' and the 2-substituent of the 4'-aryl groups [25,26]. This was confirmed by the strong NOE cross peak observed between 2"-CH_3 and H-4' in the 2D NOESY spectrum of compound **31**.

Assignments of the ^{13}C nmr resonances of the spiro-1-pyrazolines **23-44** were based on 2D HETCOR and HMBC experiments. These latter spectra were especially useful for the assignments of the quaternary carbons resonance (Table 3).

EXPERIMENTAL

Melting points were determined on a Kofler hot-stage apparatus and are uncorrected. ^1H and ^{13}C nmr spectra were recorded on a Bruker AMX 300 spectrometer at 300.13 and 75.47 MHz in deuteriochloroform at room temperature using tetramethylsilane as internal standard. ^1H Assignments were made using 2D COSY and NOESY (800 ms for mixing time) experiments, while ^{13}C assignments were made using 2D HETCOR and HMBC experiments (the delay for evolution of long-range C/H coupling constants was optimised to 7 Hz). The ir spectra were measured in potassium bromide pellets on a FT-IR Matson Polaris spectrometer. Elemental analyses were performed on a Carlo Erba 1106 analyzer. Thin-layer chromatography (tlc) was performed on silica gel 60 F_{254} (Merck) layer using hexane-acetone (7:3 v/v) as eluent. The starting materials **1-22** were synthesised according to known procedures [27,28].

Reaction of α,β-Enones **1-22** with Diazomethane. General Procedure.

A mixture of the appropriate α,β-enone (**1-22**, 5.0 mmoles), diazomethane (25.0 mmoles), anhydrous ether (30 ml) and anhydrous methylene chloride (30 ml) was allowed to stand in a refrigerator for 48 hours, the solvent was evaporated under reduced pressure, and the residue was crystallized from methanol to obtain spiro-1-pyrazolines **23-44**.

trans-(±)-3,4,4',5'-Tetrahydro-4'-(1-naphthyl)spiro{naphthalene-2(1*H*),3'-[3*H*]pyrazol}-1-one (**23**).

This compound was obtained as white crystals in 69% yield, mp 149-150°; ir: ν 1671, 1596, 1232, 906, 784 cm^{-1}; ^1H nmr: δ 1.74 (ddd, 1H, H-2_{ax}, J 13.1, 11.6 and 4.7 Hz), 1.87 (ddd, 1H, H-2_{eq}, J 13.1, 5.1 and 3.8 Hz), 2.70 (ddd, 1H, H-1_{eq}, J 17.0, 4.7 and 3.8 Hz), 3.66 (ddd, 1H, H-1_{ax}, J 17.0, 11.6 and 5.1 Hz), 4.93 (dd, 1H, H-4', J 9.0 and 2.9 Hz), 5.11 (dd, 1H, H-5'$_{cis}$, J 18.3 and 9.0 Hz), 5.42 (dd, 1H, H-5'$_{trans}$, J 18.3 and 2.9 Hz), 6.97 (d, 1H, H-2", J 7.2 Hz), 7.21 (d, 1H, H-8, J 7.7 Hz), 7.34 (dd, 1H, H-6, J 7.8 and 7.5 Hz), 7.40-7.46 (m, 2H, H-6",7"), 7.42 (dd, 1H, H-3", J 8.1 and 7.2 Hz), 7.51 (ddd, 1H, H-7, J 7.7, 7.5 and 1.2 Hz), 7.76 (d, 1H, H-4", J 8.1 Hz), 7.82-7.89 (m, 2H, H-5",8"), 8.11 (d, 1H, H-5, J 7.8 Hz); ^{13}C nmr: δ 27.0 (C-1), 29.5 (C-2), 37.0 (C-4'), 86.3 (C-5'), 102.4 (C-3'), 123.1 (C-8"), 125.0 (C-2"), 125.3 (C-3"), 125.9 and 126.7 (C-6",7"), 126.8 (C-6), 127.9 (C-4"), 128.3 (C-5), 128.9 (C-8), 129.0 (C-5"), 131.5 (C-4a), 132.3 (C-9"), 133.7 (C-10"), 134.4 (C-7), 135.4 (C-1"), 144.7 (C-8a), 192.1 (C-4).

Anal. Calcd. for $C_{22}H_{18}N_2O$: C, 80.95; H, 5.56; N, 8.58. Found: C, 80.81; H, 5.59; N, 8.51.

trans-(±)-3,4,4',5'-Tetrahydro-4'-(2-naphthyl)spiro{naphthalene-2(1*H*),3'-[3*H*]pyrazol}-1-one (**24**).

This compound was obtained as white crystals in 75% yield, mp 131-132°; ir: ν 1681, 1598, 1274, 1226, 898, 819, 769, 738 cm^{-1}; ^1H nmr: δ 1.91 (ddd, 1H, H-2_{ax}, J 14.4, 10.4 and 4.8 Hz), 2.17 (ddd, 1H, H-2_{eq}, J 14.4, 5.1 and 4.8 Hz), 2.82 (ddd, 1H, H-1_{eq}, J 16.9, 5.1 and 4.8 Hz), 3.49 (ddd, 1H, H-1_{ax}, J 16.9, 10.4 and 4.8 Hz), 4.08 (dd, 1H, H-4', J 8.1 and 3.9 Hz), 5.07 (dd, 1H, H-5'$_{cis}$, J 18.0 and 8.1 Hz), 5.18 (dd, 1H, H-5'$_{trans}$, J 18.0 and 3.9 Hz), 7.00 (dd, 1H, H-3", J 8.3 and 1.8 Hz), 7.25 (d, 1H, H-8, J 7.5 Hz), 7.35 (dd, 1H, H-6, J 7.7 and 7.4 Hz), 7.45 (s broad, 1H, H-1"), 7.53 (ddd, 1H, H-7, J 7.5, 7.4 and 1.2 Hz), 7.45-7.50 (m, 2H, H-6",7"), 7.72-7.81 (m, 2H, H-5",8"), 7.75 (d, 1H, H-4", J 8.3 Hz), 8.09 (d, 1H, H-5, J 7.7 Hz); ^{13}C nmr: δ 26.6 (C-1), 29.6 (C-2), 43.5 (C-4'), 85.0 (C-5'), 101.1 (C-3'), 126.1 and 126.5 (C-6",7"), 126.2 (C-3"), 126.9 (C-6), 127.1 (C-1"), 127.6 (C-5",8"), 128.4 (C-5), 128.5 (C-4"), 128.9 (C-8), 131.2 (C-4a), 132.5 (C-10"), 133.1 (C-9"), 134.4 (C-7), 136.1 (C-2"), 144.4 (C-8a), 192.0 (C-4).

Anal. Calcd. for $C_{22}H_{18}N_2O$: C, 80.95; H, 5.56; N, 8.58. Found: C, 80.88; H, 5.51; N, 8.62.

trans-(±)-4',5'-Dihydro-4'-(1-naphthyl)spiro{2*H*-1-benzopyran-3(4*H*),3'-[3*H*]pyrazol}-4-one (**25**).

This compound was obtained as white crystals in 93% yield, mp 172-173°; ir: ν 1679, 1604, 1475, 1448, 1213, 1145, 1033, 916, 794 cm^{-1}; ^1H nmr: δ 3.94 (d, 1H, H-2_{ax}, J 12.6 Hz), 4.27 (d, 1H, H-2_{eq}, J 12.6 Hz), 4.81 (dd, 1H, H-4', J 8.9 and 2.4 Hz), 5.11 (dd, 1H, H-5'$_{cis}$, J 18.6 and 8.9 Hz), 5.48 (dd, 1H, H-5'$_{trans}$, J 18.6 and 2.4 Hz), 6.92 (d, 1H, H-8, J 8.1 Hz), 6.96 (d, 1H, H-2", J 7.5 Hz), 7.09 (dd, 1H, H-6, J 7.7 and 7.4 Hz), 7.43 (dd, 1H, H-3", J 8.3 and 7.5 Hz), 7.42-7.51 (m, 2H, H-6",7"), 7.53 (ddd, 1H, H-7, J 8.1, 7.4 and 1.6 Hz), 7.80 (d, 1H, H-4", J 8.3 Hz), 7.83 (d, 1H, H-8", J 9.6 Hz), 7.86 (dd, 1H, H-5", J 8.4 and 1.8 Hz), 8.00 (dd, 1H, H-5, J 7.7 and 1.6 Hz); ^{13}C nmr: δ 35.8 (C-4'), 69.6 (C-2), 86.6 (C-5'), 98.7 (C-3'), 118.2 (C-8), 119.6 (C-4a), 121.9 (C-6), 122.8 (C-8"), 124.8 (C-2"), 125.3 (C-3"), 126.1 and 126.9 (C-6",7"), 128.0 (C-5), 128.6 (C-4"), 129.1 (C-5"), 132.0 (C-9"), 133.2 (C-1"), 133.7 (C-10"), 137.1 (C-7), 161.8 (C-8a), 186.0 (C-4).

Anal. Calcd. for $C_{21}H_{16}N_2O_2$: C, 76.81; H, 4.91; N, 8.52. Found: C, 76.72; H, 4.94; N, 8.46.

trans-(±)-4',5'-Dihydro-4'-(2-naphthyl)spiro{2*H*-1-benzopyran-3(4*H*),3'-[3*H*]pyrazol}-4-one (**26**).

This compound was obtained as white crystals in 76% yield, mp 173-174°; ir: ν 1681, 1602, 1475, 1299, 1263, 1052, 817, 763 cm^{-1}; ^1H nmr: δ 3.98 (dd, 1H, H-4', J 8.3 and 2.6 Hz), 4.13 (d, 1H, H-2_{ax}, J 12.5 Hz), 4.54 (d, 1H, H-2_{eq}, J 12.5 Hz), 5.03 (dd, 1H, H-5'$_{cis}$, J 18.2 and 8.3 Hz), 5.31 (dd, 1H, H-5'$_{trans}$, J 18.2 and 2.6 Hz), 6.98 (dd, 1H, H-3", J 8.9 and 1.5 Hz), 7.01 (d, 1H, H-8, J 8.0 Hz), 7.09 (dd, 1H, H-6, J 7.9 and 7.4 Hz), 7.42 (s broad, 1H, H-1"), 7.47-7.53 (m, 2H, H-6",7"), 7.56 (ddd, 1H, H-7, J 8.0, 7.4 and 1.5 Hz), 7.73-7.83 (m, 2H, H-5",8"), 7.78 (d, 1H, H-4", J 8.9 Hz), 7.96 (dd, 1H, H-5, J 7.8 and 1.5 Hz); ^{13}C nmr: δ 42.6 (C-4'), 69.6 (C-2), 85.7 (C-5'), 98.2 (C-3'), 118.2 (C-8), 119.4 (C-4a), 121.9 (C-6), 125.6 (C-3"), 126.4 and 126.7 (C-6",7"), 127.1 (C-1"), 127.7 (C-5",8"), 128.0 (C-5), 128.9 (C-4"), 132.7 (C-10"), 133.2 (C-9"), 134.3 (C-2"), 137.1 (C-7), 161.7 (C-8a), 186.0 (C-4).

Anal. Calcd. for $C_{21}H_{16}N_2O_2$: C, 76.81; H, 4.91; N, 8.52. Found: C, 76.91; H, 4.87; N, 8.58.

trans-(±)-4',5'-Dihydro-4'-(1-naphthyl)spiro{2*H*-1-benzothiopyran-3(4*H*),3'-[3*H*]pyrazol}-4-one (**27**).

This compound was obtained as white crystals in 78% yield, mp 172-173°; ir: ν 1670, 1587, 1430, 1299, 1214, 904, 779, 736 cm^{-1}; ^1H nmr: δ 3.04 and 3.08 (AB, 2H, H-2, J 14.1 Hz), 4.91 (dd, 1H, H-4', J 8.7 and 2.1 Hz), 5.06 (dd, 1H, H-5'$_{cis}$, J 18.3 and 8.7 Hz), 5.48 (dd, 1H, H-5'$_{trans}$, J 18.3 and 2.1 Hz), 6.95 (d, 1H, H-2", J 7.4 Hz), 7.23 (dd, 1H, H-6, J 8.1 and 7.8 Hz), 7.23 (d, 1H, H-8, J 7.2 Hz), 7.42 (dd, 1H, H-3", J 8.1 and 7.4 Hz), 7.42 (dd, 1H, H-7, J 7.8 and 7.2 Hz), 7.46-7.51 (m, 2H, H-6",7"), 7.79 (d, 1H, H-4", J 8.1 Hz), 7.84-7.91 (m, 2H, H-5",8"), 8.15 (dd, 1H, H-5, J 8.1 and 1.4 Hz); ^{13}C nmr: δ 31.2 (C-2), 37.6 (C-4'), 87.1 (C-5'), 99.2 (C-3'), 123.0 (C-8"), 125.0 (C-2"), 125.1 (C-6), 125.4 (C-3"), 126.1 and 126.9 (C-6",7"), 127.3 (C-8), 128.4 (C-4"), 129.1 (C-5"), 129.7 (C-4a), 130.7 (C-5), 132.3 (C-9"), 133.8 (C-10"), 134.1 (C-7), 134.6 (C-1"), 142.7 (C-8a), 188.1 (C-4).

Anal. Calcd. for $C_{21}H_{16}N_2OS$: C, 72.23; H, 4.68; N, 8.13. Found: C, 73.42; H, 4.64; N, 8.19.

trans-(±)-4',5'-Dihydro-4'-(2-naphthyl)spiro{2*H*-1-benzothiopyran-3(4*H*),3'-[3*H*]pyrazol}-4-one (**28**).

This compound was obtained as white crystals in 70% yield, mp 129-130°; ir: ν 1679, 1583, 1432, 1286, 1209, 740 cm^{-1}; ^1H nmr: δ 3.02 (d, 1H, H-2_{ax}, J 14.0 Hz), 3.77 (d, 1H, H-2_{eq}, J 14.0 Hz), 3.93 (dd, 1H, H-4', J 8.0 and 2.3 Hz), 4.91 (dd, 1H, H-5'$_{cis}$, J 17.9 and 8.0 Hz), 5.24 (dd, 1H, H-5'$_{trans}$, J 17.9 and 2.3 Hz), 7.05 (dd, 1H, H-3", J 8.4 and 1.8 Hz), 7.22 (ddd, 1H, H-6, J 7.9, 7.7 and 1.2 Hz), 7.26 (d, 1H, H-8, J 7.5 Hz), 7.44 (ddd, 1H, H-7, J 7.9, 7.5 and 1.5 Hz), 7.47 (d, 1H, H-1", J 1.8 Hz), 7.47-7.51 (m, 2H, H-6",7"), 7.74-7.83 (m, 2H, H-5",8"), 7.77 (d, 1H, H-4", J 8.4 Hz), 8.13 (dd, 1H, H-5, J 7.7 and 1.5 Hz); ^{13}C nmr: δ 31.0 (C-2), 44.7 (C-4'), 85.3 (C-5'), 98.3 (C-3'), 125.3 (C-6), 126.3 and 126.6 (C-6",7"), 126.3 (C-3"), 127.4 (C-8), 127.5 (C-1"), 127.6 (C-8"), 127.7 (C-4"), 128.5 (C-5"), 129.2 (C-4a), 130.8 (C-5), 132.6 (C-10"), 133.1 (C-9"), 134.1 (C-7), 135.5 (C-2"), 142.3 (C-8a), 187.8 (C-4).

Anal. Calcd. for $C_{21}H_{16}N_2OS$: C, 73.23; H, 4.68; N, 8.13. Found: C, 73.02; H, 4.72; N, 8.07.

trans-(±)-4',5'-Dihydro-4'-(2-naphthyl)-2-phenylspiro{2*H*-1-benzopyran-3(4*H*),3'-[3*H*]pyrazol}-4-one (**29**).

This compound was obtained as white crystals in 89% yield, mp 147-148°; ir: ν 1679, 1600, 1461, 1305, 1211, 1149, 981, 752, 694 cm^{-1}; ^1H nmr: δ 4.03 (d, 1H, H-4', J 7.7 Hz), 5.05 (dd, 1H, H-5'$_{cis}$, J 17.8 and 7.7 Hz), 5.30 (d, 1H, H-5'$_{trans}$, J 17.8 Hz), 5.57 (s broad, 1H, H-2$_{ax}$), 6.54 (d, 1H, H-3", J 8.1 Hz), 6.76 (d, 2H, H-2"',6"', J 7.7 Hz), 6.85 (s broad, 1H, H-1"), 6.88 (t, 2H, H-3"',5"', J 7.7 Hz), 6.96 (d, 1H, H-8, J 8.1 Hz), 7.04 (ddd, 1H, H-6, J 8.1, 7.7 and 0.6 Hz), 7.08 (t, 1H, H-4"', J 7.7 Hz), 7.34-7.47 (m, 4H, H-5",6",7",8"), 7.51 (dt, 1H, H-7, J 8.1 and 1.7 Hz), 7.69 (d, 1H, H-4", J 8.1 Hz), 7.93 (dd, 1H, H-5, J 7.7 and 1.7 Hz); ^{13}C nmr: δ 42.4 (C-4'), 82.0 (C-2), 88.2 (C-5'), 102.6 (C-3'), 118.8 (C-8), 120.0 (C-4a), 121.5 (C-6), 126.0 and 126.2 (C-6",7"), 125.6 (C-3"), 127.2 (C-5), 127.4 (C-4"), 127.6 (C-8"), 127.9 (C-3"',5",5"'), 128.1 (C-1",2"',6"'), 132.1 (C-10"), 132.8 (C-9"), 134.9 (C-1"'), 135.0 (C-2"), 137.5 (C-7), 159.9 (C-8a), 185.8 (C-4).

Anal. Calcd. for $C_{27}H_{20}N_2O_2$: C, 80.18; H, 4.98; N, 6.92. Found: C, 80.29; H, 4.94; N, 6.95.

trans-(±)-4',5'-Dihydro-4'-(2-naphthyl)-2-phenylspiro{2*H*-1-benzothiopyran-3(4*H*),3'-[3*H*]pyrazol}-4-one (**30**).

This compound was obtained as white crystals in 86% yield, mp 143-144°; ir: ν 1664, 1586, 1433, 1309, 1225, 1001, 824, 745, 689 cm^{-1}; ^1H nmr: δ 4.22 (d, 1H, H-4', J 7.6 Hz), 4.39 (s, 1H, H-2$_{ax}$), 5.05 (dd, 1H, H-5'$_{cis}$, J 18.1 and 7.6 Hz), 5.37 (d, 1H, H-5'$_{trans}$, J 18.1 Hz), 6.49 (d, 2H, H-2"',6"', J 7.6 Hz), 6.85 (t, 2H, H-3"',5"', J 7.6 Hz), 7.06 (t, 1H, H-4"', J 7.6 Hz), 7.72 (d, 1H, H-4", J 8.1 Hz), 7.16-7.21 (m, 3H, H-6,6",7"), 7.39-7.44 (m, 6H, H-1",3",5",7,8,8"), 8.13 (dd, 1H, H-5, J 8.1 and 1.2 Hz); ^{13}C nmr: δ 43.6 (C-4'), 48.6 (C-2), 89.6 (C-5'), 103.4 (C-3'), 124.9 (C-6), 126.1, 126.2, 127.6 and 127.7 (C-1",3",5",8,8"), 126.7 (C-2"',6"'), 127.4 (C-4",6",7"), 127.9 (C-4"'), 128.4 (C-3",5"), 129.4 (C-4a), 129.8 (C-5), 132.2 (C-10"), 132.8 (C-9"), 134.6 (C-2",7), 139,4 (C-1"'), 141.0 (C-8a), 187.4 (C-4).

Anal. Calcd. for $C_{27}H_{20}N_2OS$: C, 77.13; H, 4.79; N, 6.66. Found: C, 77.24; H, 4.82; N, 6.71.

trans-(±)-4',5',8,9-Tetrahydro-4'-(2-methylphenyl)spiro{6*H*-benzocycloheptene-6,3'-[3*H*]pyrazol}-5(7*H*)-one (**31**).

This compound was obtained as white crystals in 73% yield, mp 131-132°; ir: ν 1678, 1599, 1551, 1492, 1293, 1233, 1155, 1057, 938, 891, 760, 720 cm^{-1}; ^1H nmr: δ 1.47-1.56 (m, 1H, H-7$_{ax}$), 1.65-1.78 (m, 2H, H-7$_{eq}$,8), 2.15-2.26 (m, 1H, H-8), 2.30 (s, 3H, 2"-CH_3), 2.99 (ddd, 1H, H-9$_{eq}$, J 15.6, 6.6 and 3.0 Hz), 3.56 (ddd, 1H, H-9$_{ax}$, J 15.6, 9.9 and 3.9 Hz), 4.20 (dd, 1H, H-4', J 8.7 and 2.1 Hz), 4.57 (dd, 1H, H-5'$_{cis}$, J 18.0 and 8.4 Hz), 5.02 (dd, 1H, H-5'$_{trans}$, J 18.0 and 2.1 Hz), 6.53-6.56 (m, 1H, H-6"), 7.08-7.12 (m, 3H, H-3",4",5"), 7.23 (d, 1H, H-1, J 8.1 Hz), 7.24 (t, 1H, H-3, J 8.1 Hz), 7.38-7.42 (m, 2H, H-2,4); ^{13}C nmr: δ 20.1 (2"-CH_3), 24.1 (C-8), 31.0 (C-7), 33.1 (C-9), 39.6 (C-4'), 84.1 (C-5'), 106.6 (C-3'), 126.3 (C-3), 126.4 (C-5"), 126.9 (C-4"), 127.0 (C-6"), 128.3 (C-4), 129.4 (C-1), 130.4 (C-3"), 131.8 (C-2), 136.5 (C-2"), 137.6 (C-1"), 138.1 (C-4a), 141.7 (C-9a), 202.2 (C-5).

Anal. Calcd. for $C_{20}H_{20}N_2O$: C, 78.92; H, 6.62; N, 9.20. Found: C, 78.97; H, 6.58; N, 9.16.

trans-(±)-4',5',8,9-Tetrahydro-4'-(4-methylphenyl)spiro{6*H*-benzocycloheptene-6,3'-[3*H*]pyrazol}-5(7*H*)-one (**32**).

This compound was obtained as white crystals in 80% yield, mp 106-107°; ir: ν 1659, 1595, 1513, 1446, 1249, 1215, 972, 948, 818, 774, 749 cm^{-1}; ^1H nmr: δ 1.52-1.71 (m, 2H, H-7$_{eq}$,8), 1.87 (ddd, 1H, H-7$_{ax}$, J 14.6, 9.1 and 5.6 Hz), 2.00-2.10 (m, 1H, H-8), 2.30 (s, 3H, 4"-CH_3), 2.96 (ddd, 1H, H-9$_{eq}$, J 15.5, 7.7 and 4.0 Hz), 3.41 (ddd, 1H, H-9$_{ax}$, J 15.5, 9.1 and 4.0 Hz), 3.87 (dd, 1H, H-4', J 8.3 and 4.0 Hz), 4.73 (dd, 1H, H-5'$_{cis}$, J 17.9 and 8.3 Hz), 4.89 (dd, 1H, H-5'$_{trans}$, J 17.9 and 4.0 Hz), 6.85 (d, 2H, H-2",6", J 8.0 Hz), 7.07 (d, 2H, H-3",5", J 8.0 Hz), 7.21 (d, 1H, H-1, J 7.6 Hz), 7.26 (ddd, 1H, H-3, J 7.9, 7.3 and 0.9 Hz), 7.42 (ddd, 1H, H-2, J 7.6, 7.3 and 1.8 Hz), 7.43 (d, 1H, H-4, J 7.9 Hz); ^{13}C nmr: δ 21.0 (4"-CH_3), 23.6 (C-8), 30.6 (C-7), 33.1 (C-9), 44.6 (C-4'), 83.6 (C-5'), 105.0 (C-3'), 126.4 (C-3), 128.1 (C-2",6"), 128.4 (C-4), 129.3 (C-3",5"), 129.3 (C-1), 132.0 (C-2), 135.6 (C-1"), 136.9 (C-4"), 138.4 (C-4a), 141.1 (C-9a), 202.8 (C-5).

Anal. Calcd. for $C_{20}H_{20}N_2O$: C, 78.92; H, 6.62; N, 9.20. Found: C, 78.86; H, 6.65; N, 9.26.

trans-(±)-4',5',8,9-Tetrahydro-4'-(4-isopropylphenyl)spiro{6*H*-benzocycloheptene-6,3'-[3*H*]pyrazol}-5(7*H*)-one (**33**).

This compound was obtained as white crystals in 78% yield, mp 118-119°; ir: ν 1662, 1595, 1448, 1416, 1293, 1251, 1218, 1156, 1055, 955, 822, 772, 745 cm^{-1}; ^1H nmr: δ 1.22 (d, 6H, 2 x CH_3, J 6.9 Hz), 1.52-1.71 (m, 2H, H-7$_{eq}$,8), 1.87 (ddd, 1H, H-7$_{ax}$, J 14.6, 8.9 and 5.9 Hz), 2.01-2.11 (m, 1H, H-8), 2.86 [sept, 1H, 4"-CH(CH_3)$_2$, J 6.9 Hz], 2.97 (ddd, 1H, H-9$_{eq}$, J 15.4, 7.8 and 3.9 Hz), 3.42 (ddd, 1H, H-9$_{ax}$, J 15.4, 9.2 and 4.0 Hz), 3.88 (dd, 1H, H-4', J 8.3 and 4.1 Hz), 4.74 (dd, 1H, H-5'$_{cis}$, J 17.9 and 8.3 Hz), 4.90 (dd, 1H, H-5'$_{trans}$, J 17.9 and 4.1 Hz), 6.89 (d, 2H, H-2",6", J 8.1 Hz), 7.12 (d, 2H, H-3",5", J 8.1 Hz), 7.21 (d, 1H, H-1, J 7.5 Hz), 7.27 (t, 1H, H-3, J 7.5 Hz), 7.40-7.45 (m, 2H, H-2,4); ^{13}C nmr: δ 23.9 (2 x CH_3), 23.6 (C-8), 30.6 (C-7), 33.1 (C-9), 33.6 [4"-CH(CH_3)$_2$], 44.6 (C-4'), 83.6 (C-5'), 105.0 (C-3'), 126.4 (C-3), 126.6 (C-3",5"),128.2 (C-2",6"), 128.5 (C-4), 129.3 (C-1), 132.0 (C-2), 135.9 (C-1"), 138.5 (C-4a), 141.2 (C-9a), 147.9 (C-4"), 202.8 (C-5).

Anal. Calcd. for $C_{22}H_{24}N_2O$: C, 79.49; H, 7.28; N, 8.42. Found: C, 79.45; H, 7.31; N, 8.45.

trans-(±)-4',5',8,9-Tetrahydro-4'-(2-methoxyphenyl)spiro{6*H*-benzocycloheptene-6,3'-[3*H*]pyrazol}-5(7*H*)-one (**34**).

This compound was obtained as white crystals in 81% yield, mp 130-131°; ir: ν 1678, 1597, 1491, 1345, 1292, 1239, 1118, 1030, 945, 900, 747, 705, cm^{-1}; ^1H nmr: δ 1.47-1.68 (m, 2H, H-7$_{eq}$,8), 1.85-2.07 (m, 2H, H-7$_{ax}$,8), 2.96 (ddd, 1H, H-9$_{eq}$, J 15.4, 6.4 and 5.3 Hz), 3.40 (ddd, 1H, H-9$_{ax}$, J 19.7, 12.5 and 5.8 Hz), 3.70 (s, 3H, 2"-OCH_3), 4.17 (dd, 1H, H-4', J 8.9 and 3.6 Hz), 4.75 (dd, 1H, H-5'$_{cis}$, J 17.9 and 8.9 Hz), 4.98 (dd, 1H, H-5'$_{trans}$, J 17.9 and 3.6 Hz), 6.80 (d, 1H, H-3", J 8.2 Hz), 6.86-6.91 (m, 2H, H-5",6"), 7.17-7.25 (m, 2H, H-1,4"), 7.28 (dd, 1H, H-3, J 7.5 and 7.3 Hz), 7.42 (dd, 1H, H-2, J 7.5 and 7.3 Hz), 7.45 (d, 1H, H-4, J 7.3 Hz); ^{13}C nmr: δ 23.2 (C-8), 28.7 (C-7), 32.4 (C-9), 38.8 (C-4'), 55.1 (2"-OCH_3), 83.2 (C-5'), 104.4 (C-3'), 110.4 (C-3"), 120.6 (C-5"), 126.4 (C-3), 127.3 (C-1"), 128.3 (C-4), 129.0 (C-4"), 129.1 (C-6"), 128.5 (C-1), 131.9 (C-2), 138.7 (C-4a), 140.2 (C-9a), 157.2 (C-2"), 203.9 (C-5).

Anal. Calcd. for $C_{20}H_{20}N_2O_2$: C, 74.98; H, 6.29; N, 8.74. Found: C, 74.90; H, 6.25; N, 8.78.

trans-(±)-4',5',8,9-Tetrahydro-4'-(3-methoxyphenyl)spiro{6*H*-benzocycloheptene-6,3'-[3*H*]pyrazol}-5(7*H*)-one (**35**).

This compound was obtained as white crystals in 81% yield, mp 105-106°; ir: ν 1676, 1597, 1491, 1452, 1288, 1248, 1216, 1160, 1040, 957, 936, 899, 751, 705 cm^{-1}; ^1H nmr: δ 1.52-1.74

(m, 2H, H-7_{eq},8), 1.88 (ddd, 1H, H-7_{ax}, J 14.5, 9.0 and 5.6 Hz), 2.01-2.12 (m, 1H, H-8), 2.98 (ddd, 1H, H-9_{eq}, J 15.5, 7.5 and 3.7 Hz), 3.44 (ddd, 1H, H-9_{ax}, J 15.5, 8.9 and 3.9 Hz), 3.76 (s, 3H, 3"-OCH_3), 3.89 (dd, 1H, H-4', J 8.3 and 4.0 Hz), 4.72 (dd, 1H, H-5'$_{cis}$, J 17.9 and 8.3 Hz), 4.91 (dd, 1H, H-5'$_{trans}$, J 17.9 and 4.0 Hz), 6.52 (d, 1H, H-2", J 2.0 Hz), 6.55 (d, 1H, H-6", J 7.7 Hz), 6.77 (dd, 1H, H-4", J 8.1 and 2.0 Hz), 7.18 (dd, 1H, H-5", J 8.1 and 7.7 Hz), 7.22 (d, 1H, H-1, J 7.5 Hz), 7.26 (t, 1H, H-3, J 7.8 Hz), 7.42 (dd, 1H, H-2, J 7.8 and 7.5 Hz), 7.43 (d, 1H, H-4, J 7.8 Hz); ^{13}C nmr: δ 23.7 (C-8), 30.6 (C-7), 33.1 (C-9), 44.9 (C-4'), 55.2 (3"-OCH_3), 83.2 (C-5'), 105.2 (C-3'), 112.4 (C-4"), 114.2 (C-2"), 120.5 (C-6"), 126.4 (C-3), 128.5 (C-4), 129.4 (C-1), 129.6 (C-5"), 132.0 (C-2), 138.4 (C-4a), 140.3 (C-1"), 141.3 (C-9a), 159.6 (C-3"), 202.5 (C-5).

Anal. Calcd. for $C_{20}H_{20}N_2O_2$: C, 74.98; H, 6.29; N, 8.74. Found: C, 74.91; H, 6.32; N, 8.79.

trans-(±)-4',5',8,9-Tetrahydro-4'-(4-methoxyphenyl)spiro{6*H*-benzocycloheptene-6,3'-[3*H*]pyrazol}-5(7*H*)-one (**36**).

This compound was obtained as white crystals in 87% yield, mp 115-116°; ir: ν 1658, 1594, 1513, 1446, 1307, 1249, 1181, 1032, 941, 823, 776, 749 cm^{-1}; ^{1}H nmr: δ 1.52-1.71 (m, 2H, H-7_{eq},8), 1.88 (ddd, 1H, H-7_{ax}, J 14.6, 9.2 and 5.6 Hz), 1.99-2.09 (m, 1H, H-8), 2.97 (ddd, 1H, H-9_{eq}, J 15.5, 7.8 and 3.8 Hz), 3.41 (ddd, 1H, H-9_{ax}, J 15.5, 9.0 and 3.9 Hz), 3.77 (s, 3H, 4"-OCH_3), 3.86 (dd, 1H, H-4', J 8.3 and 4.1 Hz), 4.73 (dd, 1H, H-5'$_{cis}$, J 17.9 and 8.3 Hz), 4.88 (dd, 1H, H-5'$_{trans}$, J 17.9 and 4.1 Hz), 6.80 (d, 2H, H-3",5", J 8.7 Hz), 6.88 (d, 2H, H-2",6", J 8.7 Hz), 7.22 (d, 1H, H-1, J 7.5 Hz), 7.27 (ddd, 1H, H-3, J 7.7, 7.5 and 1.2 Hz), 7.42 (dd, 1H, H-2, J 7.7 and 7.5 Hz), 7.43 (d, 1H, H-4, J 7.5 Hz); ^{13}C nmr: δ 23.6 (C-8), 30.6 (C-7), 33.1 (C-9), 44.2 (C-4'), 55.2 (4"-OCH_3), 83.7 (C-5'), 105.0 (C-3'), 113.9 (C-3",5"), 126.4 (C-3), 128.4 (C-4), 129.2 (C-2",6"), 129.3 (C-1), 130.6 (C-1"), 132.0 (C-2), 138.4 (C-4a), 141.1 (C-9a), 158.7 (C-4"), 202.8 (C-5).

Anal. Calcd. for $C_{20}H_{20}N_2O_2$: C, 74.98; H, 6.29; N, 8.74. Found: C, 74.89; H, 6.33; N, 8.68.

trans-(±)-4',5',8,9-Tetrahydro-4'-(4-fluorophenyl)spiro{6*H*-benzocycloheptene-6,3'-[3*H*]pyrazol}-5(7*H*)-one (**37**).

This compound was obtained as white crystals in 86% yield, mp 98-99°; ir: ν 1676, 1599, 1510, 1453, 1252, 1218, 1161, 936, 834, 824, 777 cm^{-1}; ^{1}H nmr: δ 1.52-1.68 (m, 2H, H-7_{eq},8), 1.82 (ddd, 1H, H-7_{ax}, J 18.4, 8.6 and 4.3 Hz), 2.03-2.15 (m, 1H, H-8), 2.98 (ddd, 1H, H-9_{eq}, J 15.6, 7.7 and 3.3 Hz), 3.45 (ddd, 1H, H-9_{ax}, J 15.6, 9.2 and 3.3 Hz), 3.93 (dd, 1H, H-4', J 8.4 and 4.1 Hz), 4.72 (dd, 1H, H-5'$_{cis}$, J 17.9 and 8.4 Hz), 4.87 (dd, 1H, H-5'$_{trans}$, J 17.9 and 4.1 Hz), 6.96-7.00 (m, 4H, H-2",3",5",6"), 7.23 (d, 1H, H-1, J 7.5 Hz), 7.26 (dd, 1H, H-3, J 7.8 and 6.6 Hz), 7.40-7.45 (m, 2H, H-2,4); ^{13}C nmr: δ 23.8 (C-8), 31.0 (C-7), 33.2 (C-9), 44.0 (C-4'), 83.4 (C-5'), 105.3 (C-3'), 115.5 (d, J_{CF} 21.9 Hz, C-3",5"), 126.5 (C-3), 128.5 (C-4), 129.5 (C-1), 129.8 (d, J_{CF} 7.5 Hz, C-2",6"), 132.1 (C-2), 134.5 (d, J_{CF} 3.0 Hz, C-1"), 138.3 (C-4a), 141.4 (C-9a), 161.9 (d, J_{CF} 246.8 Hz, C-4"), 202.2 (C-5).

Anal. Calcd. for $C_{19}H_{17}FN_2O$: C, 74.01; H, 5.56; N, 9.08. Found: C, 74.08; H, 5.52; N, 9.11.

trans-(±)-4',5',8,9-Tetrahydro-4'-(2-chlorophenyl)spiro{6*H*-benzocycloheptene-6,3'-[3*H*]pyrazol}-5(7*H*)-one (**38**).

This compound was obtained as white crystals in 74% yield, mp 152-153°; ir: ν 1678, 1599, 1476, 1448, 1252, 1231, 1039, 939, 893, 757, 706 cm^{-1}; ^{1}H nmr: δ 1.59-1.84 (m, 3H, 2 x H-7,H-8), 2.09-2.21 (m, 1H, H-8), 3.01 (ddd, 1H, H-9_{eq}, J 15.1, 6.8 and 4.4 Hz), 3.46 (ddd, 1H, H-9_{ax}, J 15.1, 9.4 and 5.1 Hz), 4.47 (dd, 1H, H-4', J 8.6 and 2.2 Hz), 4.73 (dd, 1H, H-5'$_{cis}$, J 18.0 and 8.6 Hz), 5.06 (dd, 1H, H-5'$_{trans}$, J 18.0 and 2.2 Hz), 6.68-6.73 (m, 1H, H-6"), 7.13-7.18 (m, 2H, H-3",5"), 7.31-7.34 (m, 1H, H-4"), 7.21 (d, 1H, H-1, J 8.3 Hz), 7.27 (dd, 1H, H-3, J 7.8 and 7.4 Hz), 7.42 (dd, 1H, H-2, J 8.3 and 7.8 Hz), 7.44 (d, 1H, H-4, J 7.4 Hz); ^{13}C nmr: δ 23.5 (C-8), 29.5 (C-7), 33.5 (C-9), 41.4 (C-4'), 84.1 (C-5'), 105.5 (C-3'), 126.5 (C-3), 127.2 (C-5"), 128.4 (C-4), 128.5 (C-3"), 128.7 (C-6"), 129.1 (C-1), 129.6 (C-4"), 132.0 (C-2), 134.5 (C-2"), 137.0 (C-1"), 138.2 (C-4a), 140.6 (C-9a), 202.5 (C-5).

Anal. Calcd. for $C_{19}H_{17}ClN_2O$: C, 70.26; H, 5.28; N, 8.62. Found: C, 70.21; H, 5.31; N, 8.59.

trans-(±)-4',5',8,9-Tetrahydro-4'-(3-chlorophenyl)spiro{6*H*-benzocycloheptene-6,3'-[3*H*]pyrazol}-5(7*H*)-one (**39**).

This compound was obtained as white crystals in 74% yield, mp 107-108°; ir: ν 1680, 1596, 1571, 1476, 1444, 1428, 1275, 1249, 1202, 1082, 945, 772, 735 cm^{-1}; ^{1}H nmr: δ 1.58-1.87 (m, 2H, H-7_{eq},8), 1.82 (ddd, 1H, H-7_{ax}, J 15.1, 10.0 and 5.3 Hz), 2.06-2.17 (m, 1H, H-8), 3.00 (ddd, 1H, H-9_{eq}, J 15.4, 7.4 and 2.8 Hz), 3.49 (ddd, 1H, H-9_{ax}, J 15.4, 9.4 and 3.3 Hz), 3.93 (dd, 1H, H-4', J 8.2 and 3.9 Hz), 4.70 (dd, 1H, H-5'$_{cis}$, J 17.9 and 8.2 Hz), 4.88 (dd, 1H, H-5'$_{trans}$, J 17.9 and 3.9 Hz), 6.85-6.89 (m, 1H, H-6"), 6.99 (s broad, 1H, H-2"), 7.18-7.30 (m, 4H, H-1,3,4",5"), 7.41-7.45 (m, 2H, H-2,4); ^{13}C nmr: δ 23.9 (C-8), 31.1 (C-7), 33.2 (C-9), 44.3 (C-4'), 82.9 (C-5'), 105.5 (C-3'), 126.4 (C-3), 126.5 (C-6"), 127.5 (C-5"), 128.4 (C-2"), 128.6 (C-4), 129.5 (C-1), 129.9 (C-4"), 132.1 (C-2), 134.5 (C-3"), 138.1 (C-4a), 140.8 (C-1"), 141.6 (C-9a), 201.8 (C-5).

Anal. Calcd. for $C_{19}H_{17}ClN_2O$: C, 70.26; H, 5.28; N, 8.62. Found: C, 70.23; H, 5.25; N, 8.66.

trans-(±)-4',5',8,9-Tetrahydro-4'-(4-chlorophenyl)spiro{6*H*-benzocycloheptene-6,3'-[3*H*]pyrazol}-5(7*H*)-one (**40**).

This compound was obtained as white crystals in 84% yield, mp 101-102°; ir: ν 1679, 1597, 1551, 1414, 1277, 1253, 1202, 1089, 1012, 895, 835, 811, 733 cm^{-1}; ^{1}H nmr: δ 1.53-1.69 (m, 2H, H-7_{eq},8), 1.80 (ddd, 1H, H-7_{ax}, J 17.6, 7.7 and 4.0 Hz), 2.02-2.13 (m, 1H, H-8), 2.97 (ddd, 1H, H-9_{eq}, J 15.6, 7.7 and 3.4 Hz), 3.45 (ddd, 1H, H-9_{ax}, J 15.6, 9.2 and 3.8 Hz), 3.91 (dd, 1H, H-4', J 8.3 and 4.1 Hz), 4.70 (dd, 1H, H-3'$_{cis}$, J 17.9 and 8.3 Hz), 4.85 (dd, 1H, H-5'$_{trans}$, J 17.9 and 4.1 Hz), 6.91 (d, 2H, H-2",6", J 8.7 Hz), 7.21-7.28 (m, 2H, H-1,3), 7.24 (d, 2H, H-3",5", J 8.7 Hz), 7.39-7.44 (m, 2H, H-2,4); ^{13}C nmr: δ 23.8 (C-8), 31.0 (C-7), 33.2 (C-9), 44.1 (C-4'), 83.2 (C-5'), 105.3 (C-3'), 126.4 (C-3), 128.5 (C-4), 128.8 (C-3",5"), 129.5 (C-1), 129.6 (C-2",6"), 132.1 (C-2), 133.1 (C-4"), 137.2 (C-1"), 138.2 (C-4a), 141.4 (C-9a), 202.0 (C-5).

Anal. Calcd. for $C_{19}H_{17}ClN_2O$: C, 70.26; H, 5.28; N, 8.62. Found: C, 70.33; H, 5.24; N, 8.67.

trans-(±)-4',5',8,9-Tetrahydro-4'-(4-bromophenyl)spiro{6*H*-benzocycloheptene-6,3'-[3*H*]pyrazol}-5(7*H*)-one (**41**).

This compound was obtained as white crystals in 81% yield, mp 123-124°; ir: ν 1679, 1595, 1551, 1486, 1407, 1253, 1201, 1068, 1008, 895, 833, 809, 733 cm^{-1}; ^{1}H nmr: δ 1.55-1.67 (m, 2H, H-7_{eq},8), 1.81 (ddd, 1H, H-7_{ax}, J 18.2, 8.7 and 4.4 Hz), 2.04-2.15 (m, 1H, H-8), 2.98 (ddd, 1H, H-9_{eq}, J 15.6, 7.8 and 3.3 Hz), 3.46 (ddd, 1H, H-9_{ax}, J 15.6, 9.2 and 3.6 Hz), 3.91 (dd, 1H, H-4', J 8.2 and 4.0 Hz), 4.71 (dd, 1H, H-5'$_{cis}$, J 17.9 and 8.2 Hz), 4.86

(dd, 1H, H-5'$_{trans}$, J 17.9 and 4.0 Hz), 6.86 (d, 2H, H-2",6", J 8.4 Hz), 7.23 (d, 1H, H-1, J 7.2 Hz), 7.28 (dd, 1H, H-3, J 8.4 and 7.2 Hz), 7.39-7.45 (m, 2H, H-2,4), 7.40 (d, 2H, H-3",5", J 8.4 Hz); ^{13}C nmr: δ 23.8 (C-8), 31.1 (C-7), 33.2 (C-9), 44.1 (C-4'), 83.1 (C-5'), 105.3 (C-3'), 121.2 (C-4"), 126.4 (C-3), 128.5 (C-4), 129.5 (C-1), 130.0 (C-2",6"), 131.7 (C-3",5"), 132.1 (C-2), 137.7 (C-1"), 138.2 (C-4a), 141.5 (C-9a), 202.0 (C-5).

Anal. Calcd. for $C_{19}H_{17}BrN_2O$: C, 61.79; H, 4.64; N, 7.58. Found: C, 61.84; H, 4.67; N, 7.52.

trans-(±)-4',5',8,9-Tetrahydro-4'-(4-cyanophenyl)spiro{6*H*-benzocycloheptene-6,3'-[3*H*]pyrazol}-5(7*H*)-one (**42**).

This compound was obtained as white crystals in 76% yield, mp 162-163°; ir: ν 1670, 1596, 1452, 1253, 1218, 940, 838, 821, 776, 745 cm^{-1}; ^{1}H nmr: δ 1.55-1.82 (m, 3H, 2 x H-7,H-8), 2.08-2.19 (m, 1H, H-8), 3.01 (ddd, 1H, H-9$_{eq}$, J 15.9, 7.7 and 2.9 Hz), 3.50 (ddd, 1H, H-9$_{ax}$, J 15.9, 9.2 and 3.2 Hz), 4.04 (dd, 1H, H-4', J 8.2 and 4.2 Hz), 4.72 (dd, 1H, H-5'$_{cis}$, J 17.9 and 8.2 Hz), 4.88 (dd, 1H, H-5'$_{trans}$, J 17.9 and 4.2 Hz), 7.12 (d, 2H, H-2",6", J 8.3 Hz), 7.26 (d, 1H, H-1, J 9.0 Hz), 7.27 (dd, 1H, H-3, J 8.1 and 7.5 Hz), 7.42-7.47 (m, 2H, H-2,4), 7.59 (d, 2H, H-3",5", J 8.3 Hz); ^{13}C nmr: δ 24.1 (C-8), 31.6 (C-7), 33.3 (C-9), 44.5 (C-4'), 82.7 (C-5'), 105.9 (C-3'), 111.3 (C-4"), 118.4 (4"-*C*N), 126.5 (C-3), 129.2 (C-2",6"), 129.6 (C-1), 129.7 (C-4), 132.2 (C-2), 132.4 (C-3",5"), 138.0 (C-4a), 141.8 (C-9a), 144.3 (C-1"), 201.2 (C-5).

Anal. Calcd. for $C_{20}H_{17}N_3O$: C, 76.17; H, 5.43; N, 13.32. Found: C, 76.23; H, 5.46; N, 13.27.

trans-(±)-4',5',8,9-Tetrahydro-4'-(1-naphthyl)spiro{6*H*-benzocycloheptene-6,3'-[3*H*]pyrazol}-5(7*H*)-one (**43**).

This compound was obtained as white crystals in 87% yield, mp 147-148°; ir: ν 1673, 1596, 1448, 1243, 784, 773, cm^{-1}; ^{1}H nmr: δ 1.51-1.69 (m, 3H, 2 x H-7,H-8), 2.02-2.10 (m, 1H, H-8), 2.94 (ddd, 1H, H-9$_{eq}$, J 15.9, 6.9 and 2.7 Hz), 3.53 (ddd, 1H, H-9$_{ax}$, J 15.9, 10.0 and 3.3 Hz), 4.65 (dd, 1H, H-5'$_{cis}$, J 18.1 and 8.7 Hz), 4.95 (dd, 1H, H-4', J 8.7 and 2.3 Hz), 5.21 (dd, 1H, H-5'$_{trans}$, J 18.1 and 2.3 Hz), 6.84 (d, 1H, H-2", J 7.2 Hz), 7.20 (d, 1H, H-1, J 7.7 Hz), 7.26 (dd, 1H, H-3, J 7.2 and 7.1 Hz), 7.38 (dd, 1H, H-3", J 8.3 and 7.2 Hz), 7.40 (ddd, 1H, H-2, J 7.7, 7.1 and 1.4 Hz), 7.48 (dd, 1H, H-4, J 7.2 and 1.4 Hz), 7.50 (ddd, 1H, H-6", J 8.0, 7.4 and 1.2 Hz), 7.55 (ddd, 1H, H-7", J 8.0, 7.4 and 1.2 Hz), 7.75 (d, 1H, H-4", J 8.3 Hz), 7.85 (d, 1H, H-5", J 8.0 Hz), 8.21 (d, 1H, H-8", J 8.0 Hz); ^{13}C nmr: δ 24.3 (C-8), 31.0 (C-7), 33.3 (C-9), 38.5 (C-4'), 83.7 (C-5'), 106.9 (C-3'), 123.3 (C-8"), 124.9 (C-2"), 125.3 (C-3"), 125.9 (C-6"), 126.3 (C-3), 126.8 (C-7"), 127.9 (C-4"), 128.5 (C-4), 129.0 (C-5"), 129.6 (C-1), 131.9 (C-2), 132.5 (C-9"), 133.6 (C-10"), 135.3 (C-1"), 138.2 (C-4a), 142.2 (C-9a), 202.1 (C-5).

Anal. Calcd. for $C_{23}H_{20}N_2O$: C, 81.15; H, 5.92; N, 8.22. Found: C, 81.22; H, 5.96; N, 8.16.

trans-(±)-4',5',8,9-Tetrahydro-4'-(2-naphthyl)spiro{6*H*-benzocycloheptene-6,3'-[3*H*]pyrazol}-5(7*H*)-one (**44**).

This compound was obtained as white crystals in 82% yield, mp 144-145°; ir: ν 1671, 1594, 1425, 1247, 1201, 738 cm^{-1}; ^{1}H nmr: δ 1.51-1.59 (m, 1H, H-8), 1.68 (ddd, 1H, H-7$_{eq}$, J 14.2, 6.3 and 5.8 Hz), 1.87 (ddd, 1H, H-7$_{ax}$, J 14.2, 9.2 and 5.6 Hz), 1.97-2.06 (m, 1H, H-8), 2.97 (ddd, 1H, H-9$_{eq}$, J 15.5, 7.6 and 3.7 Hz), 3.44 (ddd, 1H, H-9$_{ax}$, J 15.5, 9.5 and 3.8 Hz), 4.10 (dd, 1H, H-4', J 8.3 and 3.8 Hz), 4.79 (dd, 1H, H-5'$_{cis}$, J 17.9 and 8.3 Hz), 5.03 (dd, 1H, H-5'$_{trans}$, J 17.9 and 3.8 Hz), 7.02 (dd, 1H, H-3", J 8.3 and 1.7 Hz), 7.21 (d, 1H, H-1, J 7.6 Hz), 7.47 (s broad, 1H, H-1"), 7.74 (d, 1H, H-4", J 8.3 Hz), 7.27 (dd, 1H, H-3, J 7.5 and 7.3 Hz), 7.42 (ddd, 1H, H-2, J 7.6, 7.5 and 1.4 Hz), 7.45-7.54 (m, 3H, H-4,6",7"), 7.73-7.78 (m, 2H, H-5",8"); ^{13}C nmr: δ 23.8 (C-8), 30.9 (C-7), 33.2 (C-9), 45.0 (C-4'), 83.5 (C-5'), 105.5 (C-3'), 126.1 and 126.4 (C-6",7" and C-3), 126.2 (C-3"), 127.1 (C-1"), 127.58 and 127.63 (C-5",8"), 128.4 (C-4"), 128.6 (C-4), 129.4 (C-1), 132.1 (C-2), 132.4 (C-10"), 133.1 (C-9"), 136.2 (C-2"), 138.4 (C-4a), 141.4 (C-9a), 202.4 (C-5).

Anal. Calcd. for $C_{23}H_{20}N_2O$: C, 81.15; H, 5.92; N, 8.22. Found: C, 81.06; H, 5.88; N, 8.28.

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[23] For sake of a simple comparison of the related stereoisomers, in our present and previous papers [17-19] those α,β-enones are considered *E*-isomers where the carbonyl and aryl groups are on the opposite sides of the double bond and the other diastereomers are the *Z*-isomers.

[24] Although the pyrazolines synthesised are racemates, only one enantiomer is depicted in Schemes 1 and 2 in each case.

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