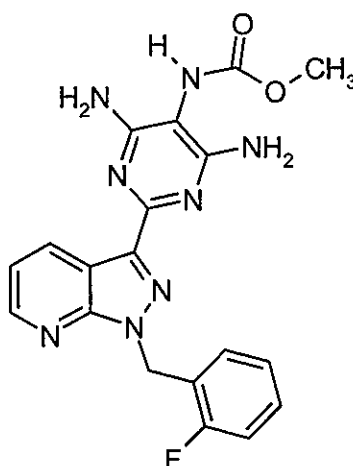


Novel polymorphic shapes of methyl {4,6-diamino-2-[1-(2-fluorobenzyl)-1H-pyrazolo[3,4-b]pyridin-3-yl]pyrimidin-5-yl}carbamate

The invention relates to novel polymorphic forms of methyl {4,6-diamino-2-[1-(2-fluorobenzyl)-1H-pyrazolo[3,4-b]pyridin-3-yl]pyrimidin-5-yl}carbamate of the formula (I), in particular to the
5 modification I, to processes for their preparation, to medicaments comprising them and to their use for fighting diseases.

Methyl {4,6-diamino-2-[1-(2-fluorobenzyl)-1H-pyrazolo[3,4-b]pyridin-3-yl]pyrimidin-5-yl}carbamate is described in WO 03/095451 and corresponds to the compound of the formula (I):



10

(I)

Preparation and use of the compound of the formula (I) for treating, for example, cardiovascular disorders and erectile dysfunction are already known from WO 03/095451. Using the procedure described therein, the compound of the formula (I) is obtained in the form of a crystal modification which is referred to as mesomorphous form hereinbelow. The mesomorphous form has no characteristic
15 melting point. It has a characteristic X-ray diffractogram, IR spectrum, Raman spectrum, FIR spectrum, NIR spectrum and ¹³C solid-state NMR spectrum (Tab. 1-7, Fig. 1-7).

It has now been found that the mesomorphous form is metastable and thus not suitable for use in pharmaceutical formulations such as, for example, solid and semi-solid preparations.

Surprisingly, four further polymorphic forms and the amorphous form have been found. Compared to
20 the mesomorphous form, known from WO 03/095451, the polymorphic forms have markedly different melting points of 244°C (modification I), 201°C (modification II), 165°C (modification III) and 141°C (modification IV), and each of these modifications has a characteristic X-ray diffractogram, IR spectrum, Raman spectrum, FIR spectrum, NIR spectrum and ¹³C solid-state NMR spectrum (Tab. 1-7, Fig. 1-7).

The present invention provides the compound of the formula (I) in modification I.

The invention provides the compound of the formula (I) in modification I which, in the X-ray diffractogram, has essentially the following preferred peak maximum of the 2 theta angle at 6.1.

5 The invention preferably provides the compound of the formula (I) in modification I which, in the X-ray diffractogram, has essentially the following preferred peak maximum of the 2 theta angle at 6.1, 14.7 and 22.2.

The invention provides the compound of the formula (I) in modification I which, in the IR spectrum, has essentially the following preferred peak maximum at 3451 cm^{-1} .

10 The present invention provides the compound of the formula (I) in modification I which, in the NIR spectrum, has essentially the following preferred peak maximum at 6834 cm^{-1} .

General aspects in connection with the present invention are pharmacological properties, processability, preparation process, side-effect profile, stability and pharmacological activity of modification I of the compound of the formula (I).

15 Surprisingly, the modification I of the compound of the formula (I) is thermodynamically stable and storage-stable even after processing to suspensions. It is therefore suitable in particular for use in pharmaceutical formulations such as, for example, suspensions or cremes, but also in other preparations prepared via suspended active compound, such as, for example, during aqueous granulation or wet grinding. By using, according to the invention, the stable modification I, it is ensured that there are no changes in solubility as a result of a conversion. This increases the safety of preparations comprising the compound of the formula (I), and patient risk is reduced.

25 In pharmaceutical formulations, the compound of the formula (I) in modification I according to the invention is employed in high purity. For reasons of stability, a pharmaceutical formulation comprises mainly the compound of the formula (I) in modification I and no major amounts of any other form of the compound of the formula (I). Preferably, the medicament comprises more than 90 per cent by weight, particularly preferably more than 95 per cent by weight, of the compound of the formula (I) in the modification I based on the total amount of the compound of the formula (I) present.

The present invention furthermore provides the use of the compound of the formula (I) in modification I for preparing a medicament for treating diseases, in particular for treating cardiovascular disorders.

30 The compound of the formula (I) in modification I brings about vasorelaxation and an inhibition of platelet aggregation and leads to a lowering of blood pressure and an increase in the coronary blood

flow. These effects are mediated by direct stimulation of soluble guanylate cyclase and an intracellular increase in cGMP.

It can therefore be employed in medicaments for the treatment of cardiovascular disorders such as, for example, for the treatment of high blood pressure and heart failure, stable and unstable Angina pectoris, peripheral and cardiac vascular disorders, of arrhythmias, for the treatment of
5 thromboembolic disorders and ischemias such as myocardial infarction, stroke, transitory and ischemic attacks, disturbances of peripheral blood flow, prevention of restenoses such as after thrombolysis therapies, percutaneous transluminal angioplasties (PTAs), percutaneous transluminal coronary angioplasties (PTCAs), bypass and for the treatment of arteriosclerosis, fibrotic disorders,
10 such as fibrosis of the liver or pulmonary fibrosis, asthmatic disorders and diseases of the urogenital systems such as, for example, prostate hypertrophy, erectile dysfunction, female sexual dysfunction and incontinence and also for the treatment of glaucoma.

It can also be used for fighting diseases of the central nervous system characterized by disturbances of the NO/cGMP system. It is suitable in particular for removing cognitive deficits, for improving
15 learning and memory performances and for treating Alzheimer's disease. It is also suitable for treating disorders of the central nervous system such as states of anxiety, tension and depression, CNS-related sexual dysfunctions and sleep disturbances, and for controlling pathological disturbances of the intake of food, stimulants and addictive substances.

It is furthermore also suitable for regulating cerebral blood flow and thus represents an effective
20 agent for controlling migraine.

It is also suitable for the prophylaxis and control of the sequelae of cerebral infarction (apoplexia cerebri) such as stroke, cerebral ischemias and craniocerebral trauma. It can likewise be employed for controlling states of pain.

In addition, it has an anti-inflammatory effect and can therefore be employed as an anti-inflammatory
25 agent.

Moreover, it is suitable for treating pulmonary arterial hypertension, impaired microcirculation, respiratory infections, reperfusion damage, respiratory disorders, pulmonary disorders and Raynaud's syndrome.

The present invention furthermore provides a method for treating disorders, in particular the disorders
30 mentioned above, using an effective amount of the compound of the formula (I) in modification I.

The compound of the formula (I) in modification I can be administered in a suitable manner, such as, for example, orally, parenterally, pulmonarily, nasally, sublingually, lingually, buccally, rectally, dermally, transdermally, conjunctivally, otically, vaginally, as stents or as an implant.

For these administration routes, the compound according to the invention can be administered in suitable administration forms.

Suitable for oral administration are administration forms working according to the prior art, which release the compound of the formula (I) in modification I rapidly and/or in modified form, such as, for example, tablets (non-coated or coated tablets, for example coated with enteric, slowly dissolving or insoluble coats which control the release of the compound according to the invention), tablets which decompose rapidly in the oral cavity or films/wafers, films/lyophilisates, capsules (for example hard gelatin capsules or soft gelatin capsules), sugar-coated tablets, granules, pellets, powders, suspensions or aerosols.

Parenteral administration can take place with circumvention of an absorption step (for example intravenous, intraarterial, intracardiac, intraspinal or intralumbar) or with involvement of an absorption (for example intramuscular, subcutaneous, intracutaneous, percutaneous or intraperitoneal). For parenteral administration, suitable administration forms are, inter alia, injection and infusion preparations in the form of suspensions, lyophilizates or sterile powders.

Suitable for the other administration routes are, for example, pharmaceutical forms for inhalation (inter alia powder inhalers, nebulizers), tablets, films/wafers or capsules to be applied lingually, sublingually or buccally, suppositories, ear or eye preparations, vaginal capsules, aqueous suspensions (lotions, shake lotions), lipophilic suspensions, ointments, creams, transdermal therapeutic systems (such as, for example, patches), pastes, dusting powders, implants or stents.

The compound according to the invention can be converted into the administration forms mentioned. This may take place in a manner known per se by mixing with inert non-toxic, pharmaceutically acceptable auxiliaries. These auxiliaries include, inter alia, carriers (for example microcrystalline cellulose, lactose, mannitol), solvents (for example liquid polyethylene glycols), emulsifiers and dispersants or wetting agents (for example sodium dodecylsulfate, polyoxysorbitan oleate), binders (for example polyvinylpyrrolidone), synthetic and natural polymers (for example albumin), stabilizers (e.g. antioxidants such as, for example, ascorbic acid), colours (e.g. inorganic pigments such as, for example, iron oxides) and taste and/or odour corrigents.

The present invention furthermore provides medicaments comprising at least the compound of the formula (I) in modification I, usually together with one or more inert non-toxic, pharmaceutically

suitable auxiliaries such as, for example, binders, fillers, etc., and their use for the purposes mentioned above.

In general, it has been found to be advantageous to administer the compound according to the invention in total amounts of from about 0.5 to about 500, preferably from 5 to 100, mg/kg of body weight per day, if appropriate in the form of a plurality of individual doses, to obtain the desired results. An individual dose contains the active compound in amounts of from about 1 to about 80, preferably 3 to 30, mg/kg of body weight.

The invention furthermore provides a process for preparing the compound of the formula (I) in modification I, by suspending the compound of the formula (I) for example in the mesomorphous form, in an inert solvent and stirring or shaking at a temperature of from 10°C to the reflux temperature of the solvent, preferably at from 15°C to 35°C, particularly preferably at from 20 to 30°C, until the desired degree of conversion has been achieved, particularly preferably to quantitative conversion into modification I. The resulting crystals of modification I are separated off and, to remove the solvent present, dried at room temperature or at elevated temperature until the weight remains constant.

Suitable inert solvents are lower alcohols, such as methanol, ethanol, n-propanol, isopropanol, n-butanol, sec-butanol, iso-butanol, 1-pentanol, or ketones, such as acetone, or alkanes, such as n-pentane, cyclopentane, n-hexane, cyclohexane, or tetrahydrofuran, acetonitrile, toluene, ethyl acetate, 1,4-dioxane or mixtures of the solvents mentioned. Preference is given to acetonitrile and acetone or mixtures of the solvents mentioned.

In general, the preparation processes are carried out under atmospheric pressure. However, it is also possible to operate under elevated or reduced pressure, for example at from 0.5 to 5 bar.

The percentages in the tests and examples below are, unless indicated otherwise, percentages by weight; parts are parts by weight. Solvent ratios, dilution ratios and concentrations of liquid/liquid solutions are in each case by volume.

Experimental part**Working examples:**

5 The DSC thermograms were recorded using a Differential Scanning Calorimeter DSC 7, Pyris-1 or Diamond from Perkin-Elmer using a heating rate of 20 Kmin⁻¹. The measurements were carried out in perforated aluminium crucibles, the purge gas used was nitrogen. There was no sample preparation.

10 The TGA measurements were carried out using TGA7 and Pyris-1-TGA thermobalances from Perkin-Elmer using a heating rate of 10 Kmin⁻¹. The measurements were carried out in open platinum crucibles, the purge gas used was nitrogen. There was no sample preparation.

The X-ray diffractograms were recorded using an STOE STADI-P transmission diffractometer having a position-sensitive detector (PSD2) at room temperature (radiation: copper, K α 1, primary monochromator: Ge [1 1 1], wavelength: 1.5406 Å).

15 The Raman spectra were recorded using RFS 100 and Multi RAM FT-Raman spectrometers from Bruker at room temperature. The resolution was 2 cm⁻¹. There was no sample preparation. The measurement was carried out in glass tubes or on an aluminium disc.

The IR spectra were recorded using Vertex 80v and IFS 66v FT-IR spectrometers from Bruker at room temperature. The resolution was 2 cm⁻¹. The measurement was carried out in a KBr matrix as pressed disc.

20 The FIR spectra were recorded using Vertex 80v and IFS 66v FT-IR spectrometers from Bruker at room temperature. The resolution was 2 cm⁻¹. The measurement was carried out in a polyethylene matrix as pressed disc.

The NIR spectra were recorded using an IFS 28/N FT-NIR spectrometer from Bruker at room temperature. The resolution was 8 cm⁻¹. There was no sample preparation.

25 The solid-state ¹³C-NMR spectra were recorded using a DRX 400 spectrometer from Bruker at room temperature. The measuring frequency was 100.6 MHz and the rotation frequencies were 8500 Hz and 10000 Hz. There was no sample preparation.

Example 1

Preparation of methyl {4,6-diamino-2-[1-(2-fluorobenzyl)-1H-pyrazolo[3,4-b]pyridin-3-yl]pyrimidin-5-yl}carbamate of the formula (I) in modification I

Example 1.1

5 About 100 mg of methyl {4,6-diamino-2-[1-(2-fluorobenzyl)-1H-pyrazolo[3,4-b]pyridin-3-yl]pyrimidin-5-yl}carbamate of the formula (I) in the mesomorphous form are suspended in 3 ml of acetonitrile and stirred at room temperature. After one week, the suspension is filtered and the residue is dried at room temperature and atmospheric humidity. The residue is examined by X-ray diffractometry and corresponds to the title compound in modification I.

10 Example 1.2

About 100 mg of methyl {4,6-diamino-2-[1-(2-fluorobenzyl)-1H-pyrazolo[3,4-b]pyridin-3-yl]pyrimidin-5-yl}carbamate of the formula (I) in the mesomorphous form are suspended in 2 ml of acetone and stirred at 50°C under reflux. After one week, the suspension is filtered and the residue is dried at room temperature and atmospheric humidity. The residue is examined by X-ray diffractometry and corresponds to the title compound in modification I.

Example 1.3

7.1 kg of methyl {4,6-diamino-2-[1-(2-fluorobenzyl)-1H-pyrazolo[3,4-b]pyridin-3-yl]pyrimidin-5-yl}carbamate of the formula (I) as di-DMSO solvate are suspended in 171.6 kg of ethyl acetate and 42 kg of ethanol and stirred at about 73°C under reflux for 20 h. The suspension is cooled to RT and filtered off with suction, and the filter cake is washed with ethyl acetate and water. The moist product is dried at 50°C under reduced pressure. The product is examined by X-ray diffractometry and corresponds to the title compound in modification I.

Example 2

Preparation of methyl {4,6-diamino-2-[1-(2-fluorobenzyl)-1H-pyrazolo[3,4-b]pyridin-3-yl]pyrimidin-5-yl}carbamate of the formula (I) in modification II

Example 2.1

110.5 g of methyl {4,6-diamino-2-[1-(2-fluorobenzyl)-1H-pyrazolo[3,4-b]pyridin-3-yl]pyrimidin-5-yl}carbamate of the formula (I) as HCl salt are suspended in 1960 ml of ethanol at room temperature. 140 ml of triethylamine are metered in, and the mixture is stirred at RT for 3 h. The solid is filtered off with suction and washed with ethanol. The moist product is dried at 50°C under re-

duced pressure overnight. The product is examined by X-ray diffractometry and corresponds to the title compound in modification II.

Example 3

Preparation of methyl {4,6-diamino-2-[1-(2-fluorobenzyl)-1H-pyrazolo[3,4-b]pyridin-3-yl]pyrimidin-5-yl} carbamate of the formula (I) in modification III

Example 3.1

3.1 g of methyl {4,6-diamino-2-[1-(2-fluorobenzyl)-1H-pyrazolo[3,4-b]pyridin-3-yl]pyrimidin-5-yl} carbamate of the formula (I) in modification II are suspended in 60 ml of methanol and stirred at RT. After one week, the suspension is filtered and the residue is dried at room temperature and atmospheric humidity. The active compound is then heat-conditioned at 125°C for 20 min. The active compound is examined by X-ray diffractometry and corresponds to the title compound in modification III.

Example 4

Preparation of methyl {4,6-diamino-2-[1-(2-fluorobenzyl)-1H-pyrazolo[3,4-b]pyridin-3-yl]pyrimidin-5-yl} carbamate of the formula (I) in modification IV

Example 4.1

3 g of methyl {4,6-diamino-2-[1-(2-fluorobenzyl)-1H-pyrazolo[3,4-b]pyridin-3-yl]pyrimidin-5-yl} carbamate of the formula (I) in modification II are suspended in 60 ml of acetone and stirred at -20°C. After two weeks, the suspension is filtered and the residue is dried at room temperature and atmospheric humidity. The active compound is then heat-conditioned at 125°C for 30 min. The active compound is examined by X-ray diffractometry and corresponds to the title compound in modification IV.

Example 5

Preparation of the amorphous form of methyl {4,6-diamino-2-[1-(2-fluorobenzyl)-1H-pyrazolo[3,4-b]pyridin-3-yl]pyrimidin-5-yl} carbamate of the formula (I)

Example 5.1

3 g of methyl {4,6-diamino-2-[1-(2-fluorobenzyl)-1H-pyrazolo[3,4-b]pyridin-3-yl]pyrimidin-5-yl}carbamate of the formula (I) in modification I are dissolved in 1.1 l of hot tetrahydrofuran, and the solution is filtered and allowed to stand at room temperature at atmospheric humidity until the solvent has evaporated. The residue is examined by X-ray diffractometry and corresponds to the title compound in the amorphous form.

Tab. 1: Differential scanning calorimetry and thermogravimetry

	Melting point (decomposition) [°C]	Mass loss [% by weight]
modification I	244	< 0.5
modification II	201	< 0.5
modification III	165	< 0.5
modification IV	141	< 1
mesomorphous	-	about 8
amorphous	-	about 10

Tab. 2: X-ray diffractometry

Peak maximum [2 theta]				
Modifica- tion I	Modifica- tion II	Modifica- tion III	Modifica- tion IV	meso- morphous
3.6	8.3	6.6	10.6	4.0
4.9	11.3	7.7	11.6	5.2
6.1	11.5	13.9	12.8	6.1
7.0	12.1	15.1	13.4	9.1
7.3	13.6	15.6	13.8	13.0
8.8	14.1	16.8	14.1	15.2
9.9	14.8	17.4	16.1	16.9
10.9	16.3	17.5	16.5	17.5
12.0	17.0	17.8	17.6	21.0
12.3	17.5	18.2	17.8	23.7
14.7	18.2	19.5	18.0	25.6
15.3	19.0	19.8	18.6	
16.5	21.1	20.5	19.0	
17.6	22.1	22.7	19.6	
18.2	22.9	23.0	20.1	
18.4	23.3	23.3	21.0	
19.8	24.0	23.7	21.4	
20.8	25.1	24.1	21.9	

Peak maximum [2 theta]				
Modifica- tion I	Modifica- tion II	Modifica- tion III	Modifica- tion IV	meso- morphous
21.1	25.4	24.4	22.8	
21.3	26.1	25.4	24.5	
21.8	26.7	26.3	25.3	
22.2	28.6	26.8	25.4	
22.9	29.3	28.1	26.2	
24.1	30.4	28.7	26.5	
24.4	34.0	30.4	27.5	
24.7	35.6	31.2	28.1	
25.6	36.9	32.8	28.3	
26.0	37.7	33.8	28.6	
26.8		35.1	30.5	
27.4		37.6	32.5	
27.8			33.5	
28.1			33.8	
28.3			35.6	
29.3			36.2	
29.7				
30.1				
30.9				

Peak maximum [2 theta]				
Modifica- tion I	Modifica- tion II	Modifica- tion III	Modifica- tion IV	meso- morphous
31.7				
32.0				
32.7				
33.0				
33.5				
34.2				
35.3				
35.6				
36.0				

Tab. 3: IR spectroscopy

Wave number [cm ⁻¹]					
Modifica- tion I	Modifica- tion II	Modifica- tion III	Modifica- tion IV	meso- morphous	amorphous
3483	3507	3503	3489	3633	3451
3470	3484	3409	3287	3443	3331
3451	3397	3365	3157	3330	3217
3387	3291	3268	2954	3222	3150
3330	3158	3092	1710	2952	2953
3276	3024	3022	1628	1705	1707
3214	2955	2987	1561	1630	1628
3133	1724	2949	1515	1566	1566
2952	1632	2843	1492	1511	1510
1712	1608	1733	1480	1492	1492
1636	1562	1627	1439	1477	1478
1567	1491	1609	1363	1437	1438
1509	1477	1563	1342	1390	1390
1478	1437	1511	1324	1351	1351
1441	1386	1492	1302	1323	1323
1387	1345	1477	1288	1288	1289
1350	1322	1454	1247	1277	1276
1323	1287	1438	1187	1247	1248
1289	1275	1388	1169	1232	1233

Wave number [cm ⁻¹]					
Modifica- tion I	Modifica- tion II	Modifica- tion III	Modifica- tion IV	meso- morphous	amorphous
1276	1235	1356	1144	1174	1175
1249	1170	1322	1112	1140	1141
1232	1141	1288	1090	1112	1112
1174	1112	1274	1075	1061	1061
1139	1087	1250	1059	1030	1031
1111	1071	1230	1031	940	940
1086	1030	1185	939	911	911
1075	995	1173	910	863	864
1062	937	1140	871	846	847
1031	907	1109	857	820	820
1004	874	1095	849	808	808
941	849	1068	822	797	796
911	812	1034	807	774	774
867	799	974	799	757	758
849	781	940	777	712	713
820	665	911	765	643	621
808	671	865	753	621	591
795	644	839	708	590	576
774	627	820	683	568	534
760	587	806	642	534	519

Wave number [cm ⁻¹]					
Modifica- tion I	Modifica- tion II	Modifica- tion III	Modifica- tion IV	meso- morphous	amorphous
715	570	795	593	519	
631	536	777	571		
594		762	531		
576		704			
535		641			
		87			
		572			
		533			
		513			

Tab. 4: Raman spectroscopy

Wave number [cm ⁻¹]					
Modifica- tion I	Modifica- tion II	Modifica- tion III	Modifica- tion IV	meso- morphous	amorphous
3452	3397	3081	3068	3067	3332
3387	3143	3023	3028	3024	3067
3331	3095	2985	2942	2956	3030
3086	3079	2947	2850	2608	2955
3054	3056	2929	1704	1704	2843
3022	3025	2844	1621	1618	2592

Wave number [cm ⁻¹]					
Modifica- tion I	Modifica- tion II	Modifica- tion III	Modifica- tion IV	meso- morphous	amorphous
2990	3006	2589	1599	1578	2329
2953	2956	1730	1576	1508	1703
2834	2843	1633	1507	1479	1617
2604	1728	1616	1486	1448	1577
1702	1641	1597	1444	1423	1508
1633	1619	1565	1421	1380	1479
1618	1567	1504	1389	1323	1447
1598	1503	1483	1373	1309	1423
1577	1478	1440	1343	1278	1380
1508	1442	1421	1323	1252	1354
1477	1434	1385	1303	1233	1323
1447	1417	1367	1251	1177	1309
1420	1385	1329	1232	1157	1250
1380	1372	1289	1170	1142	1232
1351	1344	1250	1156	1114	1176
1322	1322	1229	1145	1063	1157
1307	1308	1186	1115	1036	1142
1289	1288	1174	1062	964	1113
1277	1277	1143	1035	823	1062
1249	1244	1109	1006	798	1035

Wave number [cm ⁻¹]					
Modifica- tion I	Modifica- tion II	Modifica- tion III	Modifica- tion IV	meso- morphous	amorphous
1225	1232	1061	964	777	963
1175	1172	1031	824	742	911
1157	1144	996	807	717	823
1140	1115	958	799	645	797
1112	1059	912	773	591	776
1064	1032	820	739	560	742
1034	964	805	719	536	716
961	906	796	647	521	645
910	820	784	598	472	591
823	800	776	564	447	566
808	772	744	535	408	536
796	740	706	446	368	521
777	719	558	403	331	471
773	646	540	350	265	447
768	629	599	320	221	410
741	588	589	264	190	368
717	556	566	247	158	332
644	538	534	231		264
632	526	514	220		220
592	467	479	194		190

Wave number [cm ⁻¹]					
Modifica- tion I	Modifica- tion II	Modifica- tion III	Modifica- tion IV	meso- morphous	amorphous
559	436	439	140		157
534	349	403			117
465	316	364			
447	268	327			
265		287			
233		257			
296		231			
266		219			
246		188			
215		156			
189					
160					

Tab. 5: FIR spectroscopy

Wave number [cm ⁻¹]					
Modifica- tion I	Modifica- tion II	Modifica- tion III	Modifica- tion IV	meso- morphous	amorphous
487	461	478	454	495	496

Wave number [cm ⁻¹]					
Modifica- tion I	Modifica- tion II	Modifica- tion III	Modifica- tion IV	meso- morphous	amorphous
466	447	437	425	485	489
451	435	402	393	469	484
430	426	363	379	447	481
407	405	334	368	430	471
365	362	310	340	406	463
343	346	284	322	368	447
325	324	231	246	331	436
318	304	189	238	289	430
291	246	168	216	262	407
262	240	105	196	236	329
237	212		156	188	289
218	194		113	160	263
188	167			108	237
160	146			92	189
96	104				158
	96				96
	92				
	84				

Tab. 6: NIR spectroscopy

Wave number [cm ⁻¹]					
Modifica- tion I	Modifica- tion II	Modifica- tion III	Modifica- tion IV	meso- morphous	amorphous
9793	9786	9905	8809	8789	8797
8779	8798	8845	8462	8408	8420
7828	8534	8687	7851	7107	7109
6834	8450	8472	6857	6846	6850
6724	8152	7852	6667	6636	6637
6631	7866	7305	6011	5977	5976
6328	6949	5966	5106	5244	5236
6059	6842	5875	5064	5057	5057
5984	6784	5782	4971	4984	4984
5846	6666	5722	4795	4802	4798
5593	6357	5430	4741	4660	4660
5095	6044	5028	4659	4432	4432
5058	5971	5920	4538	4149	4148
4965	5874	5846	4486	4056	4053
4916	5811	5755	4439		
4865	5625	5720	4216		
4808	5429	5627	4155		
4646	5231	5244	4092		
4595	5107	5116			
4531	5067	5071			

Wave number [cm ⁻¹]					
Modifica- tion I	Modifica- tion II	Modifica- tion III	Modifica- tion IV	meso- morphous	amorphous
4485	5004	4010			
4419	4965	4974			
4348	4891	4899			
4268	4836	4763			
4199	4805	4665			
4062	4732	4546			
	4659	4491			
	4553	4433			
	4503	4386			
	4481	4338			
	4443	4224			
	4402	4175			
	4367	4049			
	4329				
	4262				
	4164				
	4120				
	4057				
	4037				

Tab. 7: ^{13}C solid-state NMR spectroscopy

ppm					
Modifica- tion I	Modifica- tion II	Modifica- tion III	Modifica- tion IV	meso- morphous	amorphous
52	53	31	51	22	32
95	94	44	94	26	35
116	116	52	117	31	42
123	122	95	125	35	53
126	124	116	128	41	96
128	130	123	134	52	115
130	131	133	141	96	125
133	135	142	144	115	133
138	142	150	147	124	142
141	147	158	150	128	150
149	149	161	158	132	159
150	150		161	141	162
158	154			149	
161	158			158	
	161			161	

Fig. 1: DSC and TGA thermograms of modifications I-IV, the mesomorphous form and the amorphous form

Fig. 2: X-ray diffractograms of modifications I-IV, the mesomorphous form and the amorphous form

5 **Fig. 3:** IR spectra of modifications I-IV, the mesomorphous form and the amorphous form

Fig. 4: Raman spectra of modifications I-IV, the mesomorphous form and the amorphous form

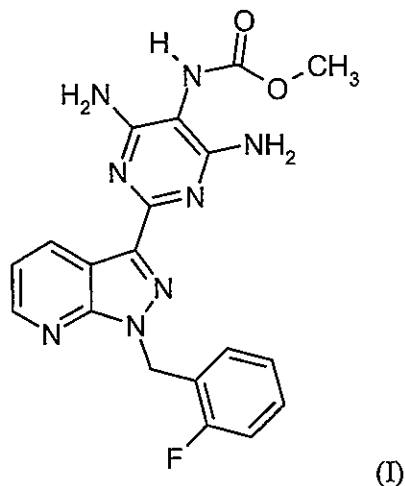
Fig. 5: FIR spectra of modifications I-IV, the mesomorphous form and the amorphous form

Fig. 6: NIR spectra of modifications I-IV, the mesomorphous form and the amorphous form

10 **Fig. 7:** ^{13}C solid-state NMR spectra of modifications I-IV, the mesomorphous form and the amorphous form

Patent claims:

1. Methyl {4,6-diamino-2-[1-(2-fluorobenzyl)-1H-pyrazolo[3,4-b]pyridin-3-yl]pyrimidin-5-yl} carbamate of the formula



- 5 in modification I.
2. Compound according to Claim 1, characterized in that the X-ray diffractogram of the compound has a peak maximum of the 2 theta angle at 6.1.
3. Compound according to Claim 1 or 2, characterized in that X-ray diffractogram of the compound has peak maxima of the 2 theta angle at 6.1, 14.7 and 22.2.
- 10 4. Compound according to any of Claims 1 to 3, characterized in that the IR spectrum of the compound has a peak maximum at 3451 cm^{-1} . Delete Claim?
5. Compound according to any of Claims 1 to 4, characterized in that the NIR spectrum of the compound has a peak maximum at 6834 cm^{-1} .
- 15 6. Compound according to any of Claims 1 to 5, characterized in that the NIR spectrum of the compound has peak maxima at 6834, 6631 and 4419 cm^{-1} .
7. Compound according to any of Claims 1 to 6 for treating diseases.
8. Medicament, comprising a compound according to any of Claims 1 to 6 and no major amounts of any other form of the compound of the formula (I).
- 20 9. Medicament, comprising a compound according to any of Claims 1 to 6 in an amount of more than 90 per cent by weight, based on the total amount of the compound of the formula (I) comprised therein.

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10. Process for preparing the compound according to any of Claims 1 to 6 by suspending the compound of the formula (I), for example in the mesomorphous form in an inert solvent and stirring or shaking at a temperature of from 10°C to the reflux temperature of the solvent until quantitative conversion into modification I has been achieved.
- 5 11. Use of the compound according to any of Claims 1 to 6 for preparing a medicament for treating cardiovascular disorders.
12. Method for treating cardiovascular disorders by administering an effective amount of a compound according to any of Claims 1 to 6.