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HETERO-COPE REARRANGEMENTS - VI[1]
SHORT AND STEREOSELECTIVE SYNTHESES OF 2-VINYLINDOLES BY A TANDEM-PROCESS

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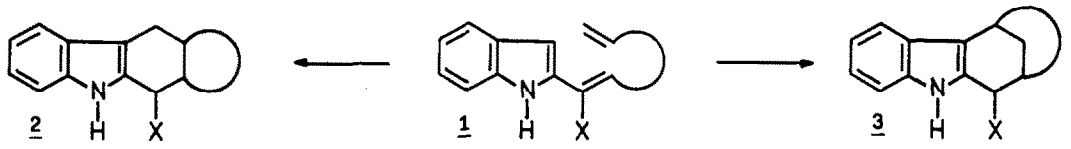
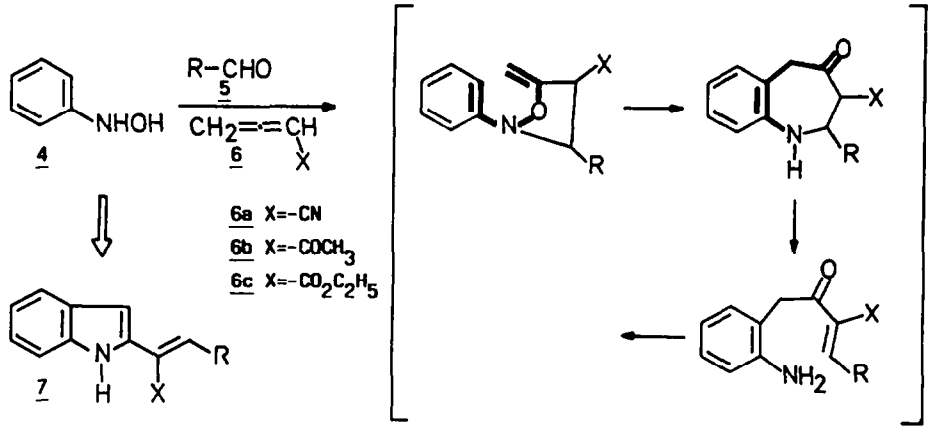
Abstract - The initially formed N-phenylnitrone-intermediates are converted by a tandem-reaction (cycloaddition, Cope rearrangement, retro-Michael addition, and indolization) to 2-vinylindoles 7. Thus these indoles can be synthesized simply and stereoselectively in a one-pot reaction from N-phenylhydroxylamine 4, aldehydes 5, and electron-deficient allenes 6.

2-Vinylindoles are enabled to undergo various cycloaddition reactions as f.i. Diels-Alder reactions. In these conversions they may react as dienes[2] as well as dienophiles[3], and they have been used in many syntheses of alkaloids and other heterocyclic compounds. Compared with the corresponding 3-substituted compounds, 2-vinylindoles are not as well accessible. In order to develop new strategies for syntheses of indole-alkaloids of the type 2 and 3 by inter- as well as intramolecular Diels-Alder reactions, we needed 2-vinylindoles of definite configuration as important key-products. Therefore we looked for a simple and variable method to synthesize these compounds.

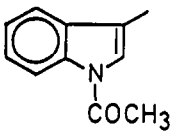
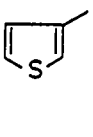
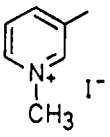


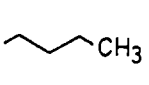
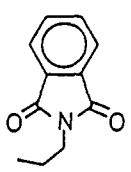
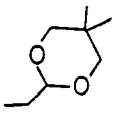
Some time ago we reported the reaction of N-phenyl-nitrones with acceptor-substituted allenes which left us with various products depending on the acceptor[4]. By reaction of ring-substituted N-phenylhydroxylamines with benzaldehyde or 3-formylpyridiniumsalts we came out with nitrones that led directly to a variety of 2-vinylindoles after addition of allene carbonitrile. Thus the vast variability of the substituents of the indole-skeleton was demonstrated. The realization of our synthetic concept required the variability of substituents on the vinyl-group. In order to direct the regio- and stereochemistry of Diels-Alder reactions, a stereoselective route to 2-vinylindoles was desirable. Here we give an account of the way we reached the goals mentioned above and introduce

scope and limitation of a method by which 2-vinylindoles can be synthesized directly from phenylhydroxylamine 4, various aldehydes 5 and acceptor-substitued allenes 6. Taking into consideration the simplicity of the starting materials and the number of reaction steps, the yields are satisfactory.



We dissolved phenylhydroxylamine and a small excess of the aldehyde in ethanol or other solvents. After complete conversion of the hydroxylamine (TLC-control) we added 1.2 - 1.5 equivalents of allene carbonitrile 6a[5]. After the termination of the reaction and distillative removal of the solvent the vinylindoles 7 can be purified either by crystallization or by chromatography. As expected we got the aryl-substituted vinylindoles 7a-d that are of interest with respect to photocyclization reactions giving carbazole derivatives[6]. The one-pot-process does not only simplify the preparative procedure but also offers the possibility to work with aliphatic aldehydes, the corresponding nitrones of which are quite un-

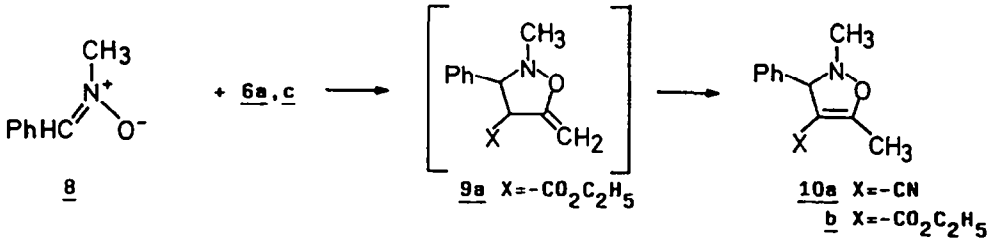
5	a	b	c	d	e	f	g
R						$-C(CH_3)_3$	$-CH(CH_3)_2$
X	-CN	-CN	-CN	-CN	$-COCH_3$	-CN	-CN
7 (%)	77	50	70	65	65	39	41

5	h	i	j	k	l	m
R			$-CH_3$			$-CO_2CH_3$
X	-CN	-CN	-CN	-CN	-CN	-CN
7 (%)	52	44	36	57	55	39

stable and f.i. tend to dimerize. Even in those cases where the existence of the nitrones is hard to prove the one-pot process comes in handy[7]. When the reaction is conducted carefully, the intermediately formed nitrone can be captured unproblematically by the allene, and even compounds like 7i or 7j are easily accessible. 7k-m prove that functional groups can be carried along. Intermediates other than the nitrones were not found.

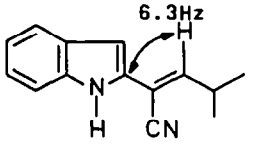
With regard to the results so far, the reaction sequence consisting of 1,3-dipolar cycloaddition, hetero-Cope rearrangement, retro-Michael addition and formation of the indole - which we aimed for and proposed in a previous communication[4] - seems to be plausible.

Little is known about cycloaddition reactions of N-phenylnitrones with allenes, but taking into consideration the molecular orbitals we expect an unproblematic cycloaddition reaction between acceptor-substituted allenes and nitrones. An expected 5-exomethylene-isoxazolidine was not observed, therefore we carried out the reaction with C-phenyl-N-methylnitrone (8) in order to support our hypothesis. At room temperature in methanol as well as benzene we came out with the isoxazoline 10 which originated from isomerization of the exomethylene-precursor. A cleavage of the N-O-bond was not observed. Reactions with other acceptor-substituted allenes took the same course. Application of 1-carbethoxyallene though led to the isolation of an unstable intermediate as a byproduct in 11% yield, the spectroscopic data of which correspond to a 5-exomethylene-isoxazolidine. The product is easily converted into 9, especially when base-catalysed. Surprisingly, our observations differ therefore from those made in recently published analogous reactions with 1-carbomethoxyallene[8].

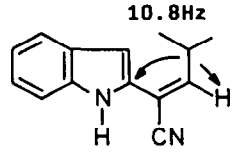


8 9a X=-$CO_2C_2H_5$ 10a X=-CN b X=-$CO_2C_2H_5$

The NMR-spectroscopic data of the vinylindoles verify the formation of products of uniform configuration. The olefins may be isomerized photochemically and can be compared with one another after chromatographic purification on silica gel. Thus we found that the tandem-reaction leads stereoselectively to Z-configurated vinylindoles. The stereochemical correlation was done by comparison of the ^{13}C-^{1}H coupling constants[9], while the ^{1}H NMR data are not suitable for this purpose. The C2-H10 coupling f.i. is 6.3 Hz for the Z- and 10.8 Hz for the E-configuration. By proton catalysis, (E)7 can be very easily and completely converted into (Z)7, but it is configurationaly stable in the course of the synthesis of vinylindoles. Until now it has not been possible to make a definite decision about whether the configuration is fixed during the cycloaddition reaction.

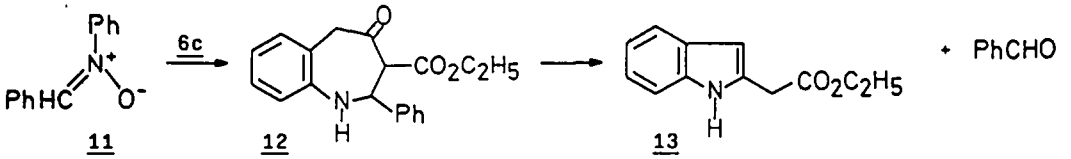


(Z)7g



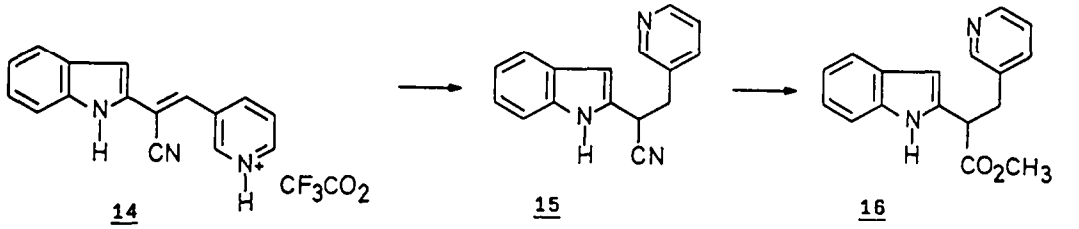
(E)7g

With regard to the allene, our synthesis of vinylindoles is also variable to a certain extent. The acceptor should not be too large, otherwise the tandem-process would come to a stop at the tetrahydrobenzazepinone-stage because obviously the retro-Michael reaction does not take place for sterical reasons. Thus reaction of the ketoallene 6[10] gives 7e very smoothly. The ketoallene is much more reactive, so that the reaction is completed after 30 minutes at room temperature. In principal aliphatic aldehydes could also find application here; unfortunately the results have not been satisfactory so far. Results of the studies with 1-carbethoxyallene correspond to our previous findings[4]. Like in the case of phenylsulfonylpropadiene, the reaction with C-phenyl-N-phenylnitrone 11 at room temperature gives us the unstable tetrahydrobenzazepinone in 70% yield. This fact underpins the reaction sequence postulated by us. As before, the following retro-Michael reaction could not be carried out. Instead we observed the formation of the indole 13 and benzaldehyde in the presence of H_2O hinting to a retro-Mannich reaction followed by hydrolysis. Ester-substituted vinylindoles of the type 1 can therefore not be made in this way. Nevertheless this method seems to be suitable for the formation of synthetically valuable precursors of alkaloids with ester groups since in many cases nitriles can be easily converted into esters[11].



11 12 13

In order to synthesize Aspidosperma-alkaloids we aimed for the 2-substituted indole 16. The use of pyridine-3-aldehyde in the sequence 4 ⟶ 7 is problematic because of the instability of the allene-carbonitrile in the presence of bases. Since in many cases this synthesis of vinylindoles has proven to be almost independent of the solvent, we could do without any troublesome application of protecting groups. After complete formation of the nitrone in acetonitrile we first added 3 equivalents CF_3COOH and next the allene. After 12 hours at room temperature we isolated the salt 14 simply by filtration in 70% yield. The vinyl-pyridinium salt 14 was reduced to the 2-substituted indole 15 with $NaBH_4$ in methanol. As an alternative, catalytic hydrogenation with $Pd/C/H_2$ is possible, but with a lower yield of only 60%. 15 can be easily converted into the corresponding ester by CH_3OH/HCl at 0°C and aqueous work-up in 80% yield.
We will give an account of further studies on the synthesis of alkaloids soon.



14 15 16

EXPERIMENTAL

General

The IR-spectra were recorded on the Perkin-Elmer 457 spectrometer, either solved in $CHCl_3$ or as KBr-pellets. UV spectra were measured with the Beckman DB-GT in methanol. ^1H NMR spectra were obtained using the Bruker WH 90, AC 200 and WH 400 instruments with tetramethylsilane as an internal standard. ^{13}C spectra were measured with the Bruker AC 200 and WP 80 instruments. Mass spectra were

run on a Finnigan MAT 312 at 70 eV at the temperatures mentioned for each case. Merck silica gel 60 (0.040 - 0.063 mm) was used for chromatographic purifications. Melting points were measured with a Reichert hot-stage microscope, they were not corrected. Combustion analyses were obtained on a C,H,N-Rapid, Heraeus.

General procedure of the synthesis of the vinylindoles (7)

2.0 mmol phenylhydroxylamine 4 and 2.4 mmol of the aldehyde 5 were dissolved in 10 ml ethanol. After complete conversion of the hydroxylamine at reaction temperatures between 20°C and 60°C (TLC-control) 30 mmol allene were added. After termination of the reaction (ca. 15 min at 60°C, TLC-control) the solvent was removed by distillation and the product was purified either by crystallization or by chromatography on silica gel.

3-(1-Acetyl-3-indolyl)-2-indolylacrylonitrile (7a)

The product was purified by crystallization from ether. 500 mg (77%) 7a was isolated as light yellow crystals (melting point 222 - 224°C). IR (KBr): 3350, 2210, 1710, 1540, 1212, 745 cm^{-1}. - UV (methanol) : λ_{max} = 222, 277, 379 nm. - ^1H NMR ([D_6]DMSO): δ = 2.75 (s;3H), 6.80 (s;1H), 7.06 (t,J=8Hz;1H), 7.22 (t,J=8Hz;1H), 7.45 (m;3H), 7.60 (d,J=8Hz;1H), 8.02 (m;1H), 8.18 (s;1H), 8.38 (m;1H), 8.57 (s;1H), 11.86 (s;1H). - MS (140°C): m/e = 325 (31%,M^+), 283 (100), 282 (97), 255 (22). - Analysis calculated for $C_{21}H_{15}N_3O$ (325.37): C,77.52;H,4.65;N,12.91; found: C,77.76;H,4.63;N,13.17%.

3-(3-Thienyl)-2-indolylacrylonitrile (7b)

The product was purified by crystallization from ether. 250 mg (50%) 7b was isolated as yellow crystals (melting point 187°C). IR (KBr): 3360, 3060, 2230, 1535, 1435, 900, 780 cm^{-1}. - UV (methanol): λ_{max} = 223, 274, 369 nm. - ^1H NMR ([D_6]DMSO): δ = 6.77 (s;1H),7.05 (t,J=9Hz;1H), 7.19 (t,J=9Hz;1H), 7.41 (d,J=9Hz;1H), 7.59 (d,J=9Hz;1H), 7.88 (m;2H), 7.95 (s;1H), 8.13 (s;1H), 11.7 (s;1H). - ^{13}C NMR($CDCl_3$): δ = 102.40 (s), 103.39 (d), 111.04 (d), 117.52 (s), 121.05 (d), 121.17 (d), 123.91 (d), 127.01 (d), 127.13 (d), 128.80 (s), 129.23 (d), 131.94 (d), 132.81 (s), 135.78 (s), 137.20 (s). - MS (110°C): m/e = 251 (21%,M^+), 250 (100), 249 (99), 248 (32), 222 (12), 216 (10), 205 (38), 125 (12). - Analysis calculated for $C_{15}H_{10}N_2S$ (250.32): C,71.97;H,4.03;N,11.19; found: C,71.99;H,4.09;N,11.34%.

3-[2-Cyano-2-(2-indolyl)vinyl]-1-methyl-pyridinium-iodide (7c)

The product crystallized from ethanole. 575 mg (70%) was isolated as light-red crystals (melting point 258 - 259°C). IR (KBr): 3430, 3220, 2930, 2235, 1605, 1580, 1508 cm^{-1}. - UV (methanol) : λ_{max} = 222, 266, 398 nm. - ^1H NMR ([D_6]DMSO): δ = 4.46 (s;3H), 7.03 (s;1H), 7.12 (t,J=8Hz;1H), 7.30 (t,J=8Hz;1H), 7.51 (d, J=8Hz;1H), 7.69 (d,J=8Hz;1H), 8.00 (s;1H), 8.32 (dd,J=6Hz,J=8Hz;1H), 8.99 (d,J=8Hz;1H), 9.07 (d,J=6Hz;1H), 9.28 (s;1H), 11.97 (s, breit;1H). - ^{13}C NMR ([D_6]DMSO): δ = 48.58 (q), 106.50 (d), 110.04 (s), 111.79 (d), 115.76 (s), 120.54 (d), 121.55 (d), 124.74 (d), 127.65 (s), 127.98 (d), 129.89 (d), 132.09 (s), 133.66 (s), 138.47 (s), 142.76 (d), 145.46 (d). - MS (270°C): m/e = 248 (2%,K^+), 245 (26), 244 (44), 243 (69), 215 (17), 188 (9), 155 (54), 142 (100), 127 (37). - Analysis calculated for $C_{17}H_{14}N_3I \cdot 0.5\ C_2H_5OH$ (410.66): C,52.65;H,4.17;N,10.23; found: C,51.80;H,4.30;N,10.16%.

2-Indolyl-3-phenylacrylonitrile (7d)

The reaction was carried out in acetonitrile. From 2 mmol hydroxylamine 317 mg (65%) 7d (light-yellow crystals, mp. 197-199°C) was obtained by crystallization.

IR (KBr): 3360, 2930, 2230, 1436, 915, 785 cm^{-1}. - UV (methanol): λ_{max} = 215, 276, 366 nm. - ^1H NMR ([D_6]DMSO): δ = 6.83 (s;1H), 7.07 (t,J=8Hz;1H), 7.22 (t,J=8Hz;1H), 7.44 (d,J=8Hz;1H), 7.58 (m;5H), 7.89 (d,J=8Hz;1H), 7.95 (s;1H), 11.74 (s;1H). - MS (100°C): m/e = 245 (18%,M^++1), 244 (99,M^+), 243 (100), 242 (51), 229 (15), 218 (16), 216 (16), 214 (13), 183 (7). - Exact mass calculated for $C_{17}H_{12}N_2$: 244.10005, found: 244.09998. - Analysis calculated for $C_{17}H_{12}N_2$ (244.30): C,83.58;H,4.95;N,11.47; found: C,81.96;H,4.82;N,11.38%.

3-(2-Indolyl)-4-phenyl-3-buten-2-on (7e)

The product was purified by chromatography on silica gel (CH_2Cl_2/CH_3OH). The yield was 340 mg (65%) of yellow crystals (mp. 135°C). IR (KBr): 3360, 1650, 1535, 1445, 1235 cm^{-1}. - ^1H NMR ($CDCl_3$): δ = 2.37 (s;3H), 6.46 (m;1H), 7.06 (dd,J=8Hz,J=1.5Hz;1H), 7.10-7.33 (m;7H), 7.56 (dd,J=8Hz,J=1.5Hz;1H), 7.66 (s;1H), 8.63 (s;1H). - MS (20°C): m/e = 261 (90%,M^+), 218 (100), 217 (80). - Analysis calculated for $C_{18}H_{15}NO$ (261.32): C,82.73;H,5.79;N,5.36; found: C,82.53;H,5.85;N,5.09%.

3-tert.Butyl-2-indolylacrylonitrile (7f)

After chromatographic purification on silica gel (ether/petroleumether) 175 mg (39%) colorless crystals (mp. 134°C) were isolated. IR (KBr): 3400, 2965, 2230, 1637, 796 cm^{-1}. - UV (methanol): λ_{max} = 210, 245, 313 nm. - ^1H NMR ($CDCl_3$): δ = 1.38 (s;9H), 6.70 (s;1H), 6.76 (s;1H); 7.12 (t,J=8Hz;1H), 7.22 (t,J=8Hz;1H), 7.35 (d,J=8Hz;1H), 7.59 (d,J=8Hz;1H), 8.24 (s;1H). - ^{13}C NMR ($CDCl_3$): δ = 29.63 (q), 34.55 (s), 102.54 (d), 104.97 (s), 110.98 (d), 116.23 (s), 120.70 (d), 121.04 (d), 123.47 (d), 128.45 (s), 132.63 (s), 136.89 (s), 153.62 (d). - MS (70°C): m/e = 224 (52%,M^+), 209 (100), 193 (17), 182 (17), 117 (17). - Analysis calculated for $C_{15}H_{16}N_2$ (224.31): C,80.32;H,7.19;N,12.49; found: C,80.19;H,7.13;N,12.42%.

(Z)-2-Indolyl-3-isopropylacrylonitrile (7g)

The product was purified by chromatography on silica gel (ether/petroleumether) 172 mg (41%) 7g (mp. 109-110°C, colorless crystals) was obtained. IR (KBr): 3392, 2958, 2220, 1590, 782, 708 cm^{-1}. - UV (methanol): λ_{max} = 210, 246, 313 nm. - ^1H NMR ($CDCl_3$): δ = 1.30 (d,J=6.5Hz;6H), 3.18 (d sept,J=10Hz,J=6.5Hz; 1H), 6.65 (d,J=10Hz;1H), 6.87 (d, J=2Hz;1H), 7.24 (t,J=8Hz;1H), 7.35 (t,J=8Hz; 1H), 7.46 (d,J=8Hz;1H), 7.71 (d,J=8Hz;1H), 8.75 (s;1H). - ^{13}C NMR ($CDCl_3$): δ = 22.14 (q), 31.75 (d), 103.11 (d), 106.22 (s), 110.96 (d), 115.63 (s), 120.60 (d), 121.02 (d), 123.51 (d), 128.22 (s), 131.32 (s), 136.97 (s), 150.14 (d). - MS (50 °C): m/e = 210 (81%,M^+), 195 (100), 168 (37), 117 (19), 77 (11). - Analysis calculated for $C_{14}H_{14}N_2$ (210.28): C,79.97;H,6.71;N,13.32; found: C,79.90;H,6.61;N,13.02%.

Isomerization into the E-configurated product

A solution of 200 mg (z)7g in 100 ml CH_2Cl_2 was irradiated (500 W-Hg-high-pressure lamp, pyrex filter) for 15 min in an argon-atmosphere at room temperature. Distillative removal of the solvent in vacuo and chromatographic separation on silica gel (ether/petroleumether) gave us, besides 60 mg starting material, 120 mg pure (E)7g. When left in $CHCl_3$ (containing a catalytic amount of acid) the starting material is regained quantitatively. ^1H NMR ([D_6]acetone): δ = 1.11 (d,J=6.4Hz;3H), 3.15 (dq,J=10.4Hz,J=6.4Hz;1H), 6.48 (d,J=10.4Hz;1H), 6.69 (d,J=2.4Hz;1H), 7.05 (dt,J=2.4Hz,J=8Hz;1H), 7.16 (dt,J=2.4Hz;J=8Hz;1H), 7.47 (d,J=8Hz;1H), 7.58 (d,J=8Hz;1H), 10.43 (s;1H). - ^{13}C NMR ([D_6]acetone): δ = 21.92 (q), 29.70 (d), 105.02 (d), 106.39 (s), 112.28 (d), 118.99 (s), 120.93 (d), 121.41 (d), 123.73 (d), 128.93 (s), 129.79 (s), 137.87 (s), 156.11 (d).

3-(4-Cyclohexenyl)-2-indolylacrylonitrile (7h)

The product was purified by chromatography on silica gel (ether/petroleumether). 258 mg (52%) 7h (colorless crystals, mp. 134-135°C) was isolated. IR (KBr): 3410, 2920, 2230, 1420, 1345, 795 cm^{-1}. - UV (methanol): λ_{max} = 214, 248, 314 nm. - ^1H NMR ($CDCl_3$): δ= 1.5-2.4 (m;6H), 3.05 (m;1H), 5.74 (m;2H), 6.61 (d, J=10Hz;1H), 6.77 (s;1H), 7.17 (m;2H), 7.34 (d,J=8Hz;1H), 7.61 (d,J=8Hz;1H), 8.31 (s;1H). - ^{13}C NMR ($CDCl_3$): δ = 23.63 (t), 27.81 (t), 30.24 (t), 36.71 (d), 102.92 (d), 106.99 (s), 110.86 (d), 115.67 (s), 119.99 (d), 120.70 (d), 123.07 (d), 124.52 (d), 126.91 (d), 127.98 (d), 128.02 (s), 131.70 (s), 137.30 (s), 147.49 (d). - MS (90°C): m/e = 248 (55%,M^+), 193 (100), 168 (89). - Analysis calculated for $C_{17}H_{16}N_2$ (248.33): C,82.22;H,6.49;N,11.28; found: C,82.60;H,6.40;N,11.23%.

3-Butyl-2-indolylacrylonitrile (7i)

The product was purified by chromatography on silica gel (ether/petroleumether). The yield was 185 mg (44%) of colorless crystals 7i (mp. 107°C). IR (KBr): 3428, 2955, 2326, 1580, 788, 730 cm^{-1}. - UV (methanol): λ_{max} = 210, 245, 312 nm. - ^1H NMR ($CDCl_3$): δ = 1.02 (t,J=7Hz;3H), 1.61 (m;2H), 2.56 (dt,J=7.5Hz, J=7Hz;2H), 6.71 (t,J=7.5Hz;1H), 6.77 (s;1H), 7.14 (t,J=8Hz;1H), 7.24 (t,J=8Hz; 1H), 7.36 (d,J=8Hz;1H), 7.61 (d,J=8Hz;1H), 8.26 (s,breit;1H). - ^{13}C NMR ($CDCl_3$): δ = 13.52 (q), 21.98 (t), 33.74 (t), 102.93 (d), 108.45 (s), 110.98 (d), 115.75 (s), 120.56 (d), 120.99 (d), 123.47 (d), 128.20 (s), 131.44 (s), 136.99 (s), 143.73 (d). - MS: m/e = 210 (99%,M^+), 195 (36), 180 (100), 168 (68), 153 (67), 127 (26), 77 (16). - Analysis calculated for $C_{14}H_{14}N_2$ (210.28): C,79.87; H,6.71;N,13.32; found: C,79.49;H,6.69;N,13.04%.

3-Methyl-2-indolylacrylonitrile (7j)

131 mg (36%) colorless crystals 7j (mp. 141°C) were obtained by chromatographic purification on silica gel (ether/petroleumether). IR (KBr): 3350, 3075, 2240, 1615, 1442, 795, 755 cm^{-1}. - UV (methanol): λ_{max} = 218, 248, 313 nm. - ^1H NMR ([D_6]acetone): δ = 2.19 (d,J=7Hz;3H), 6.68 (s;1H), 7.05 (t,J=8Hz;1H), 7.09 (q, J=7Hz;1H), 7.17 (t,J=8Hz;1H), 7.37 (d,J=8Hz;1H), 7.59 (d,J=8Hz;1H), 10.62 (s; 1H). - ^{13}C NMR ([D_6]DMSO): δ = 17.43 (q), 102.01 (d), 108.90 (s), 111.46 (d), 115.93 (s), 119.95 (d), 120.87 (d), 123.05 (d), 127.91 (s), 132.40 (s), 137.66 (s), 139.90 (d). - MS (60°C): m/e = 182 (100%,M^+), 155 (48), 127 (18), 77 (12), 63 (9). - Analysis calculated for $C_{12}H_{10}N_2$ (182.23): C,79.10;H,5.53; N,15.37; found: C,79.76;H,5.50;N,15.46%.

N-[4-Cyano-4(-2-indolyl)-3-butenyl]phthalimide (7k)

The aldehyde was generated according to a well-known procedure[12]. The synthesis of the vinylindole was performed in CH_2Cl_2. After chromatographic purification on silica gel (CH_2Cl_2/CH_3OH) we came out with 390 mg (57%) 7k (colorless crystals, mp. 185°C). IR (KBr): 3370, 2230, 1773, 1710, 1595 cm^{-1}. - UV (methanol): λ_{max} = 224, 240 (shoulder), 318 nm. - ^1H NMR ([D_6]acetone): δ = 2.99 (dt, J=7Hz,J=6.5 Hz;2H), 3.95 (t,J=6.5 Hz;2H), 6.64 (s;1H), 7.04 (t,J=7Hz;1H), 7.05 (t,J=7Hz;1H), 7.16 (t,J=7Hz;1H), 7.26 (d,J=7Hz;1H), 7.46 (d,J=7Hz;1H), 7.85 (s;4H), 10.67 (s;1H). - ^{13}C NMR ([D_6]acetone): δ = 31.98 (t), 37.16 (t), 104.05 (d), 111.38 (s), 112.09 (d), 115.85 (s), 120.99 (d), 121.78 (d), 123.86 (d), 124.22 (d), 129.14 (s), 132.94 (s), 133.12 (s), 135.08 (d), 138.78 (s), 140.12 (d), 168.69 (s), 205.97 (s). - MS (100°C): m/e = 341 (13%, M^+), 203 (11), 194 (20), 175 (33), 160 (100). - Analysis calculated for $C_{21}H_{15}N_3O_2$ (341.37): C,73.88;H4.43;N12.31; found: C,73.24;H4.56;N,11.88%.

4-(5,5-Dimethyl-1,3-dioxa-2-cyclohexyl)-2-indolyl-2-butenenitrile (7l)

The aldehyde was generated according to a well-known procedure[13]. The product was purified by chromatography on silica gel (ether/petroleumether). The yield was 325 mg (55%) 7l of colorless crystals (mp. 169°C). IR ($CHCl_3$): 3470, 2950, 2845, 2220, 1721, 1125, 1020 cm^{-1}. - UV (methanol): λ_{max} = 218, 246, 315 nm. - ^1H NMR ($CDCl_3$): δ = 0.671 (s;3H), 1.13 (s;3H), 2.86 (dd,J=4.5Hz,J=7.5Hz;2H), 3.39 (d,J=11Hz;2H), 3.57 (d,J=11Hz;2H), 4.75 (t,J=4.5Hz;1H), 6.71 (s;1H), 6.72 (t,J=7.5Hz;1H), 7.05 (t,J=8Hz;1H), 7.15 (t,J=8Hz;1H), 7.20 (d,J=8Hz;1H), 7.27 (d,J=8Hz;1H), 8.24 (s;1H). - ^{13}C NMR ([D_6]DMSO): δ = 21.36 (q), 22.86 (q), 29.79 (s), 37.29 (t), 76.21 (t), 99.28 (d), 102.56 (d), 109.68 (s), 111.42 (d), 115.78 (s), 119.91 (d), 120.86 (d), 123.18 (d), 127.67 (s), 131.99 (s), 137.69 (s), 138.08 (d). - MS (110°C): m/e = 296 (3%,M^+), 210 (4), 192 (12), 154 (14), 115 (100), 69 (94). - Analysis calculated for $C_{18}H_{20}N_2O_2$ (296.37): C,72.95;H,6.80;N,9.45; found: C,72.39;H,6.81;N,9.44%.

Methyl-3-cyano-3-(2-indolyl)acryloate (7m)

176 mg (39%) of the unstable product 7m (mp. 150°C) was isolated after purification by chromatography on silica gel (ether/petroleumether). IR (KBr): 3355 3085, 2960, 2235, 1703, 1600, 1431, 1349, 1240, 868 cm^{-1}. - UV (methanol): λ_{max} = 210, 238, 332, 363 nm. - ^1H NMR ([D_6]DMSO): δ = 3.81 (s;3H), 7.093 (t, J=8Hz;1H), 7.095 (s;1H), 7.20 (d,J=2Hz;1H), 7.29 (dt,J=8Hz,J=2Hz;1H), 7.43 (d, J=8Hz;1H), 7.65 (d,J=8Hz;1H), 11.74 (s;1H). - MS (90°C): m/e = 227 (10%,M^++1), 226 (63,M^+), 195 (35), 194 (100), 166 (24), 155 (15), 140 (27), 139 (14), 88 (14). - Exact mass calculated for $C_{13}H_{10}N_2O_2$: 226.07423, found: 226.07421.

2,5-Dimethyl-3-phenylisoxazoline-4-carbonitrile (10a)

135 mg (1 mmol) N-benzylidenemethylamine-N-oxide (8) and 0.12 ml allenecarbonitrile 6a were left in 5 ml CH_3OH for 12 hours at 20°C. After distillative removal of the solvent in vacuo and purification by chromatography on silica gel (ether/petroleumether) 150 mg (75%) 10a (colorless oil) were obtained. IR ($CHCl_3$): 3000, 2220, 1655 cm^{-1}. - UV (methanol): λ_{max} = 262 nm. - ^1H NMR ($CDCl_3$): δ = 2.12 (d,J=1.5Hz;3H), 2.94 (s;3H), 4.84 (q,J=1.5Hz;1H), 7.38 (s;5H). - ^{13}C NMR ($CDCl_3$): δ = 11.95 (q), 47.04 (q), 75.53 (d), 84.97 (s), 114.82 (s), 126.85 (d), 128.64 (s), 128.89 (d), 138.54 (s), 166.36 (s). - MS (180°C): 200 (50%,M^+), 185 (27), 183 (25), 157 (60), 123 (100). - Exact mass calculated for $C_{12}H_{12}N_2O$: 200.0950, found: 200.0944.

Reaction of (8) with ethyl-2,3-butenoate (6c)[14]

The reaction was carried out in the same manner as described before and gave the same result in benzene as well as methanol at 60°C. We isolated 28 mg (11%) 9a and 90 mg (36%) 10b. 9a can be converted quantitatively into 10b by stirring in CH_3OH/CH_3ONa (2 min). When left in substance at 0°C for longer (2 d), formation of 10b was observed, too.

Ethyl-2-methyl-5-methylene-3-phenylisoxazolidine-4-carboxylate (9a)

IR ($CHCl_3$): 2990, 1730,1670 cm^{-1}. - ^1H NMR ($CDCl_3$): δ = 1.23 (t,J=7.5Hz;3H), 2.69 (s;1H), 4.00-4.30 (m;5H), 4.38 (t,J=2.5Hz;1H), 7.25-7.65 (m;5H). - MS (180°C): m/e = 247 (73%,M^+), 204 (27), 176 (28), 174 (71), 160 (24), 158 (16), 132 (84), 131 (73), 118 (100), 103 (30), 91 (31), 77 (38), 42 (27). - Exact mass calculated for $C_{14}H_{17}NO_3$: 247.1208, found: 247.1208.

Ethyl-2,5-dimethyl-3-phenylisoxazoline-4-carboxylate (10b)

IR ($CHCl_3$): 3010, 1690, 1650 cm^{-1}. - UV (methanol) : λ_{max} = 272 nm. - ^1H NMR ($CDCl_3$): δ = 1.13 (t,J=7.5Hz;3H), 2.31 (d,J=1Hz;3H), 2.91 (s;3H), 4.09 (q, J=7.5Hz;2H), 4.89 (q,J=1Hz;1H), 7.47 (s;5H). - MS (180°C): m/e = 247 (30%,M^+), 218 (20), 186 (47), 170 (100). - Exact mass calculated for $C_{14}H_{17}NO_3$: 247.1208, found: 247.1205.

Ethyl-1,2,3,5-tetrahydro-4-oxo-2-phenyl-4H-1-benzazepine-3-carboxylate (12)

197 mg (1 mmol) N-benzylidenephenylamine-N-oxide 11 and 168 mg (1.5 mmol) 6c were left in dry THF at 20°C for 2 days. After distillative removal of the solvent in vacuo, the ^1H-NMR spectrum of the residue showed the formation of 10b in about 70% yield. The isolation could be carried out by rapid chromatography on silica gel (CH_2Cl_2), but only with high losses. A complete purification was not successful. IR ($CHCl_3$): 3010, 1740, 1710, 1600, 1470 cm^{-1}. - ^1H NMR ($CDCl_3$): δ = 1.01 (t,J=7Hz;3H); 3.70 (s,breit;1H), 3.80 (d,J=14Hz;1H), 3.93 (q, J=7Hz;2H), 4.07 (d,J=10Hz;1H), 4.26 (d,J=14Hz;1H), 5.01 (d,J=10Hz;1H), 6.63 (dd,t J=8Hz,J=1.5Hz;1H), 6.90 (dt,J=1.5Hz,J=8Hz;1H), 7.10 (m;2H), 7.37 (m;5H).

Ethyl-2-indolylethanoate (13)

Following the formation of 12 as cited above, 2 drops of H_2O were added. After 1 day the solvent was removed by distillation and we obtained 100 mg (49%) 13 (amorphous) by chromatographic purification on silica gel (ether/petroleumether). IR ($CHCl_3$): 3460, 3000, 1725, 1455 cm^{-1}. - ^1H NMR ($CDCl_3$): δ = 1.29 (t,J=7Hz;3H), 3.82 (d,J=1Hz;2H), 4.24 (q,J=7Hz;2H), 6.27 (m;1H), 7.00-7.66 (m;4H), 8.75 (s; 1H). - MS (180°C): m/e = 203 (41%,M^+), 130 (100), 103 (7), 77 (10). - Exact mass calculated for $C_{12}H_{13}NO_2$: 203.0946, found: 203.0946.

3-[2-Cyano-2-(2-indolyl)vinyl]pyridiniumtrifluoroacetate (14)

535 mg (5 mmol) pyridine-3-aldehyde and 545 (5 mmol) N-phenylhydroxylamine were dissolved in 12 ml CH_3CN. After complete formation of the nitrone 1.15 ml CF_3COOH and 0.50 ml allene were added. After a reaction time of 12 h at 20°C the product was left to crystallize at -20°C. The yield was 1.29 g (70%) 14 melting at 178°C. IR (KBr): 3340, 2230, 1780, breit, 1665 cm^{-1}, breit. - ^1H NMR ([D_6]DMSO): δ = 6.91 (d,J=1Hz;1H), 7.00-7.90 (m;5H), 8.03 (s;1H), 8.67 (dt,J=8Hz,J=1Hz;1H), 8.78 (dd,J=5Hz,J=1Hz;1H), 9.05 (d,J=1Hz;1H), 11.22 (s;2H); 11.95 (s;1H). - Analysis calculated for $C_{18}H_{12}F_3N_3O_2 \cdot 0.5\ H_2O$ (368.30): C,58.70;H,3.56;N,11.41; found: C,58.40;H,3.80;N,11.22%.

2-Indolyl-3-pyridyl-propionitrile (15)

To a solution of 1.84 g (5 mmol) 14 in 150 ml methanol $NaBH_4$ was added until complete conversion (TLC-control). 400 ml of H_2O was added. Extraction with CH_2Cl_2 and purification by chromatography on silica gel (CH_2Cl_2/CH_3OH) gave us 870 mg (70%) of amorphous 15. IR ($CHCl_3$): 3450, 2250, 1580 cm^{-1}. - ^1H NMR ($CDCl_3$): δ = 3.24 (d,J=7Hz;2H), 4.24 (t,J=7Hz;1H), 6.44 (d,J=2Hz;1H), 7.00-7.70 (m;6H), 8.42 (d,J=1.5Hz;1H), 8.51 (dd,J=5Hz,J=1.5Hz;1H), 9.60 (s;1H). - MS (180°C): m/e = 247 (47%,M^+), 156 (30), 155 (100). - Exact mass calculated for $C_{16}H_{13}N_3$: 247.1109, found: 247.1110.

Methyl-2-indolyl-3-pyridylpropionate (16)

A solution of 247 mg (1 mmol) 15 in 20 ml of absolute CH_3OH was treated with HCl-gas. After 24 h at 0°C the solution was poured onto 100 ml H_2O, neutralized with $NaHCO_3$ and extracted with CH_2Cl_2. After chromatographic purification on silica gel (CH_2Cl_2/CH_3OH) the yield was 224 mg (80%) of amorphous 16.
IR ($CHCl_3$): 3440, 3000, 2950, 1725 cm^{-1}. - ^1H NMR ($CDCl_3$): δ = 3.22 (m;2H), 3.58 (s;3H), 4.03 (t,J=7Hz;1H), 6.31 (d,J=2Hz;1H), 7.00-7.64 (m;6H), 8.40 (m; 2H), 9.02 (s;1H). - MS (180°C): m/e = 280 (25%,M^+), 190 (100), 150 (28). - Exact mass calculated for $C_{17}H_{16}N_2O_2$: 280.1212, found: 280.1210.

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