# 143. The Reaction of 3-(Dimethylamino)-2*H*-azirines with 2,3-Pyridinedicarboximide

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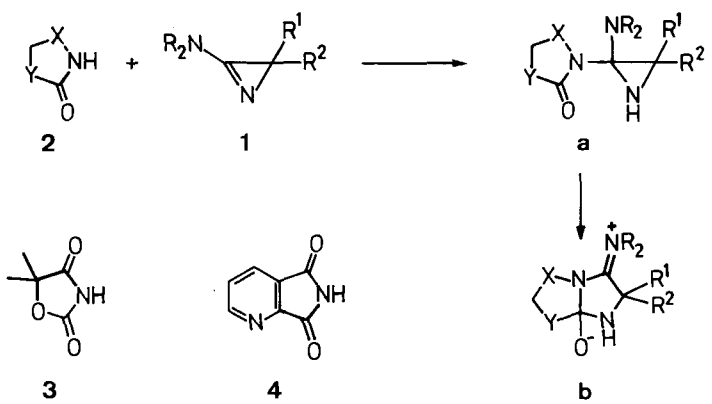
Reaction of 2,2-dialkyl-3-(dimethylamino)-2*H*-azirines **1a** and **1b** with 2,3-pyridinedicarboximide (**4**) in MeCN or DMF at room temperature yielded two regioisomeric tricyclic 1:1 adducts, the azacyclols **11/12** and **16/17**, respectively *(Schemes 3* and *4)*. The structure of **12** was established by X-ray crystallography. Methanolysis of **11/12** and **16/17** led to mixtures of methyl [4,4-dialkyl-5-(dimethylamino)-4*H*-imidazol-2-yl]pyridine carboxylates **13/14** and **18/19**, respectively. The structure of compound **14** is closely related to that of the powerful herbicide **9** *(Scheme 9)*, *i.e.* the described reactions offer a new synthetic approach to this class of compounds. A mechanistic interpretation for the formation of regioisomeric 1:1 adducts as well as methyl (imidazol-2-yl)pyridine carboxylates is depicted in *Scheme 5*.

**1. Introduction.** – A series of investigations during the last years revealed that 3-amino-2*H*-azirines **1** react with *Bronsted* acids in various ways [1–3]. The reaction of **1** with carboxylic acids, for instance, is of growing interest in peptide synthesis [3–5]. The reaction with heterocycles containing N*H*-acidic groups reveals two interesting aspects.

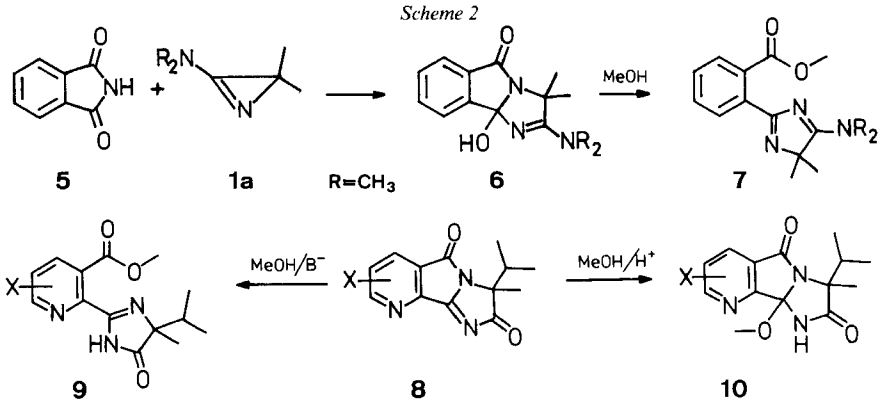
*Scheme 1*



On one hand, the reactions led to a variety of new heterocycles (*cf. e.g.* [6–9]) and on the other hand some of these reactions proceed *via* quite peculiar mechanisms (*cf. e.g.* [2] [10] [11]).

A zwitterion of type **b**, the presumed common intermediate of all these reactions, is formed by the nucleophilic attack of the aziridine *N*-atom of **a** onto the neighbouring (thio)carbonyl group *(Scheme 1)*. When X also represents a C=O group, attack onto the more electrophilic C=O C-atom in **a** is expected and also observed for the reaction of **1** with the 1,3-oxazolidine-2,4-dione **3** [11]. Additional information on mechanistic details could be expected from the reaction of **1** with asymmetric dicarboximides. 2,3-Pyridinedicarboximide (5*H*-pyrrolo[3,4-*b*]pyridine-5,7(6*H*)-dione; **4**) was chosen for this investigation on the basis of the products expected in analogy to those obtained from reaction of phthalimide (**5**) with **1a** [6] [11] [12] *(Scheme 2)*.

*Scheme 2*




The azacyclol **6**[1]) as well as the product of the subsequent methanolysis **7** are indeed closely related to compounds **9** and **10**, respectively, which are potent herbicides [14–16]. The reaction of **1b** and **4** provided a new synthetic approach to this interesting class of compounds (*cf. e.g.* [17–19]).

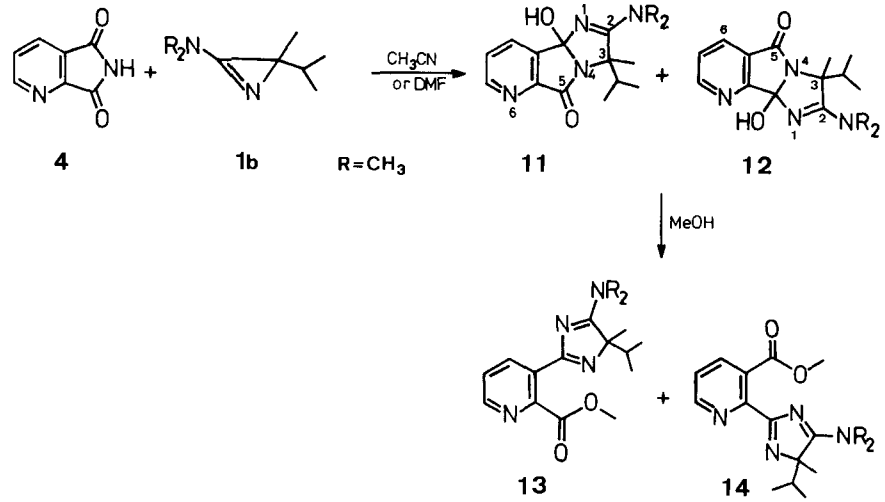
**2. Reaction of 2,3-Pyridinedicarboximide (4) with 3-(Dimethylamino)-2*H*-azirines (1).** – When a solution of 3 mmol **4** and 5 mmol 3-(dimethylamino)-2-isopropyl-2-methyl-2*H*-azirine (**1b**) [20] in 100 ml of MeCN was kept at room temperature for 5 days, a colourless precipitate was formed. Careful HPLC and NMR analysis revealed that it consisted of a 1:3 mixture of two 1:1 adducts (27% total yield). Comparison of the spectral data with those of **6** [12] led to the assignment of the structures **11** and **12** *(Scheme 3)* to these adducts.

Two signals appear for almost all C-atoms in the $^{13}$C-NMR spectrum, the most characteristic ones being those of the 'azacyclol C-atoms' (C(9b)) at *108.7*[2]) and 106.8 ppm, respectively. The signals of the other ring atoms of the major isomer **12** appear at 170.7, 167.9 (2*s*, C=O, C=N); 153.1, 131.1, 124.0 (3*d*, C(7), C(9), C(8)); 143.6, 126.4 (2*s*,

[1]) Tetrahedral products formed *via* intramolecular addition of NH, OH, SH groups onto an amide function are commonly designated as aza-, oxa-, and thiacyclols, respectively (*cf. e.g.* [13]). By this means, azatricyclic compounds of type **6** *(Scheme 2)* are designated as azacyclols.

[2]) The data in italics refer to the major isomer.

*Scheme 3*




C(5a), C(9a)), and at 73.2 ppm (*s*, C(3)). Doubling of signals for the Me groups in the $^1$H-NMR spectrum is especially striking in $CDCl_3$ (2*s* for $(CH_3)_2N$ at *3.10*/3.04, 2*s* for $CH_3$–C(3) at 1.75/*1.73*, 2*d* each for $(CH_3)_2CH$ at 1.34/*1.30*, and 1.14/*1.10* ppm), whereas the two sets of signals for the pyridine protons are more clearly separated in $(D_6)$DMSO (2*dd* at *8.74*/8.69 for H–C(7)/H–C(8), 2*dd* at 8.04/*7.97* for H–C(6)/H–C(9), and 2*dd* at 7.56/*7.47* ppm for H–C(7)/H–C(8)).

After partial evaporation of the solvent, the isomer **12** crystallized from the filtrate in pure form (m.p. 168.6–168.7°, 18% yield). These crystals were subjected to an X-ray structure determination (*cf. Chapt. 3*).

The analogous reaction in DMF, run at room temperature for 7 days, afforded a 2:3 mixture **11**/**12** upon evaporation of the solvent[3]). This material was dissolved in MeOH and kept at room temperature for 2 days. After evaporation of the solvent and chromatography of the residue, the methyl esters **13** and **14** *(Scheme 3)* were isolated in a total yield of 56% (ratio 5:1). Methanolysis at 80° afforded a 2:3 mixture of **13** and **14** (75% total yield)[4]). The structure assignment was achieved by comparison of the $^1$H-NMR data[5])

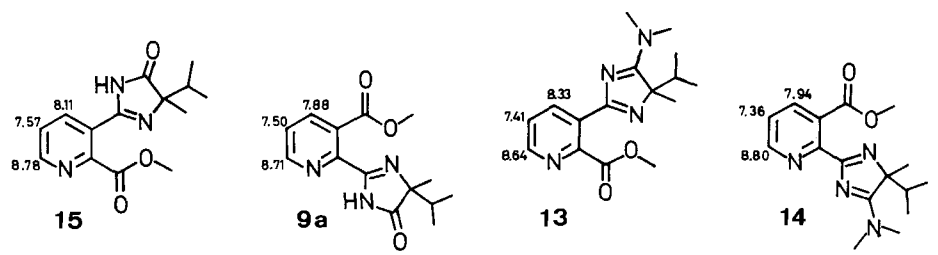



Fig. 1. *$^1$H-NMR Chemical shifts* (in $CDCl_3$) *of pyridine protons of* **9a** *and* **13–15**

[3]) The same mixture was obtained upon precipitation of the products with $Et_2O$.

[4]) Esters **13** and **14** are stable under these conditions, and no interconversion between the two isomers was observed.

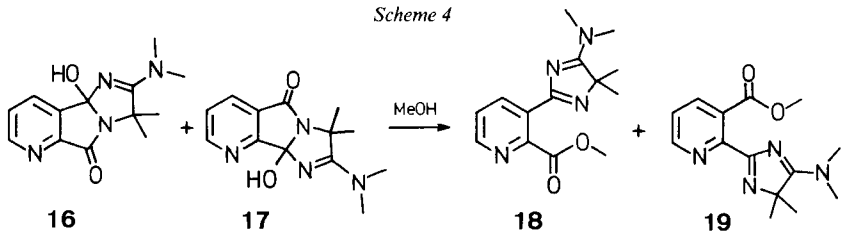
[5]) No significant differences were observed in the $^{13}$C-NMR and IR spectrum.

with those of **9a** and **15** *(Fig. 1)*, of which an X-ray structure determination also exists [21].

The remarkable observation that a 3:1 mixture **11**/**12** led to a 2:3 ratio for **13**/**14** prompted us to reflux pure **12** in MeOH for 15 h. Both esters **13** and **14** were formed in a ratio of 1:2.

The reaction of **4** with 3-(dimethylamino)-2,2-dimethyl-2*H*-azirine (**1a**) in DMF at room temperature, after precipitation with $Et_2O$, afforded a 2:5 mixture of the 3,3-dimethylazacyclols **16**/**17** *(Scheme 4)*, corresponding to **11**/**12** in *Scheme 3*, in 77% total yield. The structure assignment was also based on the chemical shifts of the pyridine protons. Methanolysis of **16**/**17** at 80° and separation of the products by chromatography yielded the pure methyl esters **18** and **19** *(Scheme 4)* in a ratio of 2:3 (65% total yield), thus, underlining the general character of the reaction sequence.

*Scheme 4*




**3. X-Ray Structure Determinations**[6]). – Crystals of **12** *(Scheme 3)* and **10a** (R = H, *Scheme 2*), obtained from $(D_6)$DMSO and hexane/AcOEt, respectively, were used for X-ray structure determination. Data were collected on

Table. *Crystallographic Data of* **12** *and* **10a**

| | **12** | **10a** |
|---|---|---|
| Crystallized from | $(D_6)$DMSO | hexane/AcOEt |
| Colour | colourless | colourless |
| Crystal temperature (*ca.*) [K] | 295 | 170 |
| Space group | $P2_1$ | $P\bar{1}$ |
| Atoms in the asymmetric unit | $C_{15}H_{20}N_4O_2$ | $C_{14}H_{17}N_3O_3$ |
| Cell parameters[a]) | | |
| *a*[Å] | 6.798(1) | 7.727(21) |
| *b*[Å] | 8.733(1) | 8.586(1) |
| *c*[Å] | 12.486(2) | 12.037(2) |
| $\alpha$[°] | 90 | 99.16(1) |
| $\beta$[°] | 91.63(1) | 107.44(1) |
| $\lambda$[°] | 90 | 102.78(1) |
| Density [Mg/m$^3$] | 1.29 | 1.27 |
| $2\theta$(max) | 60° | 50° |
| Symmetry independent reflections | 2300 | 2667 |
| Reflections used in the refinement | 2300 | 2072 |
| Variables | 269 | 177 |
| *R* | 0.049 | 0.094 |
| Rec. weighting scheme $1/w$ | $\sigma^2(F) + 0.0004F^2$ | $\sigma^2(F) + 0.001F^2$ |

[a]) The cell dimensions were obtained from 72 and 25 accurately centered reflections with $36° < |2\theta| < 42°$ and $0° < |2\theta| < 50°$, respectively.

[6]) Atomic coordinates, bond lengths, and angles have been deposited with the *Cambridge Crystallographic Data Center*, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW, England.

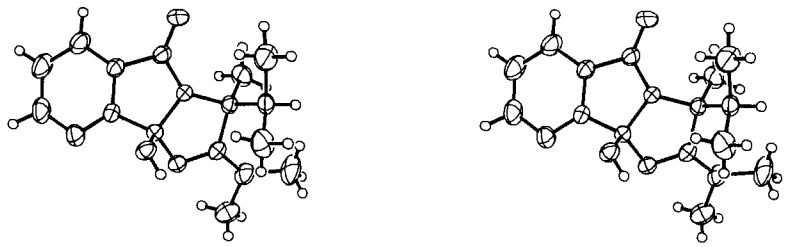


Fig. 2. *ORTEP stereoplot* [23] *of* **12**

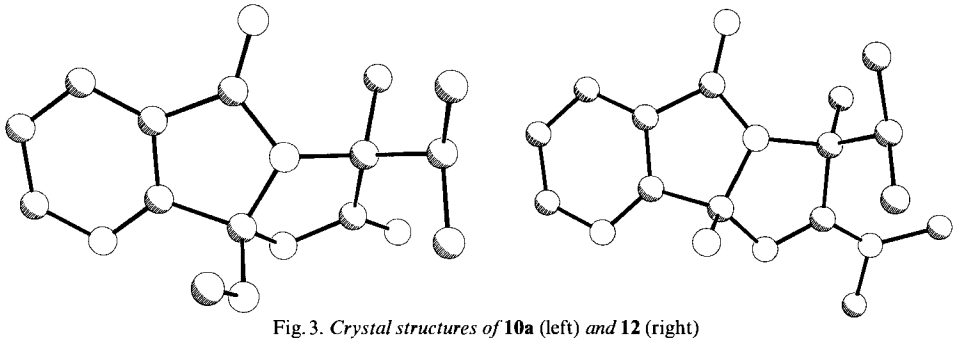


Fig. 3. *Crystal structures of* **10a** (left) *and* **12** (right)

a *Nicolet-R3* and *Nicolet-R3m* diffractometer fitted with a graphite monochromator and the LT1 cooling apparatus, respectively, in the $\omega$-scan mode using Mo$K_\alpha$ radiation. The usual corrections except for absorption were applied. The structure of **12** was determined by direct methods and refined by blocked cascade refinements (on *F*) with *ca.* 100 variables per block using the program system SHELXTL 4.1 [22]. The H-atoms were located in difference *Fourier* maps after anisotropic refinement of the other atoms and were refined with individual isotropic temperature factors. The structure of **10a** was also determined by direct methods using 39 starting phase permutations. Refinement proceeded smoothly to convergence at $R = 0.0941$ with anisotropic refinement of all non-H-atoms. All calculations were carried out with SHELXTL 3.0 [22]. The i-Pr group has been found to be disordered in two positions. The corresponding site occupation factors refined to 0.53 and 0.47, respectively. The H-atoms have been left out. Crystallographic data are given in the *Table*, and molecular drawings of **12** and **10a** in *Figs. 2* and *3*, respectively.

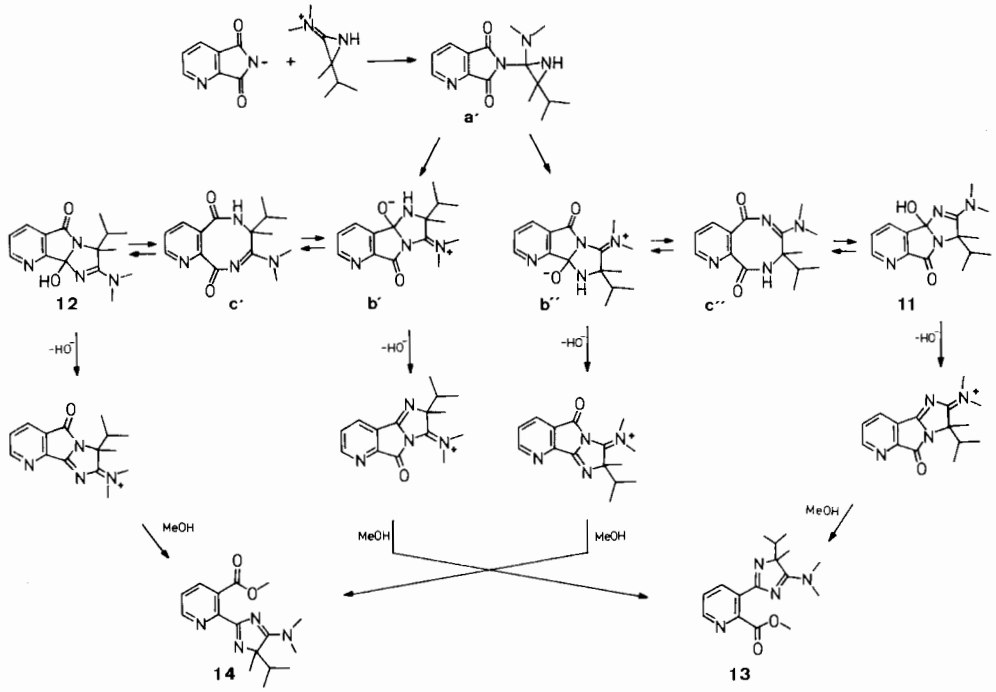
The structure of **12** corresponds to that of the recently published **6** *(Scheme 2*, R = $CH_3$) in all essential features. The i-Pr group at C(3) is *exo*-configurated and, therefore, in *cis*-position with respect to the OH group at C(9b). Crystal structures of **12** and **10a** (*cf.* [15])[7]) are shown in *Fig. 3*. The two structures are almost superimposable.

**4. Discussion.** – The aforementioned reactions of **1a** and **1b** with **4** offer a new synthetic entry to imidazopyrrolopyridines, *i.e.* **16**, **17**, and **11**, **12**, which, upon methanolysis, afford the imidazol-2-yl pyridinecarboxylates **18**, **19**, and **13**, **14**, respectively (*Schemes 3* and *4*). However, these reactions always give rise to two regioisomeric products, only one of which is of biological interest.

A mechanistic interpretation of the formation of the observed product mixtures from **1b** and **4** is depicted in *Scheme 5*. Nucleophilic attack of the aziridine N-atom of **a'** on

[7]) Compound **10a** was the only product obtained from the acid-catalyzed addition of MeOH to **8** *(Scheme 2)*. This crystal structure, for the first time, establishes clearly the *cis*-arrangement of the MeO and i-Pr groups.

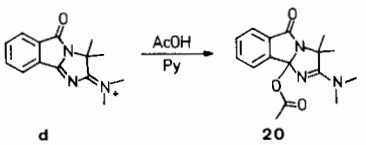
*Scheme 5*




either C=O group leads to the two zwitterions **b′** and **b″** which, *via* a transannular ring contraction, afford the azacyclols **12** and **11**, respectively. The isomer **12** is the major product which means that the nucleophilic attack in **a′** occurs preferentially at the CO group attached to C(3). This is not surprising in view of the fact that, also in the case of quinolinic anhydride (2,3-pyridinedicarboxylic anhydride), attack of nucleophiles is faster at the CO group attached to C(3) (*cf.* [24]).

In contrast to the reaction of **8** with $MeO^-$ that gives a single product **10** [14], the reaction of pure **12** with MeOH, as mentioned before, leads to a mixture **13**/**14**. This surprising observation is best explained by the *reversible* formation of the 8-membered ring intermediate **c′** and the zwitterion **b′** (*Scheme 5*). Both reaction paths had been taken into account some time ago to explain the formation of 2-(4*H*-imidazol-2-yl)benzoic-acid derivatives on treatment of 1:1 adducts of **1a** and phthalamide (**5**) with nucleophiles [6]. The new results presented here clearly indicate that the reaction, indeed, proceeds *via* both pathways simultaneously[8]).

[8]) The fact that all attempts of *O*-alkylation (including the use of 'magic methyl') of **11** and **12** failed may be due to the reversible formation of the diazocine-diones **c′** and **c″**. In contrast, from the reaction of the 1:1 adducts of **1a** and **5** with $Ac_2O$ in pyridine, a compound with the presumed structure **21** was isolated in modest yield. Its formation can be explained by the addition of AcOH to an intermediate of type **d**.



Our thanks are due to the analytical services of the Organic Chemistry Department of the University of Zürich for running the spectra and the *Swiss National Science Foundation* for financial support.

## Experimental Part

*General.* See [25].

**1. Reactions of 2,3-Pyridinedicarboximide (5*H*-Pyrrolo[3,4-*b*]pyridine-5,7(6*H*)-dione; 4) with 3-(Dimethylamino)-2*H*-azirines 1.** – 1.1. *With 3-(Dimethylamino)-2-isopropyl-2-methyl-2*H*-azirine* (**1b**). A soln. of 450 mg (3 mmol) of **4** and 700 mg (5 mmol) of **1b** [20] in *ca.* 100 ml of MeCN was stirred at r.t. for 4 days. The colourless precipitate was filtered and washed with $Et_2O$: 230 mg (27% based on **4**) of a 1:3 mixture ($^1$H-NMR, HPLC) of *2-(dimethylamino)-3,9b-dihydro-9b-hydroxy-3-isopropyl-3-methyl-5*H*-imidazo[1′,2′:1,5]pyrrolo[3,4-*b*]pyridin-5-one* (**11**) and *2-(dimethylamino)-3,9b-dihydro-9b-hydroxy-3-isopropyl-3-methyl-5*H*-imidazo[1′,2′:1,2]pyrrolo[3,4-*b*]pyridin-5-one* (**12**). IR (KBr): 3300*m* (br.), 2970*m*, 2935*w*, 2880*w*, 1685*s*, 1585*s*, 1475*m*, 1453*m*, 1380*s*, 1315*m*, 1303*m*, 1250*m*, 1225*w*, 1203*w*, 1168*w*, 1152*m*, 1127*m*, 1108*m*, 1090*m*, 1048*m*, 1030*s*, 1020*s*, 952*w*, 933*w*, 904*w*, 888*m*, 840*w*, 805*m*, 739*w*, 718*w*. $^1$H-NMR (400 MHz, $(D_6)$DMSO): 8.74/8.69 (2*dd* (3:1), $J$ = 4.9, 1.5, and 4.7, 1.5, H–C(7) of **12**, H–C(8) of **11**); 8.04/7.97 (2*dd* (1:3), $J$ = 7.8, 1.5, and 7.5, 1.5, H–C(6) of **11**, H–C(9) of **12**); 7.56/7.47 (2*dd* (1:3), $J$ = 7.8, 4.9, and 7.5, 4.8, H–C(7) of **11**, H–C(8) of **12**); 6.53/6.52 (2*s* (1:3), OH); 3.30/2.99 (2*s* (1:3), $(CH_3)_2N$); 2.26/2.18 (2 *sept.* (1:3), $J$ = 6.8, $(CH_3)_2CH$); 1.59/1.58 (2*s* (1:3), $CH_3$–C(3)); 1.13/1.11, 1.01/0.96 (2*d* each (1:3), $J$ = 6.8, $(CH_3)_2CH$). $^1$H-NMR (90 MHz, $CDCl_3$): 8.77 (*dd*, H–C(7) of **12**, H–C(8) of **11**); 8.33/8.03 (2*dd* (*ca.* 1:3), H–C(6) of **11**, H–C(9) of **12**); 7.38 (*dd*, H–C(8) of **12**, H–C(7) of **11**); 4.0 (br. *s*, OH); 3.10/3.04 (2*s* (*ca.* 3:1), $(CH_3)_2N$); 2.20 (*sept.*-like, $(CH_3)_2CH$); 1.75/1.73 (2*s*, $CH_3$–C(3)); 1.34/1.30, 1.14/1.10 (2*d*, each (1:3), $(CH_3)_2CH$). $^{13}$C-NMR (25.2 MHz, $(D_6)$DMSO): 170.7/170.5 (2*s*, (3:1), C(5)); 167.9/166.5 (2*s*, C(2)); 153.1/151.0 (2*d* (3:1), C(7) of **12**, C(8) of **11**); 149.0/143.6 (2*s* (1:3), C(9a) of **11**, C(5a) of **12**); 131.1/130.5 (2*d* (3:1), C(9) of **12**, C(6) of **11**); 126.4/124.0 (2*d* (1:3), C(7) of **11**, C(8) of **12**); 125.5 (*s*, C(9a) of **12**); 108.7/106.8 (2*s* (3:1), C(9b)); 73.4/73.2 (2*s* (1:3), C(3)); 38.8/38.7 (2*q* (*ca.* 3:1), $(CH_3)_2N$); 34.0/33.9 (2*d* (1:3), $(CH_3)_2CH$); 19.5, 19.2, 18.6 (3*q*, $CH_3$–C(3), $(CH_3)_2CH$). MS (70 eV): 288 (21, $M^{+\cdot}$), 273 (20), 271 (40), 246 (22), 245 (85), 229 (38), 228 (100), 227 (15), 218 (17), 214 (17), 213 (13), 202 (23), 201 (40), 200 (28), 199 (24), 186 (14), 185 (18), 175 (13), 173 (14), 172 (12), 167 (12), 160 (17), 159 (13), 149 (63), 148 (18), 147 (18), 144 (27), 132 (12), 131 (52), 118 (17), 106 (49), 105 (37), 104 (26), 103 (40), 97 (11), 84 (19), 79 (26), 78 (58), 77 (35), 76 (25), 72 (15), 71 (17), 70 (14), 69 (16).

After partial evaporation of the solvent, 150 mg (18%) of **12**, m.p. 168.6–168.7°, crystallized. Recrystallization from saturated DMSO soln. yielded single crystals (m.p. 177.2–177.9°) which were used for the X-ray structure determination.

In a second experiment, 450 mg (3 mmol) of **4** and 700 mg (5 mmol) of **1b** in 100 ml DMF were stirred at r.t. for 7 days. After partial evaporation of the solvent, 597 mg (69%) of a 2:3 mixture (NMR) **11**/**12** crystallized.

A similar reaction mixture was stirred at 80° for 3 days. Both 1:1 adducts **11** and **12** were formed in a ratio of *ca.* 1:3 (HPLC). Evaporation of the solvent yielded 610 mg (70%) of the 1:3 mixture as crystalline material.

1.2. *With 3-(Dimethylamino)-2,2-dimethyl-2*H*-azirine* (**1a**). A soln. of 1.0 g (6.8 mmol) of **4** and 1.3 g (11.6 mmol) of **1a** in *ca.* 150 ml of DMF was stirred at r.t. for 4 days. After addition of 150 ml of $Et_2O$, the colourless precipitate was filtered, washed with $Et_2O$, and dried i.HV.: 1.37 g (77%) of a 2:5 mixture ($^1$H-NMR) of *2-(dimethylamino)-3,9b-dihydro-9b-hydroxy-3,3-dimethyl-5*H*-imidazo[1′,2′:1,5]pyrrolo[3,4-*b*]pyridin-5-one* (**16**) and *2-(dimethylamino)-3,9b-dihydro-9b-hydroxy-3,3-dimethyl-5*H*-imidazo[1′,2′:1,2]pyrrolo[3,4-*b*]pyridin-5-one* (**17**). IR (KBr): 3360*s* (br.), 2940*w*, 1687*s*, 1592*s*, 1585*s*, 1468*w*, 1445*w*, 1430*m*, 1385*m*, 1375*m*, 1360*s*, 1345*m*, 1268*m*, 1232*w*, 1190*w*, 1142*w*, 1120*w*, 1102*m*, 1048*m*, 975*w*, 937*w*, 895*m*, 870*w*, 808*m*. $^1$H-NMR (200 MHz, $(D_6)$DMSO): 8.75/8.71 (2*dd* (5:2), $J$ = 4.9, 1.5, H–C(7) of **17**, H–C(8) of **16**); 8.08/7.99 (2*dd* (2:5), $J$ = 7.6, 1.5, H–C(6) of **16**, H–C(9) of **17**); 7.58/7.49 (2*dd* (2:5), $J$ = 7.6, 4.9, H–C(7) of **16**, H–C(8) of **17**); 6.66/6.65 (2*s*, OH); 3.00 (*s*, $(CH_3)_2N$); 1.77/1.76, 1.74/1.72 (2*s* each (2:5), $(CH_3)_2C$ of **16** and **17**). $^{13}$C-NMR (25.2 MHz, $(D_6)$DMSO): 171.9/171.7 (2*s* (2:1), C(5)); 165.7/165.1 (2*s* (3:1), C(2)); 153.1/151.1 (2*d* (5:2), C(7) of **17**, C(8) of **16**); 149.8/142.0 (2*s*, (2:3), C(9a) of **16**, C(5a) of **17**); 131.2/130.7 (2*d* (5:2), C(9) of **17**, C(6) of **16**); 126.5/124.1 (2*d*, (2:5), C(7) of **16**, C(8) of **17**); 125.8 (*s*, C(9a) of **17**); 108.7/106.9 (2*s* (3:1), C(9b)); 64.4/64.3 (2*s*, (3:5), C(3)); 39.0/38.7 (2*q* (*ca.* 3:1), $(CH_3)_2N$); 27.1, 21.2 (2*q*, $(CH_3)_2C$). MS (70 eV): 260 (6, $M^{+\cdot}$), 243 (9), 190 (8), 172 (5), 161 (5), 149 (6), 147 (6), 146 (8), 140 (8), 134 (7), 133 (8), 131 (5), 125 (6), 112 (18), 108 (11), 107 (8), 106 (5), 105 (10), 104 (6), 103 (8), 98 (12), 97 (56), 96 (14), 84 (10), 83 (12), 81 (15), 79 (16), 77 (13), 71 (13), 70 (21), 69 (55), 41 (100). Anal. calc. for $C_{13}H_{16}N_4O_2$ (260.30): C 59.99, H 6.20, N 21.52; found: C 59.80, H 6.28, N 21.70.

**2. Methanolysis of Azacyclols 11/12 and 16/17.** – 2.1. *Methyl [5-(Dimethylamino)-4-isopropyl-4-methyl-4*H*-imidazol-2-yl]pyridine Carboxylates* **13** *and* **14**. A soln. of 500 mg (1.7 mmol) of the 1:3 mixture **11/12** in 50 ml of MeOH was stirred at r.t. for 2 days. According to $^1$H-NMR, the esters **13** and **14** were formed in a ratio of 5:1. Evaporation of the solvent and chromatography ($SiO_2$, $CH_2Cl_2$/MeOH 35:1) gave 242 mg (46%) of *methyl 3-[5-(dimethylamino)-4-isopropyl-4-methyl-4*H*-imidazol-2-yl]pyridine-2-carboxylate* (**13**) and 53 mg (10%) of *methyl 2-[5-(dimethylamino)-4-isopropyl-4-methyl-4*H*-imidazol-2-yl]pyridine-3-carboxylate* (**14**).

**13:** IR ($CHCl_3$): 1740*s*, 1700*w*, 1595*s*, 1578*s*, 1460*m*, 1447*m*, 1422*m*, 1400*m*, 1385*m*, 1372*m*, 1360*s*, 1303*s*, 1265*m*, 1140*s*, 1088*m*, 1073*m*, 1055*m*, 966*m*, 912*m*. $^1$H-NMR (90 MHz, $CDCl_3$): 8.64 (*dd*, $J$ = 4, 1.5, H–C(6)); 8.38 (*dd*, $J$ = 8, 1.5, H–C(4)); 7.41 (*dd*, $J$ = 8, 4, H–C(5)); 3.91 (*s*, $CH_3O$); 3.23 (*s*, $(CH_3)_2N$); 2.29 (*sept.*, $J$ = 7, $(CH_3)_2CH$); 1.51 (*s*, $CH_3$–C(4′)); 1.24, 0.70 (2*d*, $J$ = 7, $(CH_3)_2CH$). $^{13}$C-NMR (25.2 MHz, $CDCl_3$): 188.5 (*s*, C(5′)); 167.8, 166.9 (2*s*, $COOCH_3$, C(2′)); 150.3 (*s*, C(2)); 148.7 (*d*, C(6)); 136.7 (*d*, C(4)); 127.3 (*s*, C(3)); 123.6 (*d*, C(5)); 81.0 (*s*, C(4′)); 51.6 (*q*, $CH_3O$); 38.6 (br. *q*, $(CH_3)_2N$); 33.1 (*d*, $(CH_3)_2CH$); 19.5 (*q*, $CH_3$–C(4′)); 17.5, 16.6 (2*q*, $(CH_3)_2CH$). MS (70 eV): 302 (8, $M^{+\cdot}$), 271 (5), 261 (8), 260 (60), 259 (100), 229 (11), 228 (45), 227 (27), 217 (14), 214 (21), 163 (11), 161 (24), 149 (14), 144 (25), 131 (21), 105 (17), 104 (10), 103 (43), 86 (17), 84 (25), 77 (18), 76 (12), 69 (11), 56 (87), 55 (22), 42 (45), 41 (42).

**14**: IR ($CHCl_3$): 1733*s*, 1700*w*, 1633*w*, 1590*s*, 1560*m*, 1445*w*, 1432*w*, 1422*w*, 1400*w*, 1385*w*, 1372*w*, 1338*s*, 1320*m*, 1302*s*, 1265*m*, 1141*m*, 1078*m*, 1060*w*, 972*m*. $^1$H-NMR (90 MHZ, $CDCl_3$): 8.80 (*dd*, $J$ = 4, 1.5, H–C(6)); 7.94 (*dd*, $J$ = 8, 1.5, H–C(4)); 7.36 (*dd*, $J$ = 8, 4, H–C(5)); 3.83 (*s*, $CH_3O$); 3.28 (*s*, $(CH_3)_2N$); 2.33 (*sept.*, $J$ = 7, $(CH_3)_2CH$); 1.57 (*s*, $CH_3$–C(4′)); 1.25, 0.78 (2*d*, $J$ = 7, $(CH_3)_2CH$). $^{13}$C-NMR (50.4 MHz, $CDCl_3$): 189.2 (*s*, C(5′)); 170.0, 167.8 (2*s*, $COOCH_3$, C(2′)); 150.6 (*s*, C(2)); 150.4 (*d*, C(6)); 135.9 (*d*, C(4)); 128.8 (*s*, C(3)); 122.8 (*d*, C(5)); 81.3 (*s*, C(4′)); 51.9 (*q*, $CH_3O$); 39.0 (br. *q*, $(CH_3)_2N$); 33.4 (*d*, $(CH_3)_2CH$); 19.6 (*q*, $CH_3$–C(4′)); 17.7, 16.8 (2*q*, $(CH_3)_2CH$). MS (70 eV): 302 (14, $M^{+\cdot}$), 261 (8), 260 (49), 259 (57), 229 (7), 228 (13), 227 (20), 217 (11), 214 (6), 199 (13), 163 (20), 162 (11), 161 (19), 149 (9), 131 (29), 108 (49), 107 (36), 105 (15), 104 (10), 103 (16), 92 (11), 91 (19), 90 (12), 86 (9), 84 (17), 83 (10), 82 (13), 81 (53), 80 (100), 79 (79), 78 (48), 77 (47), 76 (17), 69 (16), 67 (13), 66 (15), 65 (13), 56 (86), 55 (63), 54 (80), 53 (65), 52 (24), 51 (28), 50 (18), 43 (16), 42 (51), 41 (63).

In a second, analogous experiment, the soln. was refluxed for 6 days. $^1$H-NMR revealed the formation of **13** and **14** in a ratio of 2:3. Usual workup yielded 137 mg (26%) of **13** and 198 mg (38%) of **14**.

Refluxing a soln. of 100 mg (0.35 mmol) of **12** in 10 ml of MeOH for 15 h gave **13** and **14** in a ratio of *ca.* 1:2 in a total yield of 60%.

2.2. *Methyl [5-(Dimethylamino)-4,4-dimethyl-4*H*-imidazol-2-yl]-pyridine Carboxylates* **18** *and* **19**. In analogy to *Exper. 2.1*, a soln. of 200 mg (0.8 mmol) of the 2:5 mixture **16/17** in 30 ml of MeOH was refluxed for 15 h. According to $^1$H-NMR, *methyl 3-[5-(dimethylamino)-4,4-dimethyl-4*H*-imidazol-2-yl]pyridine-2-carboxylate* (**18**) and *methyl 2-[5-(dimethylamino)-4,4-dimethyl-4*H*-imidazol-2-yl]pyridine-3-carboxylate* (**19**) were formed in a ratio of 2:3. Chromatography on $SiO_2$ with $CH_2Cl_2$/MeOH 30:1 yielded 57 mg (26%) of **18** and 85 mg (39%) of **19**.

**18:** IR ($CHCl_3$): 1745*s*, 1600*s*, 1583*s*, 1460*w*, 1449*w*, 1426*m*, 1406*w*, 1380*w*, 1368*w*, 1340*s*, 1307*s*, 1270*m*, 1145*s*, 1090*w*, 1080*w*, 978*w*, 956*w*, 920*w*. $^1$H-NMR (90 MHz, $CDCl_3$): 8.66 (*dd*, $J$ = 4.5, 1.5, H–C(6)); 8.34 (*dd*, $J$ = 8, 1.5, H–C(4)); 7.40 (*dd*, $J$ = 8, 4.5, H–C(5)); 3.90 (*s*, $CH_3O$); 3.22 (*s*, $(CH_3)_2N$); 1.55 (*s*, $(CH_3)_2C$). $^{13}$C-NMR (50.4 MHz, $CDCl_3$): 188.6 (*s*, C(5′)); 167.5, 167.3 (2*s*, $COOCH_3$, C(2′)); 150.5 (*s*, C(2)); 149.4 (*d*, C(6)); 136.9 (*d*, C(4)); 127.9 (*s*, C(3)); 124.0 (*d*, C(5)); 74.2 (*s*, C(4′)); 51.9 (*q*, $CH_3O$); 39.1 (br. *q*, $(CH_3)_2N$); 22.3 (*q*, $(CH_3)_2C$). MS (70 eV): 274 (40, $M^{+\cdot}$), 259 (13), 243 (11), 215 (38), 204 (50), 190 (13), 189 (100), 162 (10), 161 (83), 148 (24), 144 (10), 131 (19), 105 (12), 104 (12), 103 (43), 76 (10), 56 (35), 55 (10), 42 (63), 41 (47).

**19**: IR ($CHCl_3$): 1735*s*, 1600*s* (br.), 1450*m*, 1436*w*, 1425*w*, 1406*m*, 1380*w*, 1368*w*, 1339*s*, 1306*s*, 1270*m*, 1145*s*, 1082*m*, 1062*w*, 983*w*, 956*m*, 920*w*. $^1$H-NMR (90 MHz, $CDCl_3$): 8.80 (*dd*, $J$ = 4.5, 1.5, H–C(6)); 8.00 (*dd*, $J$ = 8, 1.5, H–C(4)); 7.39 (*dd*, $J$ = 8, 4.5, H–C(5)); 3.83 (*s*, $CH_3O$); 3.27 (*s*, $(CH_3)_2N$); 1.60 (*s*, $(CH_3)_2C$). $^{13}$C-NMR (25.2 MHz, $CDCl_3$): 188.8 (*s*, C(5′)); 169.0, 167.3 (2*s*, $COOCH_3$, C(2′)); 151.0 (*s*, C(2)); 150.5 (*d*, C(6)); 136.2 (*d*, C(4)); 128.2 (*s*, C(3)); 122.9 (*d*, C(5)); 74.1 (*s*, C(4′)); 51.9 (*q*, $CH_3O$); 39.1 (br. *q*, $(CH_3)_2N$); 22.2 (*q*, $(CH_3)_2C$). MS (70 eV): 274 (100, $M^{+\cdot}$), 289 (8), 243 (5), 189 (36), 175 (13), 163 (21), 161 (43), 148 (21), 146 (18), 133 (12), 131 (28), 105 (20), 103 (25), 100 (10), 92 (12), 79 (18), 78 (15), 77 (12), 76 (10), 71 (10), 70 (71), 69 (10), 56 (14), 42 (13), 41 (13).

**3. Reaction of 2-(Dimethylamino)-3,9b-dihydro-9b-hydroxy-3,3-dimethyl-5*H*-imidazo[2,1-*a*]isoindol-5-one with $Ac_2O$.** – Treatment of the azacyclol obtained from **1a** and phthalimide [12] with $Ac_2O$ in pyridine at r.t. led to an *O*-acetyl derivative in modest yield. For this product, the structure of *2-(dimethylamino)-3,9b-dihydro-3,3-dimethyl-5*H*-imidazo[2,1-a]isoindol-9b-yl acetate* (**20**) is suggested. IR (KBr): 1780*w*, 1725*s*, 1703*s*, 1608*s*, 1570*s*, 1493*m*, 1468*w*, 1452*m*, 1397*m*, 1370*m*, 1360*s*, 1329*m*, 1292*m*, 1120*m*, 1072*m*, 1068*m*, 875*m*, 756*m*, 728*s*. $^1$H-NMR (60 MHz, $CDCl_3$): 7.9–7.7 (*m*, 4 arom. H); 2.93 (*s*, $(CH_3)_2N$); 2.18 (*s*, $CH_3CO$); 1.93 (*s*, $(CH_3)_2C$). MS (70 eV): 301 (2, $M^{+\cdot}$), 286 (34), 188 (100), 148 (27), 130 (38), 100 (17), 72 (40).

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