Stereoelectronically Controlled Cyclization Reactions on the Way to *peri*-Fused Tetrahydropyrazolo[1,5-*a*]pyridines as Aza Analogs of Ergoline Partial Structures

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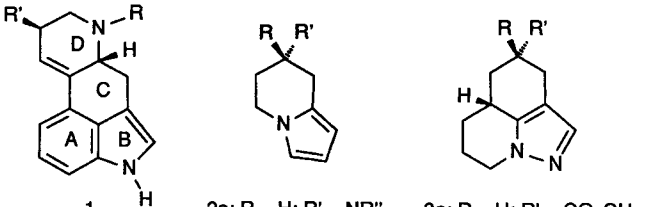
Received April 15, 1991

Key Words: Alkylation, *C*- and *O*- / Anionic cyclization / Tetrahydropyrazolo[1,5-*a*]pyridines

The synthesis of the 3-substituted tetrahydropyrazolopyridin-4-ylalkyl iodides **7a**, **7b**, **8a** and **8b** as well as their behavior towards anionic cyclization conditions have been investigated. An (enol *endo*)-*exo*-tet-type ring closure only proceeds when a seven-membered ring is annulated (**9b**, **10b**). Otherwise, treatment of the β-keto ester **7a** with NaH results in *O*-alkylation to yield the stereoelectronically favored (*Z*)-enol ether **13a**, which can be isomerized to the thermodynamically more stable (*E*) isomer **13b**. Various attemps to achieve ring closure of the methyl ketone **8a** failed; instead, β-elimination is observed. Annulation of a six-membered carbocycle is acchieved when the triester **17** is treated by a Dieckmann condensation to give the tricyclic products **18** and **19**.

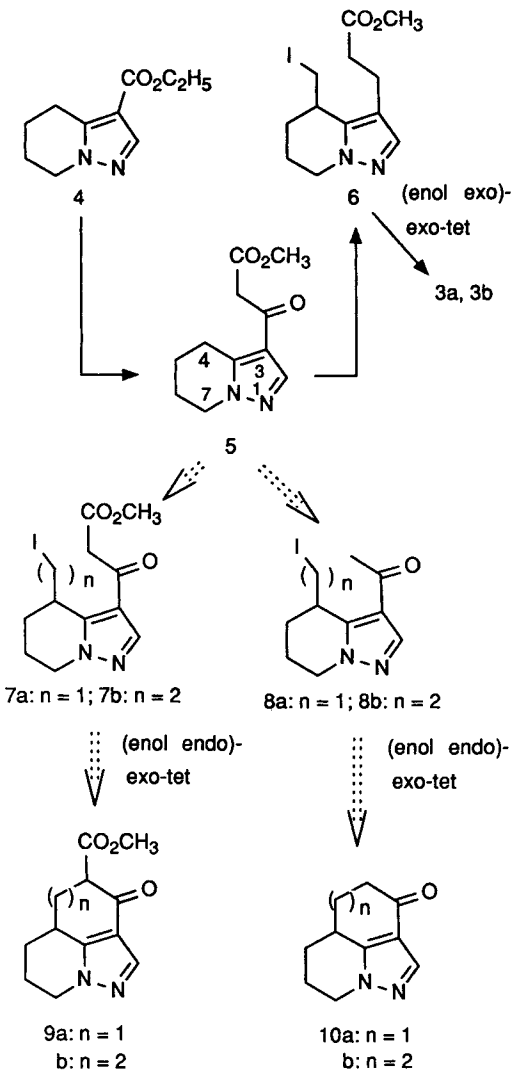
Ergoline derivatives (**1**) as well as their ABC tricyclic and BC bicyclic analogs are widely studied substrates with remarkable pharmacological properties[1]. The main characteristic of that group of compounds is their activity towards different receptors, namely the dopamine, serotonin, and adrenergic binding sites. In search of more selective dopamine agonists and antagonists which might also differentiate between dopamine receptor subtypes, we are investigating bi- and tricyclic analogs which are devoid of an aromatic NH moiety. Thus, we elaborated an EPC synthesis of the highly CNS active aminoindolizidines **2a** and **2b**[2]. We also prepared the pyrazolochinolinecarboxylate derivatives **3a** and **3b**[3], which can be converted into the pharmacologically relevant amines **3c** and **3d** in a Curtius rearrangement[4].

Scheme 1



As a continuation of this project we report in this paper on the first syntheses of cycloheptane-, oxepine-, and pyran-fused 4,5,6,7-tetrahydropyrazolo[1,5-*a*]pyridines[5]. Our recent approach[3] to the pyrazolo[2,3,4-*ji*]quinoline ring system started with the ethyl 4,5,6,7-tetrahydropyrazolo-[1,5-*a*]pyridinecarboxylate **4**[6] and involved regioselective reaction of β-keto ester **5** at C-4 after conversion into its dianion, when benzyloxymethyl chloride (BOM-Cl) was

Scheme 2

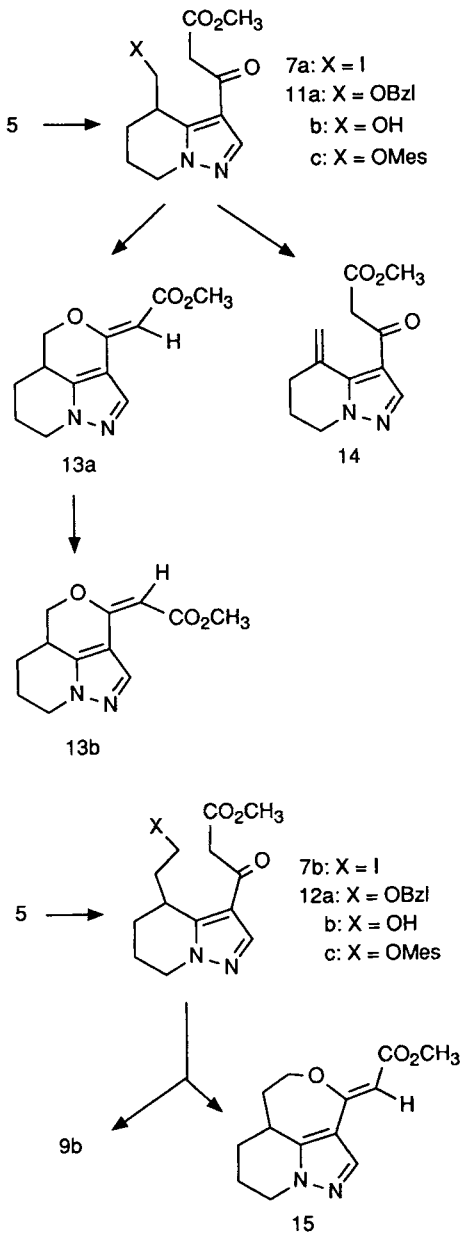


  0170–2041/91/0909–0921 $ 3.50+.25/0

used as a 1,1-dielectrophilic equivalent. Subsequent deprotection, reduction of the ketone function, and activation gave the iodide **6** which could be cyclized with the help of LDA to afford the separable diastereomers **3a** and **3b** in a 1:1 ratio. This 6-(enol *exo*)-*exo*-tet process was predicted to be favored according to the Baldwin rules[7].

It was now examined whether the cyclohexanone derivatives **9a** and **10a**, which could be further functionalized at their C=O group, can be approached by ring closure reaction of the appropriate precursors **7a** and **8a**, respectively. This would be a 6-(enol *endo*)-*exo*-tet case which is also predicted to be favored. For further SAR studies using geometrically varied substrates we also envisaged to synthesize the pyrazolopyridine-fused cycloheptanone derivatives **9b** and **10b** by 7-(enol *endo*)-*exo*-tet cyclization of **7b** and **8b**, respectively.

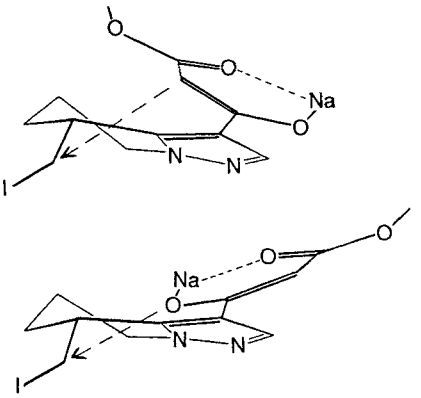
Scheme 3



For annulation of a six-membered ring the mesylate **11c** and the iodide **7a** were prepared as cyclization precursors. **11c** was obtained in 91% yield by treatment of alcohol **11b**[3] with methanesulfonyl chloride/triethylamine. **11b** was synthesized from **5** via **11a** according to a previously reported protocol[3]. Subsequently, **11c** was refluxed with NaI in acetone to yield **7a**.

In fact, deprotonation of **7a** with NaH in THF followed by stirring at 60°C resulted in ring closure. However, instead of the β-keto ester **9a** the enol ether **13a** was obtained in diastereomerically pure form. Analogously to the observations made by Baldwin[8] for isolated five-membered ring systems, we reason that the formation of our *peri*-fused ring system requires geometric restraints when the electrophile must approach *perpendicularly to the plane* of the enolate, as depicted in Scheme 4. On the other hand, the oxygen lone pair of the ambident nucleophile can be approached *in the plane* of the enolate requiring a less restrained transition state.

Scheme 4. Conformational representations of the Na enolate of **7a**



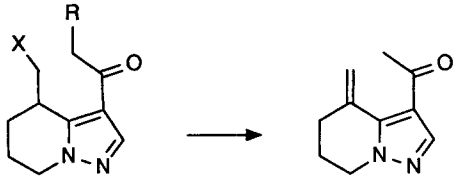
Stereospecific formation of the (*Z*)-enol ether geometry can be explained by chelation of the β-keto ester sodium salt during the reaction. Various efforts to direct the cyclization towards *C*-alkylation failed. Thus, transmetallation with cyclopentadienylthallium[9] afforded also **13a** whereas treatment of **7a** with tetrabutylammonium fluoride[10] or by triethylamine resulted in β-elimination to give **14**. Compound **13a** was also obtained by treatment of mesylate **11c** with NaH in THF. **13a** could be isomerized in refluxing xylene to yield the (*E*)-enol ether **13b** along with **13a** in a 3:1 diastereomeric mixture. Both isomers were easily separable by flash chromatography. Elucidation of the double bond geometry was carried out by proton NMR spectroscopy, indicating a strong NOE between the olefinic and the aromatic proton of **13a**.

Annulation of a seven-membered ring was also achieved by starting from β-keto ester **5**, requiring a two-carbon bis-electrophile. Since we anticipated that compounds of type $X-CH_2-CH_2-X$ (X = leaving group) tend to eliminate HX under the basic reaction conditions, the bis-electrophile should be used in protected form. By analogy with the convenient BOM−Cl we now applied 2-(benzyloxy)ethyl io-

dide, which is easily available from glycol[11]. In fact, deprotonation of **5** with 2 equivalents of LDA followed by addition of 2-(benzyloxy)ethyl iodide gave the benzyl ether **12a** in 74% yield. Hydrogenation of **12a** with Pd/C in acetic acid yielded the primary alcohol **12b**, which was converted into the mesylate **12c**. Cyclization precursor **7b** was obtained by refluxing **12c** with NaI in acetone. Upon treatment of **7b** with NaH/THF at 0–60°C, a 1:1 mixture of the tricyclic cycloheptanone **9b** and the oxepine derivative **15** was formed. Both products were easily separable by flash chromatography. This result is in accordance with observations at molecular models, which demonstrate that perpendicular approach to the enolate π system is facilitated by the extrabond length. The β-keto ester **9b** exists as a 1:1 diastereomeric equilibrium, which can be shown by the ^{1}H-NMR spectra. In accordance to the enol ether **13a** compound **15** is (*Z*)-configurated. The stereochemistry was again established by NMR spectroscopy, indicating a significant NOE between the enol ether proton and the aromatic 2-H position.

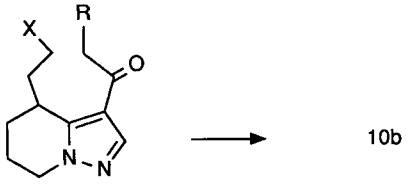
In an attempt to circumvent *O*-alkylation we approached the methyl ketones **8a** and **8b** as potential cyclization precursors. Thus, **11a** and **12a** were saponified to furnish the β-keto acids **11d** and **12d** which underwent decarboxylation to the methyl ketones **11e** and **12e**, respectively. Subsequent deprotection gave the primary alcohols **11f** and **12f** which were transformed into the iodides **8a** and **8b** via the mesylates **11g** and **12g** in 41 and 31% yields from **11a** and **12a**, respectively. In fact, selective *C*-alkylation could be achieved when iodide **8b** was treated with NaH in THF.

Scheme 5



8a: X = I; R = H
11a: X = OBzl; R = CO_2CH_3
d: X = OBzl; R = CO_2H
e: X = OBzl; R = H
f: X = OH; = H
g: X = OMes; R = H

16



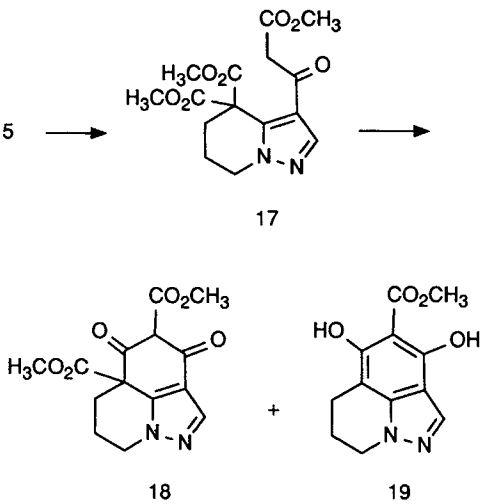
8b: X = I; R = H
12a: X = OBzl; R = CO_2CH_3
d: X = OBzl; R = CO_2H
e: X = OBzl; R = H
f: X = OH; = H
g: X = OMes; R = H

10b

The tricyclic cycloheptanone **10b** was prepared in 51% yield. On the other hand, several attempts to cyclize **8a** failed, although a range of reaction conditions were investigated (NaH/THF or DMSO, KHMDS/THF, KH/THF, LDA (+CuI)/THF. In any case, the β-elimination product **16** was isolated as the single reaction product. Treatment of mesylate **11g** with NaH, NaOMe, or KHMDS in different solvents afforded also **16**.

Finally, it could be shown that annulation of a six-membered carbocycle is possible by 6-(enol *endo*)-*exo*-trig ring closure. Thus, deprotonation of **5** by 2 equivalents of LDA, followed by quenching with methyl chloroformate gave access to the triester **17**. Treatment of **17** with NaOMe/MeOH resulted in the formation of the Dieckmann product **18** along with the dihydroxybenzoate **19** as a side product.

Scheme 6



5 → 17 → 18 + 19

We thank Prof. *F. Eiden* for stimulating discussions and generous support. Tanks are also due to *T. Müller* for technical assistance. This project is supported by the *Deutsche Forschungsgemeinschaft* and the *Fonds der Chemischen Industrie*.

Experimental

Tetrahydrofuran was distilled from $LiAlH_4$ immediately before use. Dichloromethane, acetone, diisopropylamine, and triethylamine were distilled from CaH_2. All liquid reagents were also purified by distillation. Unless otherwise noted reactions were conducted under dry nitrogen. Evaporation of final product solutions was performed under vacuo with a rotatory evaporator. – Flash chromatography: 230–400 mesh silica gel. – Melting points: Büchi melting point apparatus, uncorrected. – IR: Perkin-Elmer 881 spectrometer. – MS: Varian CH7. – NMR: Jeol 400 JNM-GX, 400 MHz, tetramethylsilane as internal standard. – Elemental analyses: Heraeus CHN Rapid instrument.

Methyl (±)-3-Oxo-3-[4,5,6,7-tetrahydro-4-(iodomethyl)pyrazolo[1,5-a]pyridin-3-yl]propionate (**7a**): A mixture of 30 mg (0.09 mmol) of **11c** and 180 mg (1.2 mmol) of NaI was stirred in 2 ml of boiling acetone for 7 h. After cooling to room temp. the solvent was removed and the residue extracted with ether. The extract was evaporated and the residue purified by flash chromatography (petroleum ether/ethyl acetate, 1:1) to give 22 mg (67%) of **7a** as a colorless oil. – IR (NaCl): $\tilde{\nu}$ = 2950 cm^{-1}, 2850, 1740, 1660. –

^{1}H NMR($CDCl_3$): δ = 1.96–2.11 (m, 3H, 5-H_{ax}, 6-H_2), 2.20–2.26 (m, 1H, 5-H_{eq}), 3.35 (t, *J* = 9.5 Hz, 1H, CH_2I), 3.62–3.66 (m, 1H, 4-H), 3.68 (dd, *J* = 9.5/2.9 Hz, 1H, CH_2I), 3.75 (s, 3H, OCH_3), 3.81 (d, *J* = 1.5 Hz, 2H, CH_2CO_2), 4.01–4.08 (m, 1H, 7-H_{ax}), 4.18–4.24 (m, 1H, 7-H_{eq}), 7.86 (s, 1H, 2-H).

$C_{12}H_{15}IN_2O_3$ (362.2) Calcd. C 39.80 H 4.17 N 7.74
Found C 39.76 H 4.30 N 7.65
Mol. mass 362 (MS)

Methyl (±)-3-Oxo-3-[4,5,6,7-tetrahydro-4-(2-iodomethyl)pyrazolo[1,5-a]pyridin-3-yl]propionate (**7b**): A mixture of 830 mg (2.41 mmol) of **12c** and 4.00 g (26.7 mmol) of NaI in 50 ml of acetone was refluxed for 4 h and worked up as described for **7a** to give 745 mg (82%) of **7b** as a colorless oil. – IR (NaCl): ṽ = 2950 cm^{-1}, 2850, 1740, 1665. – ^{1}H NMR ($CDCl_3$): δ = 1.77–2.17 (m, 5H, 5-H_2, 6-H_2, CH_2CH_2I), 2.35–2.44 (m, 1H, CH_2CH_2I), 3.23–3.36 (m, 2H, CH_2I), 3.47–3.52 (m, 1H, 4-H), 3.76 (s, 3H, CO_2CH_3), 3.79 (d, *J* = 3 Hz, 2H, CH_2CO_2), 4.02 (ddd, *J* = 13.2/11/5.1 Hz, 1H, 7-H_{ax}), 4.27 (ddd, *J* = 13.2/5.2/2.5 Hz, 1H, 7-H_{eq}), 7.85 (s, 1H, 2-H).

$C_{13}H_{17}IN_2O_3$ (376.2) Calcd. C 41.51 H 4.56 N 7.45
Found C 41.49 H 4.55 N 7.61
Mol. mass 376 (MS)

(±)-3-Acetyl-4,5,6,7-tetrahydro-4-(iodomethyl)pyrazolo[1,5-a]pyridine (**8a**): A solution of 450 mg (1.65 mmol) of **11g** and 4.00 g (26.7 mmol) of NaI in 70 ml of acetone was refluxed for 12 h and worked up as described for **7a** to give 410 mg (82%) of **8a** as a colorless solid, m.p. 96 °C. – IR (KBr): ṽ = 2960 cm^{-1}, 2950, 2870, 1660. – ^{1}H NMR ($CDCl_3$): δ = 1.91–2.25 (m, 4H, 5-H_2, 6-H_2), 2.45 (s, 3H, $COCH_3$), 3.37 (dd, *J* = 9.4/9.4 Hz, 1H, CH_2I), 3.62–3.82 (m, 1H, 4-H), 3.71 (dd, *J* = 9.4/2.1 Hz, 1H, CH_2I), 4.01–4.08 (m, 1H, 7-H_{ax}), 4.17–4.23 (m, 1H, 7-H_{eq}), 7.86 (s, 1H, 2-H).

$C_{10}H_{13}IN_2O_3$ (304.1) Calcd. C 39.49 H 4.31 N 9.21
Found C 39.49 H 4.31 N 9.21
Mol. mass 304 (MS)

(±)-3-Acetyl-4,5,6,7-tetrahydro-4-(2-iodoethyl)pyrazolo[1,5-a]pyridine (**8b**): A solution of 250 mg (0.87 mmol) of **12g** and 1.5 g (10 mmol) of NaI in 10 ml of acetone was refluxed for 4 h and worked up as described for **7a** to give 170 mg (61%) of **8b** as a colorless solid, m.p. 83 °C. – IR (KBr): ṽ = 2950 cm^{-1}, 2850, 1655. – ^{1}H NMR ($CDCl_3$): δ = 1.81–2.17 (m, 5H, 5-H_2, 6-H_2, CH_2CH_2I), 2.35–2.41 (m, 1H, CH_2CH_2I), 2.43 (s, 3H, $COCH_3$), 3.22–3.37 (m, 2H, CH_2I), 3.51–3.53 (m, 1H, 4-H), 3.99–4.06 (m, 1H, 7-H_{ax}), 4.25–4.31 (m, 1H, 7-H_{eq}), 7.86 (s, 1H, 2-H).

$C_{11}H_{15}IN_2O$ (318.2) Calcd. C 41.53 H 4.75 N 8.80
Found C 41.64 H 4.74 N 8.66
Mol. mass 318 (MS)

Methyl (±)-3,4,5,5a,6,7,8,9-Octahydro-9-oxo-2,2a-diazabenzo[cd]azulene-8-carboxylate (**9b**): A solution of 376 mg (1 mmol) of **7b** in 15 ml of THF was added to 24 mg (1 mmol) of NaH. The suspension was stirred at room temp. for 30 min, then a satd. aqueous $NaHCO_3$ solution and ether were added. The organic layer was dried ($MgSO_4$), evaporated, and the residue was purified by flash chromatography (petroleum ether/ethyl acetate, 4:6) to afford 95 mg (38%) of **9b** as a 1:1 mixture of diastereomers followed by 88 mg (35%) of **15** both as colorless solids, m.p. 150 °C for **9b**; m.p. 162 °C for **15**. **9b**: – IR (KBr): ṽ = 2950^{-1}, 2860, 1735, 1660. – ^{1}H NMR ($CDCl_3$): δ = 1.46–1.56 (m, 1H, 5-H_{ax}), 1.63–1.78 (m, 1H, 6-H_{ax}), 1.99–2.38 (m, 6H, 7-H_2, 6-H_{eq}, 5-H_{eq}, 4-H_2), 2.90–2.98 (m, 1H, 5a-H), 3.64–3.74 (m, 1H, 8-H), 3.75 (s. 0.5 x 3H, OCH_3), 3.76 (s, 0.5 × 3H, OCH_3), 3.97–4.06 (m, 1H, 3-H_{ax}), 4.28–4.34 (m, 1H, 3-H_{eq}), 7.93 (s, 0.5 x 1H, 1-H), 7.95 (s, 0.5 x 1H, 1-H). – ^{13}C NMR ($CDCl_3$): δ = 22.4, 22.6 (C-4), 24.9, 26.1 (C-7), 27.8, 28.0 (C-5), 30.3, 32.4 (C-6), 35.5, 37.6 (C-5a), 47.7, 47.8 (C-3), 52.2, 52.3 (OCH_3), 56.6, 59.7 (C-8), 120.1, 120.3 (C-2b), 140.5, 141.4 (C-1), 145, 146.1 (C-9a), 170.9, 171.4 (CO_2R), 190.5, 191.1 (CO).

$C_{13}H_{16}N_2O_3$ (248.3) Calcd. C 62.89 H 6.50 N 11.28
Found C 62.76 H 6.35 N 11.20
Mol. mass 248 (MS)

(±)-3,4,5,5a,6,7,8,9-Octahydro-9-oxo-2,2a-diazabenzo[cd]azulene (**10b**): A solution of 50 mg (0.16 mmol) of **8b** in 5 ml of THF was added to 4.8 mg (0.2 mmol) of NaH. The suspension was stirred at room temp. for 3 h, then heated to 50 °C for 4 h. After addition of further 3 mg of NaH, the mixture was stirred at 50 °C for one more hour, then quenched with 5 ml of satd. aqueous $NaHCO_3$ solution and extracted with ether. The organic layer was dried ($MgSO_4$) and evaporated. The residue was purified by flash chromatography (CH_2Cl_2/CH_3OH, 97:3) to give 15 mg (51%) of **10b** as a colorless solid, m.p. 98 °C. – IR (KBr): ṽ = 2930 cm^{-1}, 2860, 1640. – ^{1}H NMR ($CDCl_3$): δ = 1.53 (dddd, *J* = 12.8/12.8/11.5/2.8 Hz, 1H, 5-H_{ax}), 1.62–1.70 (m, 1H, 6-H_{ax}), 1.90–2.20 (m, 6H, 7-H_2, 6-H_{eq}, 5-H_{eq}, 4-H_2), 2.62 (ddd, *J* = 16.0/10.2/3.5 Hz, 1H, 8-H_{ax}), 2.73 (ddd, *J* = 16.0/7.3/3.5 Hz, 1H, 8-H_{eq}), 2.90–2.96 (m, 1H, 5a-H), 4.01 (ddd, *J* = 12.8/12.0/5.0 Hz, 1H, 3-H_{ax}), 4.30 (dd, *J* = 12.8/4.9 Hz, 1H, 3-H_{eq}), 7.93 (s, 1H, 1-H).

$C_{11}H_{14}N_2O$ (190.3) Calcd. C 69.45 H 7.42 N 14.73
Found C 69.44 H 7.49 N 14.79
Mol. mass 190 (MS)

Methyl (±)-3-Oxo-3-[4,5,6,7-tetrahydro-4-(mesyloxymethyl)-pyrazolo[1,5a]pyridin-3-yl]propionate (**11c**): To a solution of 600 mg (2.34 mmol) of **11b**[3] in 20 ml of THF were added 0.38 ml (2.73 mmol) of triethylamine and 0.212 ml (2.73 mmol) of methanesulfonyl chloride. After stirring at room temp. for 1 h the mixture was evaporated and the residue purified by flash chromatography (CH_2Cl_2/CH_3OH, 97:3) to afford 710 mg (91%) of **11c** as a colorless solid, m.p. 102 °C. – IR (KBr): ṽ = 2980 cm^{-1}, 1740, 1650, 1370, 1170. – ^{1}H NMR ($CDCl_3$): δ = 1.88–1.96 (m, 1H, 6-H_a), 2.03–2.26 (m, 3H, 6-H_b, 7-H_2), 3.06 (s, 3H, CH_3SO_3), 3.75 (s, 3H, OCH_3), 3.78–3.85 (m, 1H, 4-H), 3.81 (s, 2H, CH_2CO_2), 4.03–4.10 (m, 1H, 8-H_{ax}), 4.30 (ddd, *J* = 13.2/4.4/3.7 Hz, 1H, 8-H_{eq}), 4.35 (dd, *J* = 9.5/8.8 Hz, 1H, CH_2OSO_2), 4.51 (dd, *J* = 9.5/3 Hz, 1H, CH_2OSO_2), 7.90 (s, 1H, 2-H).

$C_{13}H_{18}N_2O_6S$ (330.4) Calcd. C 47.26 H 5.49 N 8.48
Found C 47.49 H 5.59 N 8.30
Mol. mass 330 (MS)

(±)-3-Acetyl-4-[(benzyloxy)methyl]-4,5,6,7-tetrahydropyrazolo-[1,5-a]pyridine (**11e**): A solution of 1.5 g (4.39 mmol) of **11a** in 40 ml of dioxane and 40 ml of 1 N NaOH was stirred at room temp. for 3 h. Then the solution was extracted with ether. The aqueous layer was acidified to pH = 2 with concd. HCl and subsequently extracted with ether. Finally, the organic layer (a solution of **11d**) was stirred at room temp. for 40 h to give 1.09 g (88 %) of **11e** as a colorless oil after drying ($MgSO_4$), evaporation, and flash chromatography (petroleum ether/ethyl acetate, 1:1). – IR (NaCl): ṽ = 3070 cm^{-1}, 3030, 2950, 2870, 1720, 1660. – ^{1}H NMR ($CDCl_3$): δ = 1.73–1.82 (m, 1H, 5-$H_{a,b}$ or 6-$H_{a,b}$), 1.90–1.96 (m, 1H, 5-$H_{a,b}$ or 6-$H_{a,b}$), 2.15–2.29 (m, 2H, 5-$H_{a,b}$ or 6-$H_{a,b}$), 2.41 (s, 3H, $COCH_3$), 3.59 (dd, J = 10.5/9.6 Hz, 1H, CH_2OBzl), 3.79–3.82 (m, 2H, 4-H, CH_2OBzl), 3.93–4.03 (m, 1H, 7-H_{ax}), 4.23–4.28 (m, 1H, 7-H_{eq}), 4.47 (d, *J* = 12.0 Hz, 1H, CH_2Ph), 4.65 (d, *J* = 12.0 Hz, 1H, CH_2Ph), 7.24–7.34 (m, 5H, Ph), 7.84 (s. 1H, 2-H).

$C_{17}H_{20}N_2O_2$ (284.4) Calcd. C 71.81 H 7.09 N 9.85
Found C 71.78 H 7.12 N 9.85
Mol. mass 284 (MS)

(±)-3-Acetyl-4,5,6,7-tetrahydro-4-(hydroxymethyl)pyrazolo[1,5-a]pyridine (**11f**): A mixture of 1.0 g (3.5 mmol) of **11e** and 3.5 g of Pd/C (10%) in 100 ml of acetic acid was stirred at room temp. for 3 h under a balloon of H_2. Then it was filtered (Celite® AFA), and the filtrate was evaporated. The residue was purified by flash chromatography (CH_2Cl_2/CH_3OH, 97:3) to give 510 mg (75%) of **11f** as a colorless oil. – IR (NaCl): $\tilde{\nu}$ = 3380 cm^{-1}, 2950, 2860, 1660. – ^1H NMR ($CDCl_3$): δ = 1.72–1.80 (m, 1H, 5-$H_{a,b}$ or 6-$H_{a,b}$), 1.93–1.98 (m, 1H, 5-$H_{a,b}$ or 6-$H_{a,b}$), 2.08–2.23 (m, 2H, 5-$H_{a,b}$ or 6-$H_{a,b}$), 2.40 (s, 3H, $COCH_3$), 3.57–3.60 (m, 1H, 4-H), 3.66 (dd, *J* = 10.2/7.7 Hz, 1H, CH_2OH), 3.85 (dd, *J* = 10.2/5.6 Hz, 1H, CH_2OH), 3.94–4.00 (m, 1H, 7-H_{ax}), 4.21–4.27 (m, 1H, 7-H_{eq}), 7.85 (s, 1H, 2-H).

$C_{10}H_{14}N_2O_2$ (194.2) Calcd. C 61.84 H 7.26 N 14.42
Found C 61.52 H 7.34 N 14.66
Mol. mass 194 (MS)

(±)-3-Acetyl-4,5,6,7-tetrahydro-4-[(mesyloxy)methyl)]pyrazolo-[1,5-a]pyridine (**11g**): To a solution of 450 mg (2.32 mmol) of **11f** in 25 ml of THF were added 0.50 ml (3.61 mmol) of triethylamine and 0.268 ml (3.44 mmol) of methanesulfonyl chloride. After stirring at room temp. for 1 h the mixture was evaporated, and the residue was purified by flash chromatography (petroleum ether/ethyl acetate, 1:1) to give 530 mg (84%) of **11g** as a colorless solid, m.p. 92°C. – IR (KBr): $\tilde{\nu}$ = 3010 cm^{-1}, 2960, 2875, 1660, 1350, 1175. – ^1H NMR ($CDCl_3$): δ = 1.81–1.90 (m, 1H, 5-$H_{a,b}$ or 6-$H_{a,b}$), 1.98–2.24 (m, 3H, 5-$H_{a,b}$ or 6-$H_{a,b}$), 2.40 (s, 3H, $COCH_3$), 3.05 (s, 3H, CH_3SO_3), 3.72–3.78 (m, 1H, 4-H), 3.97–4.05 (m, 1H, 7-H_{ax}), 4.23–4.29 (m, 1H, 7-H_{eq}), 4.25 (t, *J* = 9.4 Hz, 1H, CH_2OSO_2), 4.52 (dd, *J* = 9.4/3.4 Hz, 1H, CH_2OSO_2), 7.85 (s, 1H, 2-H).

$C_{11}H_{16}N_2O_4S$ (272.3) Calcd. C 48.52 H 5.92 N 10.29
Found C 48.62 H 5.91 N 10.19
Mol. mass 272 (MS)

Methyl (±)-3-{4-[2-(Benzyloxy)ethyl]-4,5,6,7-tetrahydropyrazolo-[1,5-a]pyridin-3-yl}-3-oxopropionate (**12a**): To a solution of 355 mg (1.6 mmol) of **5** in 30 ml of THF was added dropwise 10 ml of freshly prepared LDA (0.32 M in THF) at –78°C. The reaction mixture was warmed up to –20°C and then stirred at this temp. for 10 min, during which time the color turned to dark red. Then a solution of 452 mg (1.72 mmol) of 2-(benzyloxy)ethyl iodide in 5 ml THF was added dropwise. After 10 min, 20 ml of a satd. aqueous solution of $NaHCO_3$ was added, and the mixture was extracted with ether. The organic layer was dried ($MgSO_4$), evaporated, and the residue purified by flash chromatography (petroleum ether/ethyl acetate, 1:1) to give 418 mg (74%) of **12a** as a colorless oil. – IR (NaCl): $\tilde{\nu}$ = 3030 cm^{-1}, 2955, 2865, 1740, 1665. – ^1H NMR ($CDCl_3$): δ = 1.69–1.82 (m, 1H, 5-$H_{a,b}$ or 6-$H_{a,b}$), 1.93–2.01 (m, 1H, 5-$H_{a,b}$ or 6-$H_{a,b}$), 2.03–2.17 (m, 4H, BzlOCH$_2$CH_2, 5-$H_{a,b}$), or 6-$H_{a,b}$), 3.52–3.56 (m, 1H, 4-H), 3.68 (dd, *J* = 11/6.6 Hz, 2H, BzlOCH$_2$), 3.74 (s, 3H, OCH_3), 3.79 (d, *J* = 4.4 Hz, 2H, CH_2CO_2), 3.96–4.06 (m, 1H, 7-H_{ax}), 4.22–4.28 (m, 1H, 7-H_{eq}), 4,50 (d, *J* = 11.7 Hz, 1H, $PhCH_2$), 4.58 (d, *J* = 11.7 Hz, 1H, $PhCH_2$), 7.26–7.30 (m, 1H, Ph), 7.34 (d, *J* = 4.4 Hz, 4H, Ph), 7.84 (s, 1H, 2-H).

$C_{20}H_{24}N_2O_4$ (356.4) Calcd. C 67.40 H 6.79 N 7.86
Found C 67.04 H 7.13 N 7.56
Mol. mass 356 (MS)

Methyl (±)-3-Oxo-3-[4,5,6,7-tetrahydro-4-(2-hydroxyethyl)pyrazolo[1,5-a]pyridin-3-yl]propionate (**12b**): A mixture of 420 mg (1.17 mmol) of **12a** and 1 g of Pd/C (10%) in 20 ml of acetic acid was allowed to react for 1 h and worked up as described for **11f** to give 225 mg (73%) of **12b** as a colorless solid, m.p. 93°C. – IR (KBr): $\tilde{\nu}$ = 3345 cm^{-1}, 2950, 2885, 1735, 1670. – ^1H NMR ($CDCl_3$): δ = 1.71–2.16 (m, 6H, 5-H_2, 6-H_2, CH_2CH$_2$OH), 2.95 (s, 1H, OH), 3.72 (m, 3H, 4-H, CH_2OH), 3.74 (s, 3H, OCH_3), 3.81 (s, 2H, CH_2CO_2), 3.99–4.06 (m, 1H, 7-H_{ax}), 4.27–4.32 (m, 1H, 7-H_{eq}), 7.88 (s, 1H, 2-H).

$C_{13}H_{18}N_2O_4$ (266.3) Calcd. C 58.63 H 6.81 N 10.52
Found C 58.48 H 6.91 N 10.25
Mol. mass 266 (MS)

Methyl (±)-3-Oxo-3-{4,5,6,7-tetrahydro-4-[2-(mesyloxy)ethyl]-pyrazolo[1,5-a]pyridin-3-yl}propionate (**12c**): To a solution of 225 mg (0.84 mmol) of **12b** in 10 ml of THF were added 121 mg (1.2 mmol) of triethylamine and 114 mg (1 mmol) of methanesulfonyl chloride. After stirring at room temp. for 2 h, the mixture was evaporated and the residue purified by flash chromatography (CH_2Cl_2/CH_3OH, 95:5) to give 275 mg (95%) of **12c** as a colorless oil. – IR (NaCl): $\tilde{\nu}$ = 2950 cm^{-1}, 2860, 1740, 1660, 1350, 1170. – ^1H NMR ($CDCl_3$): δ = 1.73–2.27 (m, 6H, 5-H_2, 6-H_2, CH_2CH$_2$O), 3.06 (s, 3H, CH_3SO_3), 3.54–3.58 (m, 1H, 4-H), 3.74 (s, 3H, CO_2CH_3), 3.79 (s, 2H, CH_2CO_2), 4.00–4.09 (m, 1H, 7-H_{ax}), 4.26–4.33 (m, 1H, 7-H_{eq}), 4.37–4.46 (m, 2H, OCH_2), 7.86 (s, 1H, 2-H).

$C_{14}H_{20}N_2O_6S$ (344.4) Calcd. C 48.83 H 5.85 N 8.13
Found C 48.39 H 5.71 N 8.13
Mol. mass 344 (MS)

(±)-3-Acetyl-4-[2-(benzyloxy)ethyl]-4,5,6,7-tetrahydropyrazolo-[1,5-a]pyridine (**12e**): A solution of 800 mg (2.25 mmol) of **12a** in 15 ml of dioxane and 15 ml of 1 N NaOH was stirred at room temp. for 3 h. Then the solution was extracted with ether. The aqueous layer was acidified to pH = 2 with concd. HCl and subsequently extracted with ether. Finally, the organic layer (a solution of **12d**) was stirred at room temp. for 24 h to give 580 mg (86%) of **12e** as a colorless oil after drying ($MgSO_4$), evaporation, and flash chromatography (petroleum ether/ethyl acetate, 1:1). – IR (NaCl: $\tilde{\nu}$ = 3030 cm^{-1}, 2950, 2865, 1660. – ^1H NMR ($CDCl_3$): δ = 1.69–1.81 and 1.90–2.18 (2 m, 6H, CH_2CH$_2$OBzl, 5-H_2 and 6-H_2), 2.42 (s, 3H, $COCH_3$), 3.55–3.56 (m, 1H, 4-H), 3.63–3.72 (m, 2H, CH_2OBzl), 3.97–4.04 (m, 1H, 7-H_{ax}), 4.25–4.28 (m, 1H, 7-H_{eq}), 4.51 (d, *J* = 11.7 Hz, 1H, CH_2Ph), 4.59 (d, *J* = 11.7 Hz, 1H, CH_2Ph), 7.27–7.43 (m, 5H, Ph), 7.86 (s, 1H, 2-H).

$C_{18}H_{22}N_2O_2$ (298.4) Calcd. C 72.46 H 7.43 N 9.39
Found C 72.42 H 7.43 N 9.37
Mol. mass 298 (MS)

(±)-3-Acetyl-4,5,6,7-tetrahydro-4-(2-hydroxyethyl)pyrazolo-[1,5-a]pyridine (**12f**): A mixture of 470 mg (1.58 mmol) of **12e** and 100 mg of Pd/C (10%) in 20 ml of acetic acid was stirred at room temp. for 2 h under a balloon of H_2. Then it was filtered (Celite® AFA), and the filtrate was evaporated. The residue was purified by flash chromatography (petroleum ether/ethyl acetate, 2:8) to afford 290 mg (88%) of **12f** as a colorless solid, m.p. 72°C. – IR (KBr): $\tilde{\nu}$ = 3390 cm^{-1}, 2950, 2870, 1655. – ^1H NMR ($CDCl_3$): δ = 1.73–2.20 (m, 6H, 5-H_2, 6-H_2 and CH_2CH$_2$OH), 2.45 (s, 3H, $COCH_3$), 3.38 (dd, *J* = 6.1/5.8 Hz, 1H, OCH_2), 3.66–3.73 (m, 2H, 4-H OCH_2), 4.01 (ddd, *J* = 13.2/11.8/5.9 Hz, 1H, 7-H_{ax}), 4.31 (ddd, *J* = 13.2/5.8, 1.5 Hz, 1H, 7-H_{eq}), 7.88 (s, 1H, 2-H).

$C_{11}H_{16}N_2O_2$ (208.3) Calcd. C 63.44 H 7.74 N 13.45
Found C 63.45 H 7.94 N 13.40
Mol. mass 208 (MS)

(±)-3-Acetyl-4,5,6,7-tetrahydro-4-[2-(mesyloxy)ethyl]pyrazolo-[1,5-a]pyridine (**12g**): To a solution of 190 mg (0.91 mmol) of **12f** in 20 ml of THF were added 0.153 ml (1.1 mmol) of triethylamine and 0.086 ml (1.1 mmol) of methanesulfonyl chloride. After stirring at room temp. for 1 h, the mixture was evaporated. The residue was purified by flash chromatography (CH_2Cl_2/CH_3OH, 95:5) to give 230 mg (88%) of **12g** as a colorless oil. – IR (NaCl): $\tilde{\nu}$ =

3010 cm^{-1}, 2940, 2860, 1655, 1350, 1170. – ^1H NMR ($CDCl_3$): δ = 1.86–2.17 (m, 5H, 5-H_2, 6-H_2, CH_2CH_2O), 2.22–2.29 (m, 1H, CH_2CH_2O), 2.43 (s, 3H, $COCH_3$), 3.08 (s, 3H, CH_3SO_3), 3.55–3.59 (m, 1H, 4-H), 4.03 (ddd, J = 13.2/11/5.1 Hz, 1H, 7-H_{ax}), 4.29 (ddd, J = 13.2/5.1/2.5 Hz, 1H, 7-H_{eq}), 4.38–4.49 (m, 2H, CH_2O), 7.86 (s, 1H, 2-H).

$C_{12}H_{18}N_2O_4S$ (286.4) Calcd. C 50.33 H 6.34 N 9.78
Found C 50.28 H 6.29 N 9.79
Mol. mass 286 (MS)

Methyl (Z)-(±)-(5a,6,7,8-Tetrahydro-3H,5H-4-oxa-1,8a-diaza-acenaphthylen-3-ylidene)acetate (**13a**): A solution of 45 mg (0.12 mmol) of **7a** in 10 ml of THF was added to 5 mg (0.21 mmol) of NaH. The suspension was stirred at room temp. for 1 h and worked up as described for **10b** to give 21 mg (72%) of **13a** as a colorless solid, m.p. 187°C, – IR (KBr): ν̃ = 3080 cm^{-1}, 2940, 2870, 1695, 1625. – ^1H NMR ($CDCl_3$): δ = 1.23 (dddd, J = 13.2/12.3/12/3 Hz, 1H, 6-H_{ax}), 2.04–2.22 (m, 2H, 7-H_2), 2.29–2.34 (m, 1H, 6-H_{eq}), 3.18–3.26 (m, 1H, 5a-H), 3.66 (dd, J = 11.7/11 Hz, 1H, 5-H_{ax}), 3.70 (s, 3H, OCH_3), 3.94 (ddd, J = 13/12.5/5 Hz, 1H, 8-H_{ax}), 4.34 (dd, J = 12.5/5.8 Hz, 1H, 8-H_{eq}), 4.61 (dd, J = 11/5.5 Hz, 1H, 5-H_{eq}), 5.25 (s, 1H, $CHCO_2$), 7.64 (s, 1H, 2-H).

$C_{12}H_{14}N_2O_3$ (234.3) Calcd. C 61.53 H 6.02 N 11.96
Found C 61.87 H 5.90 N 11.74
Mol. mass 234 (MS)

Methyl (E)-(±)-(5a,6,7,8-Tetrahydro-3H,5H-4-oxa-1,8a-diaza-acenaphthylen-3-ylidene)acetate (**13b**): A solution of 20 mg of **13a** in 2 ml of xylene was stirred at 120°C for 3 h. The solvent was evaporated and the residue separated by flash chromatography (petroleum ether/ethyl acetate, 3:7) to give 14 mg (74%) of **13b** as a colorless solid (m.p. 124°C) followed by 5 mg (26%) of **13a**. – IR (KBr): ν̃ = 2940 cm^{-1}, 2860, 1695, 1615. – ^1H NMR ($CDCl_3$): δ = 1.25 (dddd, J = 13.2/12.3/12/3 Hz, 1H, 6-H_{ax}), 2.05–2.21 (m, 2H, 7-H_2), 2.28–2.32 (m, 1H, 6-H_{eq}), 3.15–3.23 (m, 1H, 5a-H), 3.53 (dd, J = 12.5/10.2 Hz, 1H, 5-H_{ax}), 3.72 (s, 3H, OCH_3), 3.94 (ddd, J = 12.5/12.5/5.1 Hz, 1H, 8-H_{ax}), 4.33–4.38 (m, 2H, 5-H_{eq}, 8-H_{eq}), 5.37 (s, 1H, $CHCO_2$), 8.64 (s, 1H, 2-H).

$C_{12}H_{14}N_2O_3$ (234.3) Calcd. C 61.53 H 6.02 N 11.96
Found C 61.32 H 6.01 N 12.01
Mol. mass 234 (MS)

Methyl 3-Oxo-3-(4,5,6,7-tetrahydro-4-methylenepyrazolo[1,5-a]-pyridin-3-yl)propionate (**14**): A solution of 20 mg (0.06 mmol) of **7a** and 0.2 ml (1.4 mmol) of triethylamine in 5 ml of THF was stirred at room temp. for 18 h. After addition of 3 ml of satd. aqueous $NaHCO_3$ solution and ether the organic layer was dried ($MgSO_4$), evaporated and the residue purified by flash chromatography (petroleum ether/ethyl acetate, 1:1) to give 10 mg (77%) of **14** as a colorless oil. – IR (NaCl): ν̃ = 3120 cm^{-1}, 2950, 2840, 1735, 1670. – ^1H NMR ($CDCl_3$): δ = 2.08–2.14 (m, 2H, 6-H_2), 2.60–2.63 (m, 2H, 5-H_2), 3.75 (s, 3H, OCH_3), 3.87 (s, 2H, CH_2CO_2), 4.26 (t, J = 6.2 Hz, 2H, 7-H_2), 5.50 (d, J = 1.2 Hz, 1H, CH_2 olefinic), 6.93 (d, J = 0.9 Hz, 1H, CH_2 olefinic), 7.92 (s, 1H, 2-H).

$C_{12}H_{14}N_2O_3$ (234.3) Calcd. C 61.53 H 6.02 N 11.96
Found C 61.49 H 6.27 N 11.85
Mol. mass 234 (MS)

Methyl (±)-(4,5,5a,6,7,9-Hexahydro-3H-8-oxa-2,2a-diazabenzo-[cd]azulene-9-ylidene)acetate (**15**): For preparation see **9b**. – IR (KBr): ν̃ = 3120 cm^{-1}, 2950, 2860, 1700, 1595. – ^1H NMR ($CDCl_3$): δ = 1.55 (br. q, J = 10.5 Hz, 1H, 5-H_{ax}), 1.72 (dddd, J = 14.7/8.8/3.7/2.9 Hz, 1H, 6-H_{ax}), 1.94–2.03 (m, 1H, 4-H_a), 2.10–2.19 (m, 2H, 5-H_{eq}, 4-H_b), 2.53–2.62 (m, 1H, 6-H_{eq}), 3.13–3.21 (m, 1H, 5a-H), 3.69 (s, 3H, OCH_3), 4.05 (ddd, J = 12.5/11/4.4 Hz, 1H, 3-H_{ax}), 4.21–4.35 (m, 3H, 7-H_2, 3-H_{eq}), 5.30 (s, 1H, $CHCO_2$), 7.64 (s, 1H, 1-H). – ^{13}C NMR ($CDCl_3$): δ = 22.5 (C-4), 28.0 (C-5), 31.9 (C-5a), 34.8 (C-3), 47.8 (C-9), 50.7 (CH_3), 69.4 (C-7), 93.3 ($CHCO_2$), 113.0 (C-9a), 137.9 (C-1), 1410 (C-2b),163.0 (C-9), 166.0 (CO_2).

$C_{13}H_{16}N_2O_3$ (248.3) Calcd. C 62.89 H 6.50 N 11.28
Found C 62.82 H 6.58 N 11.02
Mol. mass 248 (MS)

3-Acetyl-4,5,6,7-tetrahydro-4-methylenepyrazolo[1,5-a]pyridine (**16**): To a solution of 30 mg (0.1 mmol) of **8a** in 5 ml of THF was added dropwise 0.3 ml of freshly prepared LDA (0.32 M in THF) at –78°C. The reaction mixture was warmed up to –20°C and then stirred at this temp. for 10 min. Then 20 ml of a satd. aqueous solution of $NaHCO_3$ was added, and the mixture was extracted with ether. The organic layer was dried ($MgSO_4$), evaporated, and the residue was purified by flash chromatography (petroleum ether/ethyl acetate, 1:1) to give 9 mg (51%) of **16** as a colorless solid, m.p. 62°C. – IR (KBr): ν̃ = 3100 cm^{-1}, 2955, 1660. – ^1H NMR ($CDCl_3$): δ = 2.07–2.13 (m, 2H, 6-H_2), 2.51 (s, 3H, $COCH_3$), 2.59–2.62 (m, 2H, 5-H_2), 4.26 (t, J = 6.2 Hz, 2H, 7-H_2), 5.46 (dd, J = 2.8/1.3 Hz, 1H, CH_2 olefinic), 6.93 (d, J = 1.3 Hz, 1H, CH_2 olefinic), 7.93 (s, 1H, 2-H).

$C_{10}H_{12}N_2O$ (176.2) Calcd. C 68.16 H 6.86 N 15.90
Found C 68.38 H 6.83 N 15.99
Mol. mass 176 (MS)

Dimethyl 4,5,6,7-Tetrahydro-3-[(methoxycarbonyl)acetyl]pyrazolo[1,5-a]pyridine-4,4-dicarboxylate (**17**): To a solution of 2.4 ml (17.1 mmol) of diisopropylamine in 40 ml of THF was added 9.4 ml (15 mmol) of *n*BuLi (1.6 M in hexane) at –78°C. The mixture was allowed to warm up to 0°C. After 30 min, it was added to a solution of 1110 mg (5 mmol) of **5** in 70 ml of THF at –78°C. After 0.5 h, the temp. was raised to –20°C, and stirring was continued for further 45 min. Subsequently, 0.847 ml (12.5 mmol) of methyl chloroformate was added dropwise. Finally, stirring for 10 min, addition of 20 ml of satd. aqueous $NaHCO_3$ solution, extraction with ether, drying ($MgSO_4$), evaporation, and purification by flash chromatography (petroleum ether/ethyl acetate, 65:35) gave 830 mg (49%) of **17** as a colorless solid (m.p. 115°C) besides 300 mg of recovered **5**. – IR (KBr): ν̃ = 2950 cm^{-1}, 1735, 1675. – ^1H NMR ($CDCl_3$): δ = 2.04–2.10 (m, 2H, 6-H_2), 2.49–2.52 (m, 2H, 5-H_2), 3.72 (s, 3H, CO_2CH_3), 3.74 (s, 6H, 2 x CO_2CH_3), 3.77 (s, 2H, CH_2CO_2),4.24 (t, J = 5.8 Hz, 2H, 7-H_2), 7.94 (s, 1H, 2-H).

$C_{15}H_{18}N_2O_7$ (338.3) Calcd. C 53.25 H 5.36 N 8.28
Found C 53.37 H 5.39 N 8.30
Mol. mass 338 (MS)

Dimethyl (±)-(4,5,5a,6,7,8-Hexahydro-3,5-dioxo-3H-pyrazolo[4,5,1-ij]quinoline-4,5a-dicarboxylate (**18**) *and Methyl 7,8-Dihydro-3,5-dihydroxy-6H-pyrazolo[4,5,1-ij]quinoline-4-carboxylate* (**19**): To a solution of 147 mg (0.44 mmol) of **17** in 10 ml of methanol was added 0.88 ml (0.44 mmol) of sodium methoxide (0.5 M solution in methanol). The reaction mixture was stirred at room temp. for 18 h. After addition of 5 ml of satd. aqueous $NaHCO_3$ solution the solution was extracted with ether, the organic layer dried ($MgSO_4$) and evaporated. Purification of the residue by flash chromatography gave 26 mg (24%) of **19** as a colorless solid (m.p. 119°C) followed by 37 mg (28%) of **18**.

18: IR (NaCl): ν̃ = 2950 cm^{-1}, 2860, 1740, 1735, 1715, 1695. – ^1H NMR ($CDCl_3$): δ = 2.01–2.25 (m, 4H, 6-H_2, 7-H_2), 3.74 (s, 3H, OCH_3), 3.78 (s, 3H, OCH_3), 4.07–4.14 (m, 1H, 8-H_{ax}), 4,26–4.31 (m, 1H, 8-H_{eq}), 4.27 (s, 1H, 4-H), 7.90 (s. 1H, 2-H).

$C_{14}H_{14}N_2O_6$ (306.3) Calcd. C 54.90 H 4.61 N 9.15
Found C 55.06 H 4.59 N 9.17
Mol. mass 306 (MS)

19: IR (KBr): $\tilde{\nu}$ = 3390 cm^{-1}, 2950, 2850, 1650. – ^1H NMR ($CDCl_3$): δ = 2.23 (quint, J = 6 Hz, 2H, 7-H_2), 2.83 (t, J = 6 Hz, 2H, 6-H_2), 4.09 (s, 3H, CO_2CH_3), 4.27 (t, J = 5.6 Hz, 2H, 8-H_2), 7.98 (s, 1H, 2-H).

$C_{12}H_{12}N_2O_4$ (248.2) Calcd. C 58.06 H 4.87 N 11.28
Found C 57.93 H 4.85 N 11.14
Mol. mass 248 (MS)

CAS Registry Numbers

5: 132255-60-8 / **7a**: 134706-47-1 / **7b**: 134706-48-2 / **8a**: 134706-49-3 / **8b**: 134706-50-6 / *cis*-**9b**: 134706-51-7 / *trans*-**9b**: 134706-52-8 / **10b**: 134706-53-9 / **11a**: 132255-62-0 / **11b**: 132255-63-1 / **11c**: 134706-54-0 / **11d**: 134706-55-1 / **11e**: 134706-56-2 / **11f**: 134706-57-3 / **11g**: 134706-58-4 / **12a**: 134706-59-5 / **12b**: 134706-60-8 / **12c**: 134706-61-9 / **12d**: 134706-62-0 / **12e**: 134706-63-1 / **12f**: 134706-64-2 / **12g**: 134706-65-3 / **13a**: 134706-66-4 / **13b**: 134706-67-5 / **14**: 134706-68-6 / **15**: 134706-69-7 / **16**: 134706-70-0 / **17**: 134706-71-1 / **18**: 134706-72-2 / **19**: 134706-73-3

[1] For review, see: A. S. Horn in *Comprehensive Medicinal Chemistry* (C. Hansch, P. G. Sammes, J. B. Taylor, Eds.), Pergamon Press, Oxford 1990.
[2] P. Gmeiner, H. Lerche, *Heterocycles* **31** (1990) 9.
[3] P. Gmeiner, J. Sommer, *Arch. Pharm. (Weinheim, Ger.)* **323** (1990) 991.
[4] Publication in preparation.
[5] For syntheses of *peri*-fused pyrazolopyridines, see: Y. Miki, N. Nishikobu, H. Kinoshita, S. Takemura, *Heterocycles* **22** (1984) 2467: G. Baum, A. Fridrichs, A. Kümmell, W. Massa, G. Seitz, *Chem. Ber.* **121** (1988) 411; Y. Miki, M. Uragi, S. Takemura, *J. Chem. Soc., Perkin Trans. 1*, **1985**, 379; Y. Miki, O. Tomii, M. Utsunomiya, S. Takemura, M. Ikeda, *Chem. Pharm. Bull.* **34** (1986) 3588; Nissan Chemical Industries, Ltd. (N. Tanaka, E. Oya, M. Baba, Inv.), Eur. Pat. Appl. EP 344,775 (December 6, 1982) [*Chem. Abstr.* **112** (1990) P 216923g]; Duphar International Research B. V. (I. Van Wijngaarden, D. Hamminga, H. H. Haeck, W. Wouters, Inv.), Eur. Pat. Appl. EP 350,130 (January 10, 1990) [*Chem Abstr.* **113** (1990) P 40668g].
[6] P. Gmeiner, J. Schünemann, *Arch. Pharm. (Weinheim, Ger.)* **321** (1988) 517.
[7] J. E. Baldwin, M. J. Lusch, *Tetrahedron* **38** (1982) 2939.
[8] J. E. Baldwin, L. I. Kruse, *J. Chem. Soc., Chem. Commun.* **1977**, 233.
[9] E. C. Taylor, G. H. Hawks, A. Mc Killop, *J. Am. Chem. Soc.* **90** (1968) 2421.
[10] J. H. Clark, J. M. Miller, *J. Chem. Soc., Perkin Trans. 1*, **1977**, 1743.
[11] S. M. Ludemann, D. L. Bartlett, G. Zon, *J. Org. Chem.* **44** (1979) 1163.

[85/91]