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Halogen dance in pyrazole 1-oxides: synthesis of pyrazolo[3,4-*c*]quinoline 1-oxides

Jørgen Eskildsen,[a] Niels Østergaard,[a,b] Per Vedsø[a,†] and Mikael Begtrup[a,*]

[a]*Department of Medicinal Chemistry, The Royal Danish School of Pharmacy, Universitetsparken 2, DK-2100 Copenhagen, Denmark*
[b]*ACADIA Pharmaceuticals A/S, Fabriksparken 58, DK-2600 Glostrup, Denmark*

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Abstract—The synthesis of a new series of 3-substituted pyrazolo[3,4-*c*]quinoline 1-oxides is presented. Regioselective bromine–magnesium exchange of 2-benzylated 3,4,5-tribromopyrazole 1-oxides and subsequent halogen dance of the resulting monometalated intermediates was used to synthesize fused pyrazoloquinoline 1-oxides.

1. Introduction

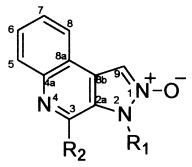
Recent reports have shown that pyrazolo[3,4-*c*]quinoline ring systems display significant biological activities, such as good affinity and selectivity for adenosine A3 receptors,[1a,b] benzodiazepine receptor activity,[1c,d] and NMDA receptor inhibition.[1e]

In these ring systems, the pyrazole moiety is typically constructed at a late stage in the sequence making the synthetic route lengthy and non-flexible. For example rearrangement of phenylhydrazones of 3-acylindoles,[1f] thermal cyclization of 4-diazomethylquinolinones,[1h] addition of diazomethane to cinnamates followed by reduction and condensation,[1g] and especially hydrazine condensations[1b,d,e] have afforded pyrazolo[3,4-*c*]quinoline ring systems. In order to make the synthesis more flexible, a methodology based on diversification at a late stage of the pyrazoloquinoline ring system synthesis would be desirable.

The introduction of substituents at the 4-position of 1-benzyloxypyrazole via iodination followed by magnesium iodine exchange[2] and at C-5 via directed *ortho* metalation has previously been reported.[3,4] These methods were extended to furnish quinoline- and iso-quinoline-1-alkoxypyrazoles fused across the C-4–C-5 bond of the 1-benzyloxypyrazole moiety.[5,6] These methodologies, however, failed to provide access to pyrazoloquinolines or isoquinolines fused across the C-3–C-4 bond, since direct metalation at the 3-position of 1-alkylpyrazoles is hampered by the adjacent lone pair effect.[7,8]

Recently, we reported the access to the 3-position in *N*-1 oxidized pyrazoles via regioselective mono bromination of 2-alkylpyrazole 1-oxides.[9] Subsequent bromine–magnesium exchange with *i*-PrMgCl at −78°C afforded C-3 magnesiated pyrazole 1-oxides which could be either acylated upon addition of an acid chloride[10] or arylated[11] via transmetalation with $ZnCl_2$ and Pd(0) catalyzed cross-coupling to afford C-3 functionalized pyrazole 1-oxides. *N*-debenzylation gave access to C-3 functionalized 1-hydroxypyrazoles.

This prompted us to develop a synthetic methodology for the synthesis of pyrazolo[3,4-*c*]quinoline 1-oxides (**1**, Scheme 1).



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Scheme 1.

2. Results and discussion

Herein, we wish to report the extension of C-3 functionalization of 2-alkylpyrazole 1-oxides to the facile synthesis of 3-substituted 2-benzylpyrazolo[3,4-*c*]quinoline 1-oxides.

2.1. Functionalization of pyrazole 1-oxide

We speculated that the access to the 3-position in pyrazole 1-oxides could be utilized to prepare pyrazoloquinoline 1-oxides fused across the C-3–C-4 bond (**1**) of the starting pyrazole 1-oxide as outlined in Scheme 2.

Keywords: pyrazole 1-oxides; metalation; halogen dance; pyrazolo[3,4-*c*]quinolines.

* Corresponding author. Tel.: +45-35-30-60-00; fax: +45-35-30-60-40; e-mail: mb@dfh.dk

† Present address: Novo Nordisk A/S, Medicinal Chemistry Research, DK-2760 Måløv, Denmark.

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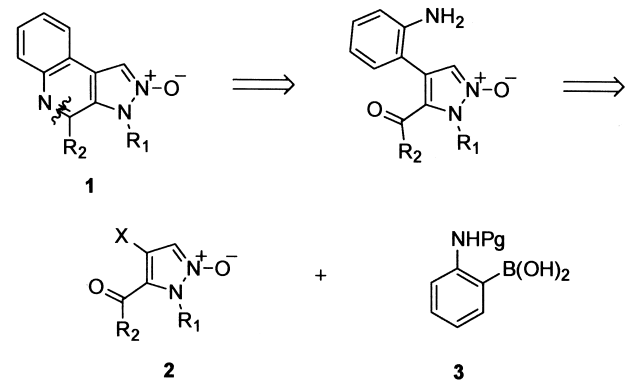
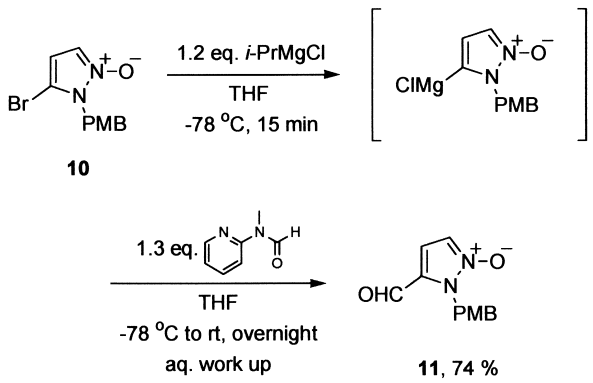


Scheme 2. Retrosynthetical analysis.

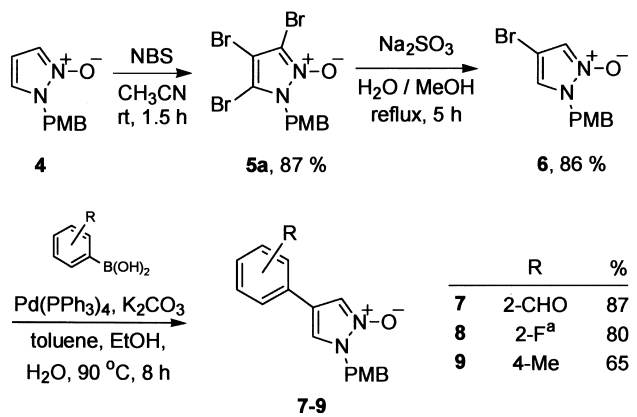


Scheme 4. Synthesis of 3-formyl-2-PMB-pyrazole 1-oxide **11**.

This strategy would require a 3-formyl- or acyl 4-halopyrazole 1-oxide of type **2** and a suitably protected *ortho* amino phenylboronic acid building block **3**.[12] Thus two issues had to be addressed with respect to **2** and later combined: (1) introduction of aryl groups at C-4 and (2) introduction of formyl- and acyl-groups at C-3.

2.1.1. Synthesis of 4-arylated 2-(4-methoxybenzyl)pyrazole 1-oxides. 2-PMB‡-pyrazole 1-oxide[11] (**4**) was readily tribrominated using NBS in acetonitrile[13] affording the tribrominated pyrazole 1-oxide **5a** in 87% yield. Subsequent treatment with aqueous Na_2SO_3[14] caused ready debromination at C-3 and C-5 whereas the C-4 bromine was totally inert towards reduction during these conditions.

While iodine magnesium exchange provided a route for C–C bond formation at C-4 in 4-iodo-1-benzyloxypyrazoles[2] attempted bromine–magnesium exchange in compound **6** was unsuccessful, since treatment of **6** with 1.2 equiv. *i*-PrMgCl in THF at 0°C for 1 h resulted in C-5 deprotonation. Subsequent quenching with MeOD produced 4-bromo-5-deutero-2-PMB-pyrazole 1-oxide in quantitative yield. Instead, C-4 arylation[16] was accomplished by treatment of **6** with aryl boronic acids under classical Suzuki–Miyaura[17] conditions (Scheme 3).



	R	%
7	2-CHO	87
8	2-F[a]	80
9	4-Me	65

Scheme 3. Synthesis of 4-aryl-2-PMB-pyrazole 1-oxides via 4-bromo-2-PMB-pyrazole 1-oxide (**6**). (a) The neopentylglycol ester of 2-fluoro benzeneboronic acid[15] was used.

‡ 4-Methoxybenzyl.

2.1.2. Synthesis of 3-formyl-2-(4-methoxybenzyl)pyrazole 1-oxide. The 3-magnesiated intermediate formed by bromine–magnesium exchange in 3-bromo-2-PMB-pyrazole 1-oxide (**10**)[11] reacted sluggishly with DMF giving complex mixtures. However, *N*-methyl-*N*-(2-pyridyl)formamide (Meyers formylating agent)[18] smoothly produced the formylated 1-oxide **11** (Scheme 4) which was slightly unstable on silica thus reducing the isolated yield of analytically pure material to 74%.

In general, the 3-acylated pyrazole 1-oxides were easily de-*para*-methoxybenzylated upon treatment with acids at rt.[10]

A combination of the two basic protocols thus established was anticipated to provide access to building blocks of type **2**. However, attempts to brominate **11** with NBS in CH_3CN or with bromine in $CHCl_3$ failed. Therefore, an alternative approach to **2** using **5a** as precursor was investigated.

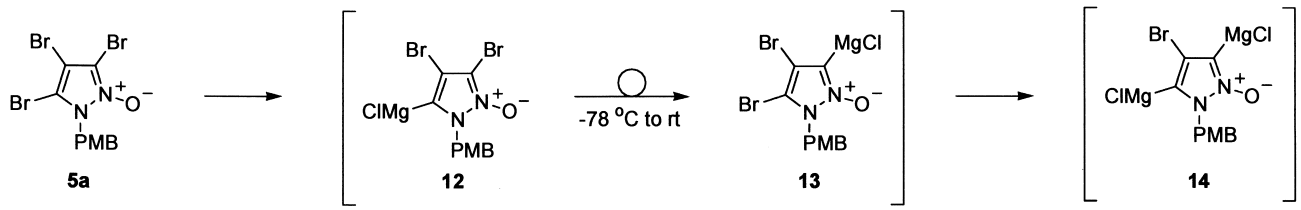
2.2. Halogen dance in pyrazole 1-oxides

An intriguing selectivity was observed when the bromine–magnesium exchange reactions were performed with the tribrominated pyrazole **5a** at different temperatures (Table 1).

Compound **5a** first underwent bromine–magnesium exchange at C-3 (Table 1, entry 1) to give **12** despite that exchange at C-5 would give a less basic, thermodynamically favored **13**[19] and despite that C-3 is more congested than C-5. This regioselectivity may be due to the low solubility of **12** which precipitated at −78°C. By heating to rt, compound **12** was converted to **13**, stable at rt and readily soluble in THF even at −78°C. The halogen dance[21,22] **12→13** may involve remaining tribromo compound **5a**. It entails halogen–metal exchange and is thus distinct from most reported halogen dance reactions which involve proton–metal exchange.[23a–c]

Treatment of **5a** with 2.1 equiv. *i*-PrMgCl afforded the 3,5-dimagnesio pyrazole dianion intermediate **14**, a white solid stable in THF at rt.[24] The 3-position of this dimagnesio complex reacted more rapidly with electrophiles like Me_2S_2 to give **15** in 60% isolated yield[25] along with **16** and **6**. The formation of **16** is probably the result of higher solubility of the 3-methylsulfanyl 5-magnesio intermediate. This approach provides a route for 3,5-disubstituted

Table 1. Halogen dance in pyrazole 1-oxides. The distribution of **5a**, **12**–**14** was determined by ^{1}H NMR of aliquots quenched with HCl in diethyl ether



Entry	*T* (°C)	*i*-PrMgCl (equiv.)	*T* (min)	**5a**	**12**[a]	**13**	**14**
1	−78	1.1	10	–	71	21	8
2	−78–rt	1.2	At rt[b]	–	–	88	12
3	Rt	1.0	10	3	2	89	6
4	Rt	1.0	5[c]	–	–	100	–
5	Rt	2.1	10	–	–	–	100

[a] A 2% NOE was observed between the CH_2 on PMB and H-3 on pyrazole after quenching.
[b] Quenched with MeOH.
[c] Quenched with excess TMS-Cl.[20]

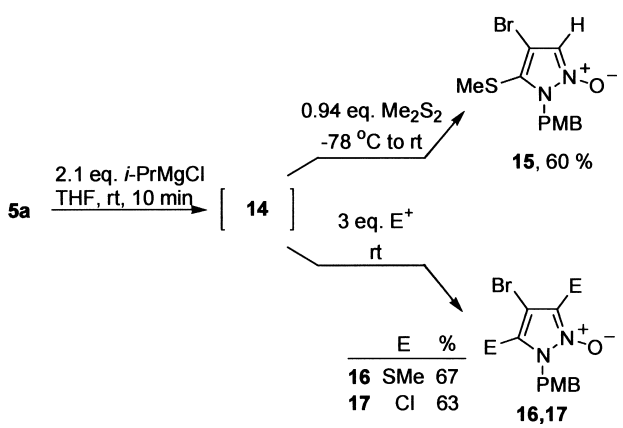
pyrazole 1-oxides exemplified by the syntheses of **16** and **17** (Scheme 5).

2.3. 4-Bromo-3-formylpyrazole 1-oxides

In order to access the desired pyrazole 1-oxides such as **2**, the halogen dance sequence observed when reacting **5a** with 1 equiv. of *i*-PrMgCl in THF (Table 1, entry 4) was exploited to in situ protect the 5-position with a trimethylsilyl group. A subsequent bromine–magnesium exchange at C-3 followed by reaction with Meyers formylating reagent gave 4-bromo-3-formyl-2-PMB-pyrazole 1-oxide (**19a**) in one pot from **5a** (Scheme 6).

The 5-TMS protected intermediates were not purified, as the only byproduct was $MgCl_2(2THF)$.[20] Aqueous work-up followed by treatment with K_2CO_3 in MeOH–water smoothly removed the TMS group. In contrast, the use of TBAF resulted in lower isolated yields.

Unfortunately, the 3-formylated pyrazole 1-oxide **19a** was unstable during the work-up conditions, especially towards silica, hence the lower isolated yield. Performing the halogen dance sequence using 3,4,5-tribromo-2-benzylpyrazole 1-oxide (**5b**)[14] instead did not improve the stability.



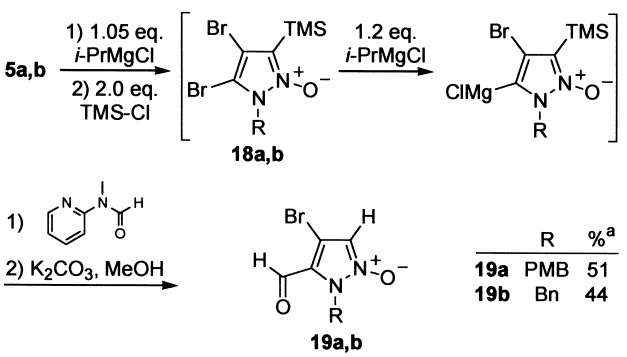
Scheme 5. Reaction of intermediate **14** with electrophiles.

2.3.1. 3-Acylated 4-bromopyrazole 1-oxides.

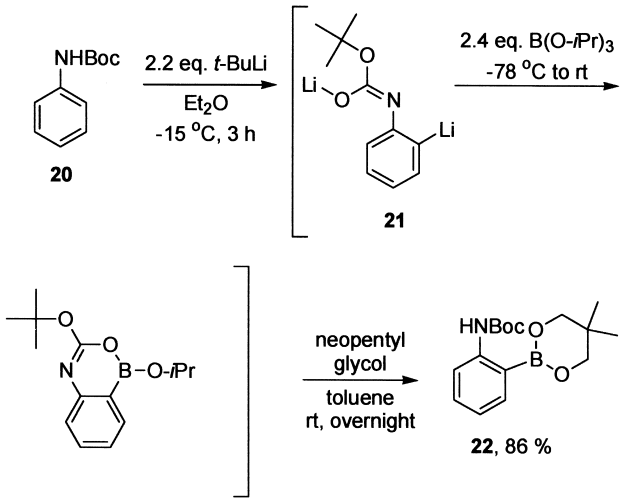
Direct addition of acid chlorides at −78°C to 3-magnesio pyrazole 1-oxide successfully gave rise to 3-acylated pyrazole 1-oxides.[10] Therefore, the same sequence as for the synthesis of 3-formylated pyrazole 1-oxides of type **2** was adopted to access 3-acylated derivatives. However, initial tests following the sequence outlined in Scheme 6 replacing Meyers reagent with an acid chloride gave low yields, when tribromide **5a** was used. This may be due to readily de-*para*-methoxybenzylation of 3-acylated 4-bromo-2-PMB-pyrazole 1-oxide, as substantial amounts of *p*-anisaldehyde were formed. The 3-acylated 2-benzylpyrazole 1-oxides, synthesized from **5b**, were less sensitive than the corresponding 2-PMB compounds. The NMR yield was at least 70% depending on which acid chloride was used. Unfortunately, these compounds were unstable on silica gel, as was the case for the formylated compounds **19a**,**b**. Therefore, the crude 3-acylated 2-benzyl-4-bromopyrazole 1-oxides were used directly in the synthesis of pyrazolo[3,4,-*c*]quinoline 1-oxides.

2.4. *ortho*-Aminophenylboronic acid building block 3

N-Boc-2-aminophenylboronic acids have previously been prepared in moderate yields as pinacol boronates by Pd catalyzed borylation of 2-halo *N*-Boc-aniline[26] or by



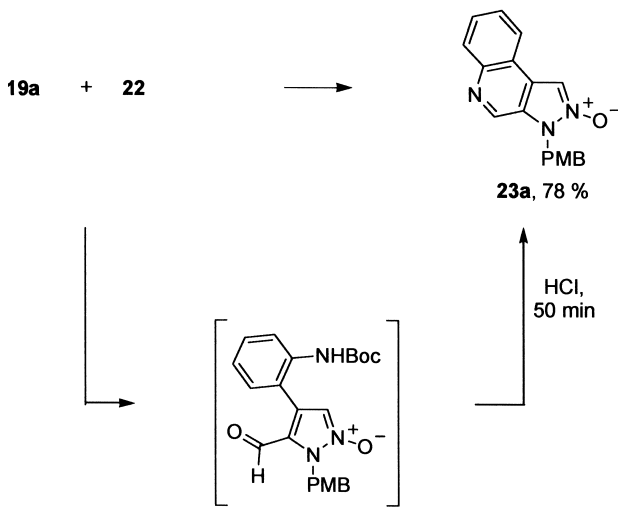
Scheme 6. Synthesis of 4-bromo-3-formylpyrazole 1-oxides via halogen dance in tribrominated pyrazole 1-oxides **5a** or **5b**. (a) Isolated yield based starting tribromides **5a** or **5b**.



Scheme 7. Synthesis of [2-(5,5-dimethyl-[1,3,2]dioxaborinan-2-yl)-phenyl]carbamic acid *tert*-butyl ester (**22**).

stepwise double lithiation/bromine–lithium exchange of 2-bromo-*N*-Boc-aniline.[27] In a different study, Stanetty et al. studied directed *ortho* lithiation of *N*-Boc-aniline (**20**) to dilithio intermediates.[28] Using this methodology, we developed a facile synthetic route to multigram quantities of the *N*-Boc-2-aminophenylboronic acid ester **22** (Scheme 7).

Since *t*-BuLi is significantly more stable in diethyl ether than in THF[29] it was essential to carry out dilithiation of **20** to **21** and the subsequent reaction with $B(O\text{-}i\text{-}Pr)_3$ in diethyl ether. The isolation as the neopentylglycol ester **22** was crucial as well to achieve a close to quantitative yield. Previous procedures by other groups to isolate the free *ortho* boronic acids of the related *N*-pivaloyl-aniline failed to give yields higher than about 60%. This was probably due to inevitable proto-deboronation occurring during the acidic conditions required for boronic ester hydrolysis.[30] The crude boronic acids are likely to form boroxines upon drying and to be contaminated with boronic salts.[27] However, cyclic boronic esters like **22** are stable white solids that are easily recrystallized from heptane. They do not form boroxines and they react readily in ordinary Suzuki–Miyaura cross-coupling reactions.[15]



Scheme 8. Synthesis of 2-PMB-pyrazolo[3,4-*c*]quinoline 1-oxide (**23a**).

2.5. Synthesis of pyrazolo[3,4-*c*]quinoline 1-oxides

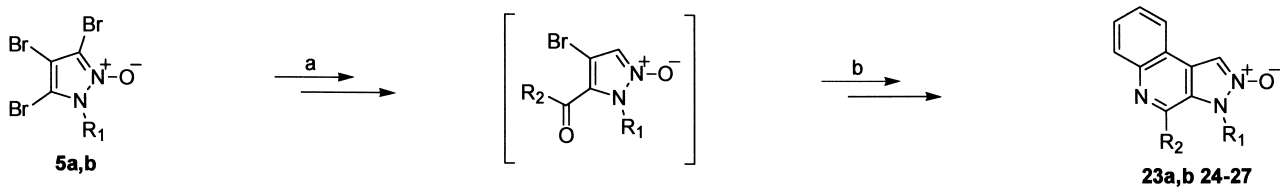
The C–C bond formation to C-4 combined with the introduction of formyl- and acyl groups in pyrazole 1-oxides via the observed halogen dance presented the desired components for the synthesis of pyrazolo[3,4-*c*]quinoline 1-oxides.

2.5.1. Condensation into pyrazolo[3,4-*c*]quinoline 1-oxides. When the crude reaction mixture from the cross-coupling between **19a** and the boronic acid ester **22** was quenched with aqueous HCl condensation into the desired pyrazolo[3,4-*c*]quinoline systems took place (Scheme 8) to give **23a** in 78% isolated yield.

Because of the sensitivity of 3-formyl- and 3-acyl 4-bromopyrazole 1-oxides, the construction of the fused ring systems was conveniently carried out using the crude reaction mixtures from the acylation reactions (Table 2).

Thus the pyrazolo[3,4-*c*]quinoline 1-oxides **23a** and **23b** were obtained in 38 and 40% isolated yield, respectively,

Table 2. Synthesis of pyrazolo[3,4-*c*]quinoline 1-oxides



Entry	R_1	R_2	Conditions	Product	Yield (%)[c]
1	PMB	H	A	**23a**	38
2	Bn	H	A	**23b**	40
3	Bn	Me	A	**24**	48
4	Bn	Et	B	**25**	52
5	Bn	Cyclopropyl	B	**26**	43
6	Bn	Ph	B	**27**	26

(a) (i) 1.05 equiv. *i*-PrMgCl, THF, 0°C, 20 min, then 2.0 equiv. TMS-Cl, 0°C to rt, 1.5 h; (ii) 1.2 equiv. *i*-PrMgCl, THF, 0°C, 15 min, then Meyers reagent or an acid chloride, −78°C to rt; (iii) 2.0 equiv. 2 M K_2CO_3(aq.), MeOH, rt, 10 min. (b) (i) 1.5 equiv. **22**, 0.06 equiv. $Pd(PPh_3)_4$, 3 equiv. 2 M K_2CO_3(aq.), EtOH, toluene, 90°C, 4 h; (ii) Method A: aq. HCl, rt, 50 min, Method B: TFA, DCM, 30 min. (c) Isolated yields over 5 steps based on starting tribromides **5a** or **5b**.

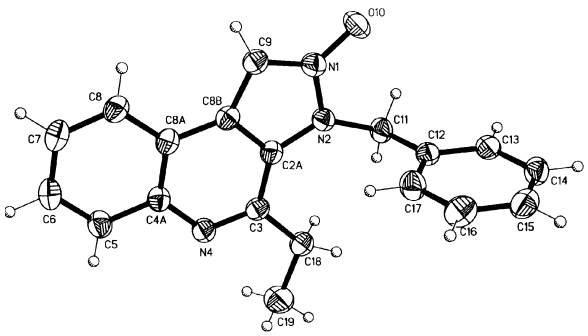


Figure 1. X-Ray structure of **25**.[31]

and the 3-substituted pyrazolo[3,4-*c*]quinoline 1-oxides **24**–**27** were obtained in 26–52% isolated yield over 5 steps (76–88% average). In case of derivative **26**, 4-chlorobutyryl chloride was used in the acylation step.

The entire five-step sequence could be carried out within one working day, providing access to the pyrazolo[3,4-*c*]-quinoline 1-oxide ring systems in a time efficient and flexible approach, in which further ring-functionalizations can be envisaged.

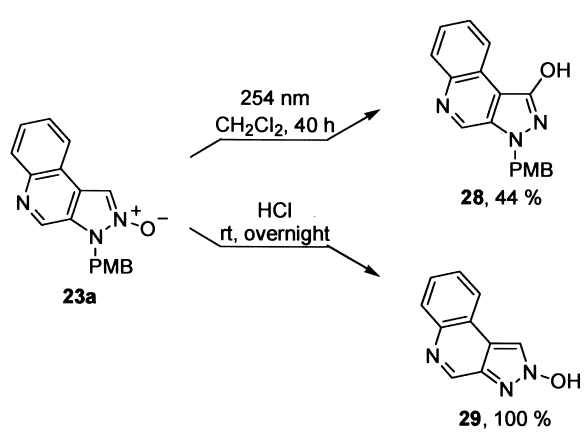
After obtaining suitable crystals of the 3-ethyl derivative **25**, an X-ray structure unambiguously confirmed the structural assignment. In the crystal structure the two ethyl carbons and the benzylic carbon are all in the plane of the planar tricyclic system within the accuracy of the experiment (Fig. 1).

2.6. Derivatization of 23a

The pyrazolo[3,4-*c*]quinoline 1-oxides described above could be further functionalized to produce free *C*- and *N*-hydroxy compounds (Scheme 9). By way of example, exposure of **23a** to light caused rearrangement to the 9-hydroxycompound **28** in 44% isolated yield.[32] Acidic cleavage of the PMB group quantitatively afforded the free *N*-hydroxy compound **29**.

3. Conclusion

A new series of pyrazolo[3,4-*c*]quinoline 1-oxides have been prepared under mild conditions from tribrominated 2-alkylpyrazole 1-oxide via a controlled halogen dance sequence. The approach is flexible and gives access to an array substituted derivatives.



Scheme 9. Further functionalization of **23a**.

4. Experimental

4.1. General

All reactions involving air- or moisture-sensitive reagents were performed under N_2 using syringe-septum cap technique. All glassware was flame-dried prior to use. Flash chromatography (FC) was performed using silica gel Merck 60 (230–400 mesh). Melting points are uncorrected. NMR spectra were recorded on a 300 MHz Varian instrument with TMS as internal standard and were run at 20°C in $CDCl_3$ unless otherwise stated. For clarity, the coupling patterns are reported as they appear (J_{app}). Thus the AA′XX′ coupling pattern observed in e.g. 4-methoxybenzyl groups are reported as $J_{app}=J_{AX}+J_{AX'}$. Solvents and reagents were obtained from Fluka or Aldrich and used without further purification. THF was distilled from Na/benzophenone ketyl under N_2. *i*-PrMgCl was titrated prior to use.[33] $Pd(PPh_3)_4$ was prepared as previously described.[34]

4.1.1. 3,4,5-Tribromo-2-(4-methoxybenzyl)pyrazole 1-oxide (5a). 2-(4-Methoxybenzyl)pyrazole 1-oxide (**4**)[11] (2.11 g, 10.4 mmol) was dissolved in CH_3CN (25 mL). NBS (5.72 g, 31.1 mmol) was added in small portions over 5 min keeping the internal temperature below 40°C. After stirring at rt for 1.5 h, the light orange suspension was poured into water (150 mL), stirred vigorously for 10 min and then filtered. The crystals were washed with cold diethyl ether to obtain white crystals. After drying in a dessicator over P_2O_5 at 1 mbar overnight the title compound was obtained as colorless crystals (3.96 g, 87%): mp 125–126°C; R_f=0.53 (heptane/EtOAc 1:1); ^{1}H NMR δ 3.78 (s, 3H), 5.42 (s, 2H), 6.84 (d, J_{app}=8.4 Hz, 2H), 7.40 (d, J_{app}=8.4 Hz, 2H); ^{13}C NMR δ 49.3, 55.2, 95.9, 101.6, 108.4, 114.3, 125.7, 130.3, 160.0. Anal. calcd for $C_{11}H_9Br_3N_2O_2$: C, 29.96; H, 2.06; N, 6.35. Found C, 30.21; H, 2.20; N, 6.32.

4.1.2. 4-Bromo-2-(4-methoxybenzyl)pyrazole 1-oxide (6). Compound **5a** (6.58 g, 14.9 mmol) was refluxed for 5 h in a suspension of $Na_2SO_3{\cdot}7H_2O$ (25.2 g, 99.9 mmol) in water/methanol (300 mL+300 mL). After cooling to rt the MeOH was removed by rotary evaporation and the aqueous layer was extracted with CH_2Cl_2 (100+3×50 mL). The combined organic layers were dried over $MgSO_4$. Evaporation to dryness gave the title compound as colorless crystals (3.62 g, 86%). This crude product was >95% pure according to ^{1}H NMR and used without further purification. An analytical sample was obtained by recrystallization from toluene: mp 98–98.5°C; R_f=0.37 (EtOAc); ^{1}H NMR δ 3.82 (s, 3H), 5.21 (s, 2H), 6.76 (d, J=1.4 Hz, 1H), 6.92 (d, J_{app}=8.8 Hz, 2H), 7.21 (d, J=1.4 Hz, 1H), 7.27 (d, J_{app}=8.8 Hz, 2H); ^{13}C NMR δ 48.6, 55.3, 88.6, 114.6, 118.3, 120.0, 125.2, 130.4, 160.1; Anal. calcd for $C_{11}H_{11}BrN_2O_2$: C, 46.67; H, 3.92; N, 9.89. Found: C, 46.70; H, 3.84; N, 9.58.

4.2. 4-Arylation of 4-bromo-2-(4-methoxybenzyl)-pyrazole 1-oxide (6)

4.2.1. 4-(2-Formylphenyl)-2-(4-methoxybenzyl)pyrazole 1-oxide (7). Compound **6** (229 mg, 0.809 mmol) and 2-formylbenzeneboronic acid (209 mg, 1.39 mmol) were dissolved in toluene (10 mL) and EtOH (1.0 mL) and to this mixture was added 2.0 M aqueous K_2CO_3 (1.0 mL, 2.0 mmol). The mixture was degassed with N_2 for 10 min prior to addition of $Pd(PPh_3)_4$ (25 mg, 0.046 mmol) and stirred under N_2 at 90°C for 8 h. The mixture was poured into CH_2Cl_2 (80 mL) and washed with saturated aqueous $NaHCO_3$ solution (10 mL) and brine (20 mL). Drying over Na_2SO_4 and evaporation yielded 305 mg of an orange wax. This was purified by FC (EtOAc) to give the title compound (216 mg, 87%) as yellow crystals: mp 105–108°C; R_f=0.19 (EtOAc); ^{1}H NMR (200 MHz) δ 3.85 (s, 3H), 5.35 (s, 2H), 6.85 (d, J=1.5 Hz, 1H), 6.93 (d, J_{app}=9.4 Hz, 2H), 7.31–7.38 (m, 3H), 7.43 (d, J=1.5 Hz, 1H), 7.46–7.52 (m, 1H), 7.57–7.66 (m, 1H), 7.94–7.98 (m, 1H), 10.15 (d, J=0.8 Hz, 1H); ^{13}C NMR (75 MHz) δ 48.6, 55.2, 113.3, 114.4, 117.7, 119.0, 125.2, 128.0, 128.4, 130.1, 130.3, 133.3, 133.8, 133.9, 159.6, 191.0. Anal. calcd for $C_{18}H_{16}N_2O_3$: C, 70.11; H, 5.23; N, 9.09. Found: C, 70.00; H, 5.32; N, 8.94.

4.2.2. 4-(2-Fluorophenyl)-2-(4-methoxybenzyl)pyrazole 1-oxide (8). Compound **8** was prepared from **6** and 2-(2-fluorophenyl)-5,5-dimethyl-[1,3,2]dioxaborinane[15] in a manner similar to that described for the preparation of **7**. Compound **8** was obtained as colorless crystals (80%): mp 104–106°C; R_f=0.27 (EtOAc); ^{1}H NMR (200 MHz) δ 3.81 (s, 3H), 5.31 (s, 2H), 6.93 (d, J_{app}=9.4 Hz, 2H), 7.05–7.19 (m, 3H), 7.22 (dd, J=1.5, 1.6 Hz, 1H), 7.32–7.43 (m, 3H), 7.64 (dd, J=1.5, 1.6 Hz, 1H); ^{13}C NMR (50 MHz) δ 48.1, 55.0, 111.5, 114.5, 116.4, 116.0 (d, J=24 Hz), 116.6, 116.8 (d, J=10 Hz), 117.7, 117.8 (d, J=10 Hz), 118.3, 118.5 (d, J=14 Hz), 124.6, 124.5 (d, J=3 Hz), 125.9, 127.0, 127.1 (d, J=4 Hz), 128.5, 128.6 (d, J=9 Hz), 130.2, 157.1, 162.1 (d, J=268 Hz), 160.0. Anal. calcd for $C_{17}H_{15}FN_2O_2$: C, 68.45; H, 5.07; N, 9.39. Found: C, 68.52; H, 5.05; N, 9.22.

4.2.3. 4-(4-Tolyl)-2-(4-methoxybenzyl)pyrazole 1-oxide (9). Compound **9** was prepared from **6** and in a manner similar to that described for the preparation of **7**. Compound **9** was obtained as colorless crystals (65%): mp 150–150.5°C; R_f=0.21 (EtOAc); ^{1}H NMR (200 MHz) δ 2.34 (s, 3H), 3.81 (s, 3H), 5.28 (s, 2H), 6.93 (d, J_{app}=9.4 Hz, 2H), 6.97 (d, J=1.5 Hz, 1H), 7.16 (d, J_{app}=8.7 Hz, 2H), 7.25 (d, J_{app}=8.7 Hz, 2H), 7.32 (d, J_{app}=9.4 Hz, 2H), 7.50 (d, J=1.5 Hz, 1H); ^{13}C NMR (50 MHz) δ 20.7, 48.2, 55.1, 114.0, 114.5, 117.0, 118.0, 125.1, 126.0, 127.7, 129.7, 130.3, 137.3, 160.1. Anal. calcd for $C_{18}H_{18}N_2O_2$: C, 73.45; H, 6.16; N, 9.52. Found: C, 73.42; H, 6.00; N, 9.47.

4.2.4. 3-Formyl-2-(4-methoxybenzyl)pyrazole 1-oxide (11). A solution of 3-bromo-2-PMB-pyrazole 1-oxide (**10**)[11] (1.03 g, 3.64 mmol) in THF (40 mL) was cooled to −78°C. (If left for more than 10 min crystals may form.) A solution of *i*-PrMgCl in THF (2.1 M, 2.0 mL, 4.2 mmol) was added dropwise and the solution containing a white precipitate was stirred for 15 min. Meyers reagent (*N*-methyl-*N*-(2-pyridyl)-formamide, 647 mg, 4.75 mmol in 10 mL THF) was added dropwise and after 20 min the cooling bath was removed. After stirring for an additional 1.5 h the reaction mixture was quenched by addition of 4 M aqueous HCl (25 mL) and extracted with EtOAc (6×50 mL). The combined organic layers were washed with 2 M aqueous HCl (30 mL), brine and dried over Na_2SO_4 before evaporation to dryness. This gave almost pure title compound (757 mg, 90%) as judged by ^{1}H NMR, however the compound slowly decomposed on silica requiring fast purification. After purification by FC (heptane/EtOAc 1:1→EtOAc) the title compound was obtained as colorless crystals (629 mg, 74%): mp 116–118°C; R_f=0.37 (EtOAc); ^{1}H NMR δ 3.76 (s, 3H), 5.70 (s, 2H), 6.81 (d, J_{app}=8.6 Hz, 2H), 6.87 (d, J=2.7 Hz, 1H), 7.25 (d, J=2.7 Hz, 1H), 7.45 (d, J_{app}=8.6 Hz, 2H), 9.44 (s, 1H); ^{13}C NMR δ 47.1, 55.1, 113.8, 114.0, 120.3, 126.7, 127.1, 130.4, 159.7, 176.4. Anal. calcd for $C_{12}H_{12}N_2O_3$: C, 62.06; H, 5.21; N, 12.06. Found: C, 61.52; H, 5.03; N, 11.91.

4.2.5. 4-Bromo-3-methylsulfanyl-(4-methoxybenzyl)-pyrazole 1-oxide (15). To a solution of compound **5a** (385 mg, 0.87 mmol) in THF (10 mL) at rt was added dropwise *i*-PrMgCl (1.89 M in THF, 0.97 mL, 1.83 mmol). The resulting suspension was stirred for further 10 min at rt and then cooled to −78°C. Me_2S_2 (90 mg, 0.96 mmol in 1 mL THF) was added dropwise and the mixture was stirred for 10 min before removal of the cooling bath. After stirring for an additional hour without cooling the mixture was quenched by addition of a saturated aqueous solution of NH_4Cl (10 mL). The aqueous layer was extracted with CH_2Cl_2 (5×10 mL) and the combined organic layers were washed with H_2O (10 mL), dried over $MgSO_4$ and evaporated to dryness. Purification by FC (heptane/EtOAc 1:1→1:2) gave the title compound as a hygroscopic colorless oil (173 mg, 60%): ^{1}H NMR δ 2.11 (s, 3H), 3.77 (s, 3H), 5.48 (s, 2H), 6.85 (d, J_{app}=8.8 Hz, 2H), 7.26 (s, 1H), 7.36 (d, J_{app}=8.8 Hz, 2H); ^{13}C NMR δ 19.1, 46.6, 55.2, 98.7, 114.2, 120.5, 122.9, 127.2, 129.8, 159.6. Anal. calcd for $C_{12}H_{13}BrN_2O_2S{\cdot}1.5H_2O$: C, 42.24; H, 4.23; N, 8.21. Found: C, 42.04; H, 3.91; N, 8.00.

4.2.6. 4-Bromo-3,5-dimethylsulfanyl-2-(4-methoxybenzyl)pyrazole 1-oxide (16). To a solution of compound **5a** (310 mg, 0.70 mmol) in THF (10 mL) at rt was added dropwise *i*-PrMgCl (1.89 M in THF, 0.78 mL, 1.47 mmol). The resulting suspension was stirred for further 10 min at rt and then cooled to −78°C. Me_2S_2 (0.20 mL, 2.25 mmol) was added dropwise and the mixture was stirred for 70 min and then allowed to reach rt overnight. The solution was finally heated to 50°C for 4 h before quenched by addition of a saturated aqueous solution of NH_4Cl (10 mL). The aqueous layer was extracted with CH_2Cl_2 (4×10 mL). The combined organic layers were washed with H_2O (10 mL), dried over $MgSO_4$ and evaporated to dryness. Purification by FC (heptane→heptane/EtOAc 1:1) gave the title compound as a colorless oil that very slowly solidified (177 mg, 67%): mp 64.5–65°C; R_f=0.31 (heptane/EtOAc 1:1); ^{1}H NMR δ 2.15 (s, 3H), 2.48 (s, 3H), 3.79 (s, 3H), 5.51 (s, 2H), 6.89 (d, J_{app}=8.8 Hz, 2H), 7.41 (d, J_{app}=8.8 Hz, 2H); ^{13}C NMR δ 15.3, 19.0, 47.3, 55.2, 104.7, 114.1, 121.9, 125.5, 127.1, 130.0, 159.6. Anal. calcd for $C_{13}H_{15}N_2BrO_2S_2$: C, 41.60; H, 4.03; N, 7.46. Found: C, 41.71; H, 3.99; N, 7.47.

4.2.7. 4-Bromo-3,5-dichloro-2-(4-methoxybenzyl)pyrazole 1-oxide (17). Prepared as described for compound **16**, except adding C_2Cl_6 (931 mg, 3.93 mmol) at rt to the dimagnesio intermediate (**14**) derived from **5a** (493 mg, 1.12 mmol) in 16 mL THF. After FC (heptane/EtOAc 4:1→2:1) the title compound was obtained as colorless crystals (247 mg, 63%); mp 113.5–114°C; R_f=0.58 (heptane/EtOAc 1:1); ^{1}H NMR δ 3.79 (s, 3H), 5.39 (s, 2H), 6.87 (d, J_{app}=8.8 Hz, 2H), 7.41 (d, J_{app}=8.8 Hz, 2H); ^{13}C NMR δ 47.9, 55.3, 89.3, 114.2, 115.1, 120.1, 125.4, 130.2, 159.9. Anal. calcd for $C_{11}H_9N_2O_4BrCl_2$: C, 37.53; H, 2.58; N, 7.96. Found: C, 37.80; H, 2.59; N, 7.68.

4.2.8. 4-Bromo-3-formyl-2-benzylpyrazole 1-oxide (19b). A solution of **5b**[14] (410 mg, 1.00 mmol) in THF (10 mL) was cooled to 0°C. A 1.90 M *i*-PrMgCl solution in THF (0.55 mL, 1.05 mmol) was added dropwise and the initially formed white suspension was left with stirring for 20 min at 0°C to give a clear, yellow solution. After addition of TMS-Cl (0.25 mL, 1.98 mmol) the cooling bath was removed and the mixture was left at rt for 1.5 h and then evaporated to dryness. The resulting orange foam of 3,4-dibromo-5-TMS-2-benzylpyrazole 1-oxide was redissolved in THF (10 mL), cooled to 0°C and slowly added *i*-PrMgCl solution in THF (0.63 mL, 1.20 mmol). After stirring for 15 min the solution was cooled to −78°C and Meyers reagent (0.16 mL, 1.34 mmol) was added dropwise. After stirring at −78°C for 20 min the cooling bath was removed and the mixture left for 2.5 h before addition of 2 M aqueous HCl (10 mL). The mixture was extracted with CH_2Cl_2 (4×25 mL) and after washing of the combined organic layers with brine the organic layer was evaporated to dryness. The semicrystalline mass was dissolved in MeOH (30 mL), 2.0 M aqueous K_2CO_3 (2.00 mL, 4.0 mmol) was added and after stirring for 1.5 h at rt brine (30 mL) was added. The MeOH was removed by rotary evaporation and the aqueous layer was extracted with CH_2Cl_2 (4×25 mL). The combined organic layers were washed with brine (10 mL), dried over $MgSO_4$ and evaporated to dryness. After purification by FC (heptane/EtOAc 1:1) the title compound was obtained as colorless crystals (123 mg, 44%): mp 99.5–100°C; R_f=0.35 (heptane/EtOAc 1:1); ^{1}H NMR δ 5.67 (s, 2H), 7.20–7.25 (m, 4H), 7.33–7.37 (m, 2H), 9.47 (s, 1H); ^{13}C NMR δ 47.3, 103.2, 121.1, 123.5, 128.5, 128.71, 128.73, 134.4, 175.6. Anal. calcd for $C_{11}H_9N_2O_2Br$: C, 47.00; H, 3.23; N, 9.97; Found: C, 47.25; H, 3.35; N, 9.85.

4.2.9. 4-Bromo-3-formyl-2-(4-methoxybenzyl)pyrazole 1-oxide (19a). In a procedure similar to the preparation of **19b**, compound **19a** was obtained as colorless crystals (51%): mp 118–119°C; R_f=0.4 (heptane/EtOAc 1:1); ^{1}H NMR δ 3.77 (s, 3H), 5.70 (s, 2H), 6.83 (d, J_{app}=8.8 Hz, 2H), 7.25 (s, 1H), 7.43 (d, J_{app}=8.8 Hz, 2H), 9.56 (s, 1H); ^{13}C NMR δ 47.12, 55.17, 103.27, 114.03, 121.25, 123.48, 126.68, 130.62, 159.85, 175.75. Anal. calcd for $C_{12}H_{11}N_2O_3Br$: C, 46.32; H, 3.56; N, 9.00. Found: C, 46.45; H, 3.41; N, 8.78.

4.2.10. [2-(5,5-Dimethyl-[1,3,2]dioxaborinan-2-yl)phenyl]-carbamic acid *tert*-butyl ester (22). A solution of phenylcarbamic acid *tert*-butyl ester **20**[35] (8.52 g, 44.1 mmol) in diethyl ether (90 mL) was cooled to −20°C. *tert*-Butyllithium (57 mL, 96.3 mmol) was added dropwise keeping the temperature between −20 and −10°C. The mixture was stirred at an internal temperature between −15 and −10°C for 3 h and was then cooled to −78°C. Tri-*i*-propylborate (25 mL, 108 mmol) was added slowly and the mixture was left overnight. Saturated aqueous NH_4Cl solution (85 mL) was added and the mixture stirred vigorously for 20 min before extraction of the aqueous layer with EtOAc (2×400 mL). The combined organic layers were washed with water and evaporated to almost dryness. Toluene (500 mL) was added and the mixture was stirred with neopentylglycol (11.3 g, 0.109 mol) at rt overnight to give a two phase mixture. Dilution with diethyl ether (500 mL), washing with water (4×100 mL) and evaporation to dryness yielded the title compound quantitatively as colorless crystals: mp 85–88°C. This compound was used as well as a recrystallized sample without any difference in the reaction outcome. Recrystallization from heptane gave the title compound as colorless crystals (11.6 g, 86%): mp 90–91°C; R_f=0.36 (heptane/EtOAc, 10:3, with substantial tailing); ^{1}H NMR δ 1.04 (s, 6H), 1.52 (s, 9H), 3.82 (s, 4H), 6.97 (ddd, J=7.4, 7.3, 1.1 Hz, 1H), 7.39 (ddd, J=8.4, 7.3, 1.7 Hz, 1H), 7.77 (dd, J=7.4, 1.7 Hz, 1H), 8.20 (br d, J=8.4 Hz, 1H), 8.92 (br s, 1H); ^{13}C NMR (the B *ipso* carbon was not observed) δ 21.7, 28.3, 31.7, 72.4, 79.7, 117.6, 121.4, 132.1, 135.6, 145.2, 153.3. Anal. calcd for $C_{16}H_{24}BNO_4$: C, 62.97; H, 7.93; N, 4.59. Found: C, 62.95; H, 7.99; N, 4.86.

4.3. Synthesis of pyrazolo[3,4-*c*]quinoline 1-oxides

4.3.1. 2-(4-Methoxybenzyl)pyrazolo[3,4-*c*]quinoline 1-oxide (23a). Compound **22** (1.37 g, 4.50 mmol) and compound **19a** (940 mg, 3.02 mmol) were dissolved in a mixture of toluene (40 mL), EtOH (4 mL) and 2.0 M K_2CO_3 (4.5 mL, 9.0 mmol). After passing N_2 through the solution for 15 min $Pd(PPh_3)_4$ (212 mg, 0.18 mmol, 6 mol%) was added and the mixture was refluxed under N_2 for 4 h. Aqueous 4 M HCl (30 mL) was added with vigorous stirring and after 50 min the mixture was neutralized by addition of a saturated aqueous solution of $NaHCO_3$ (approx. 70 mL). The aqueous layer was extracted with CH_2Cl_2 (150+2×50 mL). The combined organic layers were washed with $NaHCO_3$ (sat. aq, 50 mL), H_2O (3×50 mL) and then dried over $MgSO_4$. The crude product was adsorbed onto silica gel (about 2 g) and purified by FC (heptane/EtOAc 1:1→1:3) to yield the title compound as light yellow crystals (717 mg, 78%): mp 196–198°C; R_f=0.48 (EtOAc); ^{1}H NMR δ 3.76 (s, 3H), 5.67 (s, 2H), 6.86 (d, J_{app}=8.8 Hz, 2H), 7.34 (d, J_{app}=8.8 Hz, 2H), 7.61–7.74 (m, 2H), 7.97–8.00 (m, 1H), 8.06 (s, 1H), 8.12–8.15 (m, 1H), 8.77 (s, 1H); ^{13}C NMR δ 46.2 (t), 55.2 (q), 111.8 (d), 114.6 (d), 119.5 (s), 119.7 (s), 123.0 (d), 124.6 (s), 126.1 (s), 127.81 (d), 127.83 (d), 129.6 (d), 130.2 (d), 133.2 (d), 143.3 (s), 159.9 (s). Anal. calcd for $C_{18}H_{15}N_3O_2$: C, 70.51; H, 4.95; N, 13.76. Found: C, 70.54; H, 4.97; N, 13.34.

When the same procedure was carried out using crude **19a** (worked up but not chromatographed), compound **23a** was obtained in 38% overall yield based on the tribromide **5a**.

4.3.2. 2-Benzylpyrazolo[3,4-*c*]quinoline 1-oxide (23b). Compound **23b** was obtained as described for **23a** using

the crude **19b** (worked up but not chromatographed) in 40% overall yield based on **5b**: mp 206–209°C (decomp.); R_f= 0.49 (EtOAc); ^{1}H NMR δ 5.73 (s, 2H), 7.31–7.36 (m, 5H), 7.62–7.67 (m, 2H), 7.96–7.99 (m, 1H), 8.01 (s, 1H), 8.08–8.14 (m, 1H), 8.76 (s, 1H); ^{13}C NMR δ 46.4, 111.9, 119.5, 119.6, 123.0, 124.7, 127.84, 127.85, 127.9, 128.7, 129.3, 130.3, 133.2, 134.2, 143.4; Anal. calcd for $C_{17}H_{13}N_3O$: C, 74.17; H, 4.76; N, 15.26. HRMS (EI): calcd for $C_{17}H_{13}N_3O$: 275.1059. Found: 275.1053

4.3.3. 2-Benzyl-3-methylpyrazolo[3,4-*c*]quinoline 1-oxide (24). *Preparation of building block **2***. A solution of tribromide **5b**[14] (511 mg, 1.24 mmol) in THF (13 mL) was cooled to 0°C. A solution of *i*-PrMgCl in THF (1.91 M, 0.68 mL, 1.30 mmol) was added dropwise and the mixture was stirred at 0°C for 20 min to produce a light orange solution. TMS-Cl (0.31 mL, 2.45 mmol) was added, cooling was removed and the mixture was stirred at rt for 1 h before evaporation to dryness to remove excess TMS-Cl. The mixture was redissolved in THF (13 mL) and cooled to 0°C. A solution of *i*-PrMgCl in THF (1.91 M, 0.72 mL, 1.38 mmol) was added dropwise and after stirring the solution for 15 min at 0°C it was cooled to −78°C. Acetyl chloride (0.11 mL, 1.52 mmol) was added dropwise and the mixture was stirred for 1 h and then allowed to slowly reach rt. After 30 min, a solution of saturated aqueous NH_4Cl (10 mL) was added and the mixture extracted with CH_2Cl_2 (4×25 mL). The combined organic layers were evaporated to almost dryness and the semicrystalline residue was dissolved in MeOH (30 mL). A solution of 2.0 M aqueous K_2CO_3 (0.62 mL, 1.24 mmol) was added and after stirring for 30 min at rt brine (30 mL) was added. The MeOH was removed by rotary evaporation and the aqueous layer was extracted with CH_2Cl_2 (5×25 mL). The combined organic layers were washed with brine (20 mL), dried over $MgSO_4$ and evaporated to dryness to give the crude **2**.

*Suzuki cross-coupling with building block **22***. The crude intermediate **2** and **22** (502 mg, 1.64 mmol) were dissolved in a mixture of toluene (40 mL), EtOH (4 mL) and 2.0 M K_2CO_3 (4.5 mL, 9.0 mmol). After passing N_2 through the solution for 15 min $Pd(PPh_3)_4$ (80 mg, 0.069 mmol, 6 mol%) was added and the mixture was heated to 90°C under N_2 for 3 h.

Ring closure. Aqueous 4 M HCl (30 mL) was added with vigorous stirring and after 50 min the mixture was neutralized by addition of a saturated aqueous solution of $NaHCO_3$ (approx. 70 mL). The aqueous layer was extracted with CH_2Cl_2 (150+2×50 mL). The combined organic layers were washed with $NaHCO_3$ (sat. aq., 50 mL), H_2O (3×50 mL) and then dried over $MgSO_4$. The crude product was adsorbed onto silica gel (about 2 g) and purified by FC (heptane/EtOAc 3:2→2:3) to yield the title compound as colorless crystals (174 mg, 48%, 5 steps from **5b**): mp 167–168°C; R_f=0.23 (heptane/EtOAc 1:1); ^{1}H NMR δ 2.84 (s, 3H), 5.95 (s, 2H), 7.06–7.08 (m, 2H), 7.26–7.33 (m, 3H), 7.57–7.68 (m, 2H), 7.96–7.99 (m, 1H), 8.03–8.06 (m, 1H), 8.14 (s, 1H); ^{13}C NMR δ 23.1, 47.1, 112.0, 118.8, 120.0, 122.6, 124.9, 126.0, 127.1, 127.9, 128.1, 129.2, 129.3, 135.8, 142.3, 142.8. HRMS (ESI): calcd for $C_{18}H_{16}N_3O$ $(M+H)^+$: 290.1293. Found: 290.1297.

4.3.4. 2-Benzyl-3-ethylpyrazolo[3,4-*c*]quinoline 1-oxide (25). Compound **25** was obtained as described for **24** in 1 mmol scale using propionyl chloride (111 mg, 1.2 mmol) as acid chloride. After the Suzuki cross-coupling step the following procedure was used for ring closure.

The reaction mixture was poured into CH_2Cl_2 (50 mL) and washed with saturated aqueous $NaHCO_3$ solution (10 mL) and brine (20 mL). The aqueous phase was extracted CH_2Cl_2 (2×50 mL) and the combined organic layers were then dried over Na_2SO_4 and evaporated to dryness. The crude intermediate was dissolved in CH_2Cl_2 (5 mL) and TFA (5 mL) was added. After stirring for 1 h at rt, the reaction mixture was evaporated to dryness. The crude mixture was redissolved in CH_2Cl_2, adsorbed onto silica gel and purified by FC (heptane/EtOAc 3:1→1:2) to yield the title compound as colorless crystals (157 mg, 52%, 5 steps from **5b**): mp 160–161°C (EtOAc/heptane); R_f=0.36 (heptane/EtOAc 1:1); ^{1}H NMR δ 1.34 (t, J= 7.5 Hz, 3H), 3.11 (q, J=7.5 Hz, 2H), 5.94 (s, 2H), 7.02–7.07 (m, 2H), 7.24–7.33 (m, 3H), 7.55–7.68 (m, 2H), 7.97 (br d, J=7.8 Hz, 1H), 8.07 (br d, J=7.8 Hz, 1H), 8.16 (s, 1H); ^{13}C NMR δ 12.9, 28.6, 47.4, 112.3, 118.9, 120.4, 122.8, 124.5, 126.1, 127.1, 128.0, 128.4, 129.3, 129.7, 135.9, 143.0, 147.2. HRMS (ESI): calcd for $C_{19}H_{18}N_3O$ $(M+H)^+$: 304.1450. Found: 304.1449.

4.3.5. 2-Benzyl-3-cyclopropylpyrazolo[3,4-*c*]quinoline 1-oxide (26). Compound **26** was obtained as described for **25** in 1 mmol scale using 4-chlorobutyryl chloride (169 mg, 1.2 mmol) as acid chloride. Purification by FC (heptane/EtOAc 3:1→1:2) gave the title compound as colorless crystals (135 mg, 43%, 5 steps from **5b**): mp 158–159°C (EtOAc/ heptane); R_f=0.48 (heptane/EtOAc 1:1); ^{1}H NMR δ 0.97–0.99 (m, 2H), 1.31–1.37 (m, 2H), 2.26–2.36 (m, 1H), 6.10 (s, 2H), 7.10–7.14 (m, 2H), 7.26–7.33 (m, 5H), 7.53–7.65 (m, 2H), 7.94–8.02 (m, 2H), 8.14 (s, 1H); ^{13}C NMR δ 8.7, 14.8, 47.7, 112.2, 119.9, 122.7, 125.6, 126.2, 126.9, 127.9, 128.2, 129.3, 129.7, 136.0, 143.0, 146.2. HRMS (ESI): calcd for $C_{20}H_{18}N_3O$ $(M+H)^+$: 316.1450. Found: 316.1443.

4.3.6. 2-Benzyl-3-phenylpyrazolo[3,4-*c*]quinoline 1-oxide (27). Compound **27** was obtained as described for **25** in 1 mmol scale using benzoyl chloride (169 mg, 1.2 mmol) as acid chloride. Purification by FC (heptane/EtOAc 3:1→1:2) gave the title compound as colorless crystals (91 mg, 26%, 5 steps from **5b**): mp 194–195°C (EtOAc/ heptane); R_f=0.36 (heptane/EtOAc 1:1); ^{1}H NMR δ 5.94 (s, 2H), 6.51–6.54 (m, 2H), 7.03–7.15 (m, 3H), 7.44–7.56 (m, 5H), 7.61–7.72 (m, 2H), 8.04 (br d, J=7.6 Hz, 1H), 8.07 (br d, J=7.6 Hz, 1H), 8.23 (s, 1H); ^{13}C NMR δ 47.5, 112.8, 119.1, 121.8, 122.9, 124.2, 126.8, 127.7, 127.9, 128.4, 128.7, 128.9, 129.3, 129.8, 130.4, 135.2, 137.9, 143.1, 145.0. HRMS (ESI): calcd for $C_{23}H_{18}N_3O$ $(M+H)^+$: 352.1450. Found: 352.1434.

4.3.7. 9-Hydroxypyrazolo[3,4-*c*]quinoline (28). Compound **23a** (62 mg, 0.203 mmol) was dissolved in CH_2Cl_2 (15 mL) and the solution was degassed with N_2 for 10 min. The solution was irradiated at 254 nm for 40 h with an UV lamp (Vilber Lourmat VL-4LC 4 W) used for TLC plate visualization. After purification by FC (CH_2Cl_2→CH_2Cl_2/

EtOAc 6:4) the title compound was obtained as light yellow crystals (27 mg, 44%): mp 219–220°C; R_f=0.69 (EtOAc); ^{1}H NMR (dmso-d_6) δ 3.70 (s, 3H), 5.57 (s, 2H), 6.87 (d, J_{app}=8.3 Hz, 2H), 7.26 (d, J_{app}=8.3 Hz, 2H), 7.56–7.69 (m, 2H), 8.07–8.09 (m, 1H), 8.31–8.34 (m, 1H), 9.38 (s, 1H), 11.40 (br s, the signal only integrates to approx. 0.5H). Carrying out a NOE difference experiment with irradiation of the benzylic protons at δ 5.57 ppm, a 20% NOE was observed on the d 9.38 ppm singlet along with a 8% NOE on the δ 7.26 doublet. ^{13}C NMR (dmso-d_6) δ 51.4, 55.0, 107.9, 114.0, 122.2, 122.6, 125.7, 127.8, 129.1, 129.3, 129.4, 134.8, 137.8, 141.4, 155.7, 158.9. Anal. calcd for $C_{18}H_{15}N_3O_2$: C, 70.81; H, 4.95; N, 13.76. Found: C, 70.60; H, 5.02; N, 13.52.

4.3.8. 1-Hydroxypyrazolo[3,4-*c*]quinoline (29). Compound **23a** (23 mg, 0.075 mmol) was stirred at rt in conc. aqueous HCl (10 mL) overnight. The solution was diluted with conc. aqueous HCl (10 mL) and washed with toluene (2 mL) before evaporation to dryness. Addition of toluene (30 mL) and evaporation was subsequently carried out twice and the mixture was dried at rt at 1 mbar overnight to give the HCl salt of the title compound as white crystals (17 mg, 100%): mp 235–237°C; ^{1}H NMR (dmso-d_6) δ 7.84–7.92 (m, 2H), 8.30–8.36 (m, 1H), 8.48–8.53 (m, 1H), 9.11 (s, 1H), 9.84 (s, 1H); ^{13}C NMR (dmso-d_6) 117.9, 121.0, 121.8, 123.3, 124.9, 129.27, 129.34, 132.1, 133.6, 139.8. HRMS (EI): calcd for $C_{10}H_7N_3O$: 185.0589. Found: 185.0589.

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