# Preparation and Reactions of 3*H*-Pyrazolo[1,5-*a*]indole Derivatives[1)]

Jing-Kang SHEN and Hajime KATAYAMA*

*Niigata College of Pharmacy, 5–13–2 Kamishin'ei-cho, Niigata City, Niigata 950–21, Japan.*
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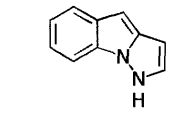
**3*H*-Pyrazolo[1,5-*a*]indole derivatives were prepared for the first time starting from 3-oxo-2-phenyl-3*H*-pyrazolo[1,5-*a*]indole, which was obtained by the 2,3-dichloro-4,5-dicyano-*p*-benzoquinone (DDQ) oxidation of 3-hydroxy-2-phenyl-3a,4-dihydro-3*H*-pyrazolo[1,5-*a*]indole. Their reactions were briefly investigated.**

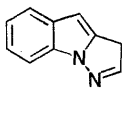
**Keywords** 3*H*-pyrazolo[1,5-*a*]indole; isomerization; electrophilic substitution; mechanism; 3-oxo-3*H*-pyrazolo[1,5-*a*]indole; reduction

Pyrazolo[1,5-*a*]indoles are of interest from a chemical interests as well as biological standpoint.[2–5)] Among the three isomers of pyrazolo[1,5-*a*]indole (Chart 1), we have already reported the preparation of 1*H*- and 4*H*-pyrazolo[1,5-*a*]indole derivatives.[3,4)] In this report we present the first examples of 3*H*-pyrazolo[1,5-*a*]indole derivatives.

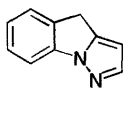
We initially attempted to prepare the 3*H*-isomer by introducing a double bond between C-3a and C-4 of the alcohol **1** (Chart 1).[2)] When **1** was dehydrogenated with 2,3-dichloro-4,5-dicyano-*p*-benzoquinone (DDQ) in THF, a dark red crystalline material **2** was obtained as a sole product. The yield became 97% when 2 eq of DDQ was employed. This product **2** had a maximum absorption ($\lambda_{max}$) in the visible region at 504 nm (log $\varepsilon$ 3.52), and showed a carbonyl absorption band at 1688 $cm^{-1}$ in the IR spectrum, which is lower than the 4-keto absorption of 4-oxo-4*H*-pyrazolo[1,5-*a*]indole (1724 $cm^{-1}$).[4)] In the



1*H*-pyrazolo[1,5-*a*]indole



3*H*-pyrazolo[1,5-*a*]indole



4*H*-pyrazolo[1,5-*a*]indole

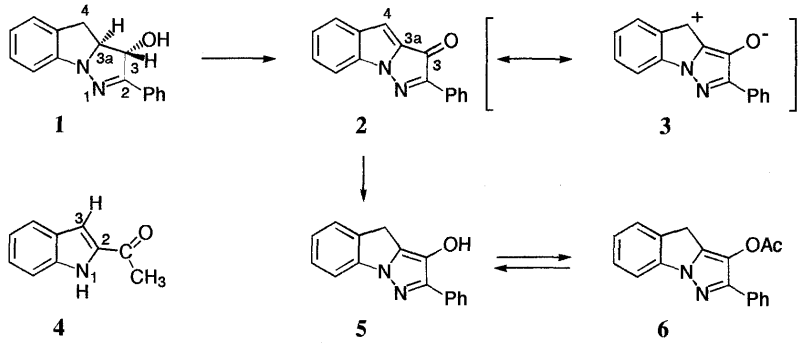


Chart 1

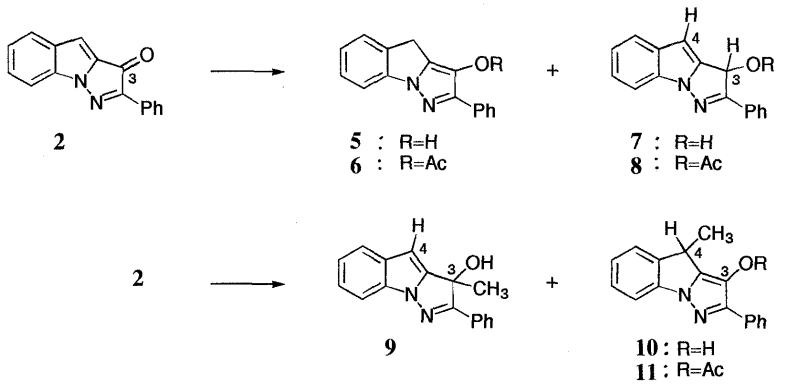


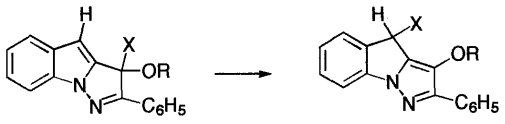
Chart 2

$^1$H-NMR spectra, the product **2** revealed a singlet vinylic proton (4-H) at $\delta$ 7.19 ppm, identical with 3-H of 2-acetylindole **4** ($\delta$ 7.19).[6] In the $^{13}$C-NMR spectrum, C-4 of the product **2** ($\delta$ 111.0) appeared quite close to C-3 of 2-acetylindole **4** ($\delta$ 110.0). These spectral observations allowed us to assign the 3-ketone structure **2** to this dark red product. The carbonyl carbon (C-3) signal of **2** was detected at higher magnetic field ($\delta$ 180.7) than that of the 2-acetylindole **4** ($\delta$ 190.6) in the $^{13}$C-NMR spectrum. This big difference implies an important contribution of the resonance form **3** which involves the stable pyrazole ring.[7] A similar resonance form is not possible for 2-acetylindole **4**. When the ketone **2** was reduced with $NaBH_4$ in methanol, the dark red color of the solution faded away instantly and colorless product **5** was formed, which was isolated as the acetate **6**. In $^1$H-NMR spectrum the acetate **6** has a singlet signal at $\delta$ 4.01 which is characteristic of the 4-methylene group of the 4*H*-isomer,[4] so the structure **6** was confirmed. The air-sensitive phenol **5** was formed by hydrolyzing the acetate **6** with sodium hydroxide in an inert atmosphere.

Since the selective 1,2-reduction of the conjugated ketone **2** allows the formation of derivatives of the 3*H*-isomer, reduction of the ketone **2** was conducted with $NaBH_4$ in the presence of an equivalent amount of cerium chloride.[8] This reaction afforded new air-resistant product **7** in 96% yield. Trace contamination with the 4*H*-isomer **5** was detected by TLC analyses of the mother liquor from the recrystallization. The combination of $NaBH_4$–$CaCl_2$[9] was also effective and the same product **7** (81%) was obtained together with slight increase of the 4*H*-isomer **5** (14%). In these reductions, the pH of the solution was kept almost neutral as measured with pH paper. The structure of the new product **7** was deduced as follows. In the UV spectrum, the product **7** had two absorption maxima at 279 (log $\varepsilon$ 3.76) and 362 nm (3.84), whilst the 4*H*-isomer **5** showed a single maximum at 311 nm (4.06). The OH group was detected in both the IR (3361 cm$^{-1}$) and $^1$H-NMR ($\delta$ 2.28, d, $J$=10.0 Hz) spectra. The secondary carbinol proton (3-H) was observed at $\delta$ 5.87 as a double doublet ($J$=1.5, 10.0 Hz), the bigger coupling of which disappeared on $D_2O$ addition. This carbinol proton signal moved to lower magnetic field at $\delta$ 6.76 (d, $J$=1.5 Hz) in the acetate **8**, *vide infra*. The vinylic 4-H of the product **7** appeared at higher magnetic field ($\delta$ 6.61, br s) than that of the ketone **2** ($\delta$ 7.19, s), supporting the successful 1,2-reduction of the ketone **2**. As the 3*H*-isomer **7** was in hand, the reduction of the ketone **2** with $NaBH_4$ in methanol without any additive was reinvestigated. When this reduction was carried out at 0 °C and the reaction progress was monitored with TLC, the 3*H*-isomer **7** was, in fact, formed as an initial product. However, the initial product **7** was gradually transformed into the 4*H*-isomer **5**. This isomerization became fast at room temperature (r.t.). Similar isomerization was also found during melting point (mp) measurement. The 3*H*-isomer **7** melted first at 148.0—149.0 °C but further heating resulted in solidification, and this solid melted again at 240.0—242.0 °C which is the mp of the 4*H*-isomer **5**. When the alcohol **7** was acetylated with acetic anhydride and 1 eq of 4-dimethylaminopyridine (DMAP), the acetate of the 4*H*-isomer **6** (93%) was obtained as a sole product. However, the employment of 0.05 eq of DMAP afforded the acetate of the 3*H*-isomer **8** in 79% yield, together with a small amount of the 4*H*-isomer **6** (13%). In the $^1$H-NMR spectrum, the acetate **8** showed a long range coupling ($J$=1.5 Hz) between 3-H ($\delta$ 6.76) and 4-H ($\delta$ 6.65) as observed in the alcohol **7**. Another long range splitting ($J$=0.7 Hz) between 4-H and 8-H ($\delta$ 7.70) was also detected, corresponding to the long range coupling between 3-H and 7-H in the indole series.[10]

As the 3*H*-isomers prepared above were quite susceptible to isomerization (*vide infra*), stable derivatives of the 3*H*-isomer were prepared using the ketone **2** (Chart 2). When the ketone **2** was reacted with methylmagnesium bromide in THF, both 1,2- and 1,4-addition products, **9** (61%) and **10** (30%), were obtained. The 1,4-adduct became dominant when lithium dimethyl cuprate[11] was employed (86%). These two products were readily separated by column chromatography. In their $^1$H-NMR spectra, the methyl signal of the 1,2-adduct **9** appeared at $\delta$ 1.81 as a singlet and the 4-H signal at $\delta$ 6.45 as a singlet, whereas the methyl protons of the 1,4-adduct **10** resonated at $\delta$ 1.53 as a doublet ($J$=7.3 Hz) due to coupling with 4-H ($\delta$ 4.03). The phenolic 4*H*-isomer **10** was labile to air as the phenol **5**, so it was transformed into the stable acetate **11**. The 3*H*-isomers **7**, **8** and **9** prepared above constitute the first reported examples of 3*H*-pyrazolo[1,5-*a*]indole derivatives. Among the three isomers of pyrazolo[1,5-*a*]indole, no registry number has been given to the parent 3*H*-isomer, although numbers have been assigned to the 1*H*-(42318-55-8) and 4*H*-isomers (247-75-6).

The 3*H*-isomers isomerized quite readily into the 4*H*-isomers as observed above, and the details of this reaction were investigated. Reaction conditions which allow




**7** : R=X=H
D-**7** : R=H, X=D
**8** : R=Ac, X=H
D-**8** : R=Ac, X=D

**5** : R=X=H
D-**5** : R=H, X=D
**6** : R=Ac, X=H
D-**6** : R=Ac, X=D

Chart 3

TABLE I. Reaction Conditions for the Isomerization of the 3*H*-Isomer **7** into the 4*H*-Isomer **5**

| Entry | Reaction conditions[a] | Isomerization (%)[b] |
|---|---|---|
| 1 | $BF_3 \cdot OEt_2$(1eq)/$CH_2Cl_2$/−40 °C/1 h | 100 [93][c] |
| 2 | NaOH(1eq)/MeOH/r.t./0.5 h | 100 [100][c] |
| 3 | AcOH/r.t./1 h | 100 [96][c] |
| 4 | $d_6$-Acetone/r.t./13.5 h | 80 |
| 5 | $d_6$-DMSO/r,t,/2 h | 66 |
| 6 | MeOD/r.t./53 h | 22 |
| 7 | $CDCl_3$/r.t./48 h | 7 |
| 8 | Neat/170 °C/1 h | 65 |

*a*) r.t.: room temperature. *b*) Isomerization ratio was calculated from the integrations of 3-H and 4-H for **7** and those of 4-$H_2$ for **5** in the $^1$H-NMR spectra. *c*) Isolated yield of **5** (%).

isomerization are summarized in Table I. The isomerization proceeded slowly even under neutral conditions (entries 4 to 7) and the solvent polarity affected the isomerization (entries 4 to 6). Heating was effective, as observed during mp measurement (*vide supra*) (entry 8). The acetate of the 3*H*-isomer **8** was also isomerized into the 4*H*-isomer **6** by heating (63%). Both acid and base were found to be effective for the isomerization (entries 1, 2, 3).

In order to examine the mechanism of these acid- and base-catalyzed isomerizations, the 3-deuterated 3*H*-isomers, D-**7** and D-**8**, were prepared by reduction of the ketone **2** with $NaBD_4$, followed by acetylation. The incorporated deuterium ratio of D-**7** (91%) and D-**8** (98%), and the deuterated position were determined by MS (calculation), $^1$H-NMR (disappearance of 3-H signal) and $^{13}$C-NMR (weakening of C-3 signal with multiple splittings) examinations. For acid-catalyzed isomerization, acetic acid (AcOH) and $d_1$-acetic acid (AcOD) were used. The 3*H*-isomer was dissolved in dichloromethane and isomerized with 5 eq of acetic acid at r.t. for the period indicated. The results are summarized in Table II. The phenolic products **5** and D-**5** (entries 1 and 2) were collected as precipitates, washed with water and dried. The acetates **8** and D-**8** (entries 3 and 4) were reacted similarly, but were recovered almost intact (entries 3 and 4). Deuterium incorporations were deduced from the integrational decrease of the 4-$H_2$ signal using *ortho* protons of the phenyl group as a reference in the $^1$H-NMR spectra. As shown on Table II, the isomerization of the 3*H*-isomers **7** and D-**7** was completed within 24 h but almost no isomerization took place with their acetates, **8** and D-**8**. No remarkable difference in isomerization rate between **7** and D-**7** was observed by TLC. Deuterium (60%) was incorporated into C-4 when **7** was isomerized in AcOD (entry 1), but no deuteration occurred at the same position when the isomerization of D-**7** was carried out with AcOH (entry 2). No deuterium was detected in the recovered 3*H*-isomer **8**, as far as $^1$H-NMR precision concerned (entry 3). No deuterium incorporation into the 4*H*-isomers **5** and **6** took place when these 4*H*-isomers were exposed to AcOD for 24 h. Based upon these observations, the following mechanism is proposed for the acid-catalyzed isomerization (Chart 4).

The initial step of the isomerization leading to the salt **12** is not reversible but is rate-determining, since no deuterium incorporation was detected in the recovered 3*H*-isomer **8** (entry 3) and no di-deuteration was observed in the isomerization of the 3*H*-isomer **7** with AcOD in $CH_2Cl_2$ (entry 1). Once the salt **12** is formed, the subsequent isomerization leading to stable pyrazole-ring formation is quick and gives the 4*H*-isomer **5**. The formation of the 4*H*-isomer **5** in entry 1 is explained by protonation from AcOH formed by the quick exchange of 3-OH with AcOD. The transformation of 3-OH into 3-OAc resulted in dramatic deceleration of the isomerization. The 3-OAc group reduces the electron density at C-3 then at C-4, so retarding protonation at C-4. The steric crowding at C-4 due to the 3-OAc group also makes it difficult for a proton to approach the C-4 position. The combination of these electronic and steric retarding effect eventually block the protonation at the C-4 position. The precipitation of the phenolic product **5** from the solution should aid the isomerization of the 3*H*-isomer **7** as well.

The base-catalyzed isomerization of the 3*H*-isomer was carried out with DMAP as a base. The 3*H*-isomer was treated with 1 eq of DMAP in $CH_2Cl_2$–MeOH (2 : 1) at r.t. and the progress of the reaction was followed by TLC. The reaction was continued until the starting material was completely consumed. The phenolic products were collected as precipitates (entries 1 and 2) and the acetates were purified by flash column chromatography (entries 3 to 5). The results are summarized in Table III.

The base-catalyzed isomerization was found to be faster than the acid-catalyzed one. In particular, the acetate **8**, which was resistant to the acid-catalyzed isomerization,

Table II. The Acid-Catalyzed Isomerization of the 3*H*-Isomers into the 4*H*-Isomers[a]

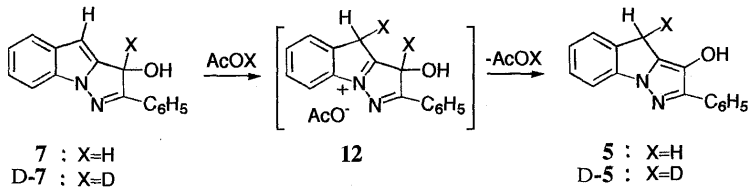
| Entry | Substrate | AcOX | RT (h) | Yield (%)[b] | Products[c] |
|---|---|---|---|---|---|
| 1 | **7** | AcOD | 24 | 92 | **5** (40), D-**5** (60) |
| 2 | D-**7** | AcOH | 24 | 90 | **5** (100), D-**5** (0) |
| 3 | **8** | AcOD | 48 | 100 | **8** |
| 4 | D-**8** | AcOH | 48 | 98 | D-**8**[d] |

*a*) A solution of the substrate in $CH_2Cl_2$ containing AcOX (5 eq) was stirred at r.t. for the period indicated under reaction time (RT, hour). *b*) Isolated yields (%). *c*) Products ratios were calculated from 4-$H_2$ integration data using the *ortho* proton signal of the phenyl group as a reference. *d*) The 4*H*-isomer (8%) was also present.

Table III. The Base-Catalyzed Isomerization of 3*H*-Isomers into the 4*H*-Isomers[a]

| Entry | Substrate | MeOX | RT (h) | Yield (%)[b] | Products[c] |
|---|---|---|---|---|---|
| 1 | **7** | MeOD | 6 | 88 | **5** (60), D-**5** (40) |
| 2 | D-**7** | MeOH | 24 | 88 | **5** (44), D-**5** (56) |
| 3 | **8** | MeOD | 0.2 | 94 | **6** (32), D-**6** (68) |
| 4 | D-**8** | MeOH | 0.5 | 85 | **6** (94), D-**6** (6) |
| 5 | D-**8** | — | 0.5 | 100 | **6** (4), D-**6** (96) |

*a*) A solution of the substrate and DMAP (1 eq) in a mixture of $CH_2Cl_2$–MeOH (2 : 1) was stirred at r.t. for the period indicated under reaction time (RT, hour). b) Isolated yields (%). *c*) Products ratios were calculated from the result of 4-$H_2$ integration using the *ortho* proton signals of the phenyl group as a reference.




**7** : X=H
D-**7** : X=D

**12**

**5** : X=H
D-**5** : X=D

Chart 4

underwent complete isomerization within 0.2 h (entry 3). The isotope effect was observed with 3-deuterated substrates. Isomerizations of the 3*H*-isomers D-**7** and D-**8** (entries 2, 4 and 5) were slower, compared with the corresponding non-deuterated 3*H*-isomers **7** and **8** (entries 1 and 3). Deuteration at C-4 occurred during these isomerizations but was incomplete (Table III). Some deuterium transfer from C-3 to C-4 took place even when MeOH was employed as the proton source (entries 2, 4). Deuterium incorporation into C-4 became almost quantitative giving D-**6**, when no X-source was present during isomerization (entry 5). This result confirms the precision of the experimental procedures. In separate experiments, the 4*H*-isomers **5** and **6** were kept with DMAP in MeOD at r.t. for 24 h, but no deuterium incorporation was detected. The influence of base concentration was also checked (Fig. 1). Increase of the base concentration

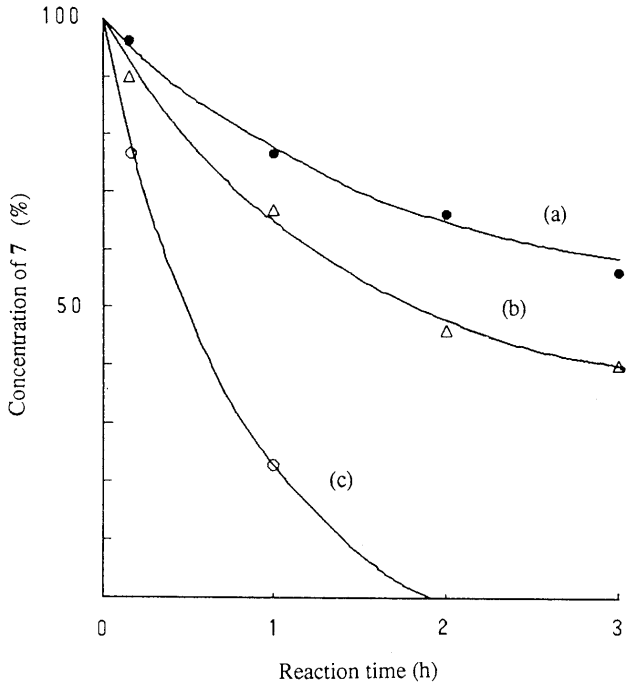



Fig. 1. Base-Catalyzed Isomerization of the 3*H*-Isomer **7**

Internal standard, $Cl_2CHCHCl_2$; solvent, $CDCl_3$; concentration of **7**: 14 mg/0.7 ml; concentration of base (DMAP), (a) 0.1 eq, (b) 0.5 eq, (c) 1.0 eq; reaction temperature, 25±2 °C.

accelerated the isomerization rate. Thus, the following mechanism is postulated for the base-catalyzed isomerization of the 3*H*-isomers (Chart 5).

The direct abstraction of X from C-3 of the 3*H*-isomer with base leads to the formation of the anion **13**, which is stabilized by resonance with the anion **14**. The alternative pathway *via* the alkoxide **15** can also occur to produce the anion **13**. The canonical form **14** (the 4*H*-isomer) is better suited than the other form **13** (the 3*H*-isomer), and protonation or deuteration of the anion **14** gives the 4*H*-isomer, *i.e.*, the preferred isomerization of the 3*H*-isomers into the 4*H*-isomers. In the last stage of the reaction, both $BX^+$ and MeOX may participate. The species $BX^+$ is formed by the direct reaction of base with both 3-X and 3-OH. Either protonation or deuteration of the anion **13** regenerates the 3*H*-isomer but this reaction does not take place, since no 4-dideuterated 4*H*-isomer was detected in the isomerization of the 3*H*-isomer **7** (entry 1). In entry 5, there is no other acid besides $BD^+$, so total deuteration took place at C-4. Sterically it is not possible to transfer the deuterium intramolecularly from C-3 to C-4. The partial deuteration at C-4 even in the presence of MeOH (entries 2, 4) can be explained in terms of the participation of $BD^+$, which is held close to the anion **13** and **14**. The observed isotope effects of D-**7** and D-**8** and the dependence of isomerization rate on the base concentration support the hypothesis that the irreversible X abstraction from C-3 of the 3*H*-isomer with base is rate-determining.

In contrast to the acid-catalyzed isomerization, the base-catalyzed isomerizations of the acetate **8** and D-**8** were faster than those of the corresponding alcohols. The 3-OAc in the acetates is more electron-attracting than 3-OH. The decrease of the electron density at C-3 increases the acidity of 3-H, thus easing the abstraction of 3-H(D) by base, and accelerates the isomerization. The C-4 deuteration during the isomerization of the acetate D-**8**, *i.e.*, deuterium transfer from C-3 to C-4 with $BD^+$ in MeOH, was found to be much smaller than that of the alcohol D-**7** (ratio 6:56 in entries 4, 2). This difference can be explained as follows. The anionic intermediate **14** (R = Ac) derived from the acetates is more stable than that (**14**, R = H) from the alcohols, so the more stable anion is better solvated with MeOH than the one from the

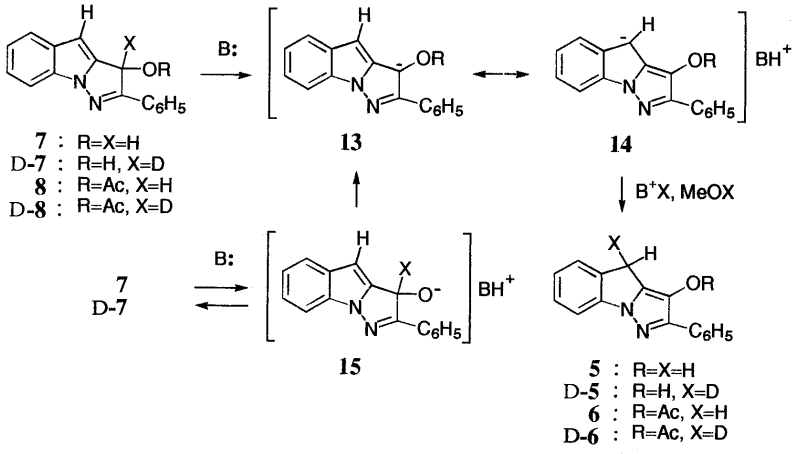



Chart 5

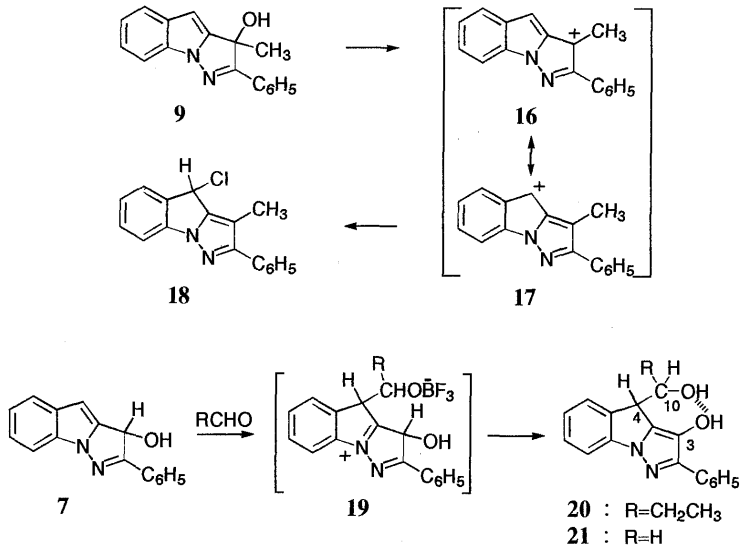



Chart 6

alcohol, and consequently the anion from the acetate, **14** (R = Ac) is less available to $BD^+$ compared with the anion from the alcohol, **14** (R = H). The stabilized anion **13** and the intramolecular proton abstraction of the anion **15** are reminiscent of the mechanism of benzoin condensation.[12]

When the stable 3*H*-isomer **9** was mesylated, no mesylate or olefinic product was formed but the chloride **18** was obtained in 78% yield. The presence of one chlorine atom was suggested by the characteristic peaks at *m/z* 280 ($M^+$) and 282 ($M^+ + 2$) (3 : 1) in the MS. The broad singlet signal at $\delta$ 5.90 ppm (4-H) in the $^1$H-NMR spectrum allowed us to identify the position of a chlorine atom and the methyl signal (3-Me) at $\delta$ 2.37 ppm (d, $J = 0.7$ Hz: long-range coupling with 4-H) was consistent with the proposed structure. The formation of the chloride **18** can be rationalized in terms of initial mesylation and subsequent formation of the cation **16**, which is stabilized by resonance with the cation **17**. The cation **17** (the 4*H*-isomer) is more stable than the cation **16** (the 3*H*-isomer) as in the case of the corresponding anions, **13** and **14** (Chart 5). Subsequent attack of the chlorine atom on the cation **17** gives the *SN*1′-type product **18**.

As the 3*H*-isomer contains an indole nucleus, a similar range of reactivity to that of indole can be expected.[13] Although the 3*H*-isomer is readily isomerizable into the 4*H*-isomer in the presence of either acid or base (Table I), the 3*H*-isomer **7** was reacted with propionaldehyde in the presence of boron trifluoride etherate and the addition product with isomerization, **20**, was obtained in 85% yield. The product **20** consisted of a single isomer according to the $^1$H-NMR and $^{13}$C-NMR analyses. A similar reaction was effected with formaldehyde generated by heating paraformaldehyde,[14] giving the adduct **21** in 76% yield. The compositions of these products were determined by high resolution MS. The position of the carbinol unit was confirmed by the $^1$H-NMR spectrum. The 4-H signal of the adduct **20** appeared at $\delta$ 4.49 with splitting into a doublet ($J = 5.1$ Hz) due to one adjacent proton (10-H) after exchange with $D_2O$. The 4-H signal ($\delta$ 4.27) of the adduct **21** appeared as double doublets ($J = 6.8$, 5.1 Hz) because of the adjacent two diastereotopic protons (10-$H_2$). Two hydroxy groups in these adducts are intramolecularly hydrogen-bonded and were detected in the $^1$H-NMR spectra, in which the signal of the phenolic 3-OH appeared at the lower magnetic field than that of the alcoholic 10-OH. The formation of these adducts can be understood in terms of the formation of the intermediate **19** and its isomerization into the stable pyrazole ring (Chart 6).

In summary, we were able to prepare 3*H*-pyrazolo[1,5-*a*]indole derivatives for the first time and we established the following reactivities of the 3*H*-isomers. 1) The 3*H*-isomer with 3-H is readily isomerized into the more stable 4*H*-isomer upon heating, or under neutral, acidic or basic conditions. 2) The C-3 anion and cation of the 3*H*-isomer are stabilized by resonance with the C-4 anionic and cationic forms and the reactions *via* these ions give the products derived from the more stable C-4 ions. 3) The C-4 position of the 3*H*-isomer has similar nucleophilic character to the C-3 position of indole.

**Experimental**

All melting points (mp) were determined with a Yanaco micro melting point apparatus without correction. Spectra were measured with the following spectrometers: IR (KBr pellet unless otherwise stated), Perkin-Elmer FT-IR 1720; $^1$H- and $^{13}$C- NMR, JEOL JNM-FT 200 and JNM-ALPHA 400 in $CDCl_3$ at ambient temperature (25—27 °C) with tetramethylsilane as an internal standard; MS and high resolution MS (HRMS), Hitachi RMU-7MG; UV and visible spectra (VIS), Shimadzu UV-200. Anhydrous THF was prepared by distillation in the presence of ketyl radical and $CH_2Cl_2$ and *N*,*N*-dimethylformamide (DMF) were dried by refluxing with calcium hydride and distillation. Unless otherwise noted, the quenched reaction mixture was extracted with ether or $CH_2Cl_2$ and the extracts were washed twice with saturated brine, dried over anhydrous magnesium sulfate and evaporated *in vacuo*. The crude product was purified by flash column chromatography on silica gel with a combination of petroleum ether and ethyl acetate. The TLC analyses were used for fractionation of the eluates.

**3-Oxo-2-phenyl-3*H*-pyrazolo[1,5-*a*]indole (2)** DDQ (2.658 g, 11.71 mmol) was added to a solution of the alcohol **1**[2] (1.332 g, 5.32 mmol) in THF (20 ml). The dark red solution was stirred at r.t. for 2 h, diluted with $CH_2Cl_2$, then quenched with 10% NaOH. The crude product was recrystallized from ethyl acetate to give the product **2** (1.277 g, 97%),

mp 165.0—168.0 °C (dec., sublimed at 157 °C). MS *m/z*: 246 ($M^+$, 73), 143 (100), 115 (88), 88 (18). UV-VIS $\lambda_{max}^{CH_3CN}$ nm (log ε): 210 (4.35), 238 (sh, 4.11), 291 (4.06), 391 (4.01), 504 (3.52). IR: 3056, 1688, 1614, 1525, 1350, 1297, 1166, 787, 750, 690 $cm^{-1}$. $^1$H-NMR δ: 7.10 (1H, td, *J*=7.8, 1.2 Hz, 6-H), 7.19 (1H, s, 4-H), 7.41—7.56 (5H, m, Ar-H), 7.62 (1H, d, *J*=7.8 Hz, 5-H), 7.23 (2H, m, 2′, 6′-H). $^{13}$C-NMR δ: 110.0 (C-8). 111.0 (C-4), 122.4 (C-6), 125.7 (C-5), 127.5 (C-2′, 6′), 128.4 (C-3a, 1′), 128.7 (C-3′, 5′), 130.0 (C-7), 130.5 (C-4a), 130.7 (C-4′), 134.5 (C-8a), 152.8 (C-2), 180.7 (C-3). *Anal.* Calcd for $C_{16}H_{10}N_2O$: C, 78.04; H, 4.09; N, 11.38. Found: C, 78.16; H, 3.89; N, 11.25.

**3-Acetoxy-2-phenyl-4*H*-pyrazolo[1,5-*a*]indole (6)** a) When $NaBH_4$ (27 mg, 0.71 mmol) was added into a solution of **2** (175 mg, 0.71 mmol) in MeOH (20 ml) under a nitrogen atmosphere, the dark red solution instantly became colorless. The reaction mixture was stirred at r.t. for 15 min then evaporated. The residue was acetylated with a mixture of pyridine (1 ml) and acetic anhydride (0.20 ml, 2.12 mmol) overnight. The solution was poured into 1 M HCl containing ice and extracted with ether. The usual work-up yielded the acetate **6** (67 mg, 33%), colorless crystals, mp 98.0—98.5 °C (from ethyl acetate). MS *m/z*: 290 ($M^+$, 15), 248 (100), 145 (17), 144 (15), 117 (97), 116 (50), 104 (12), 90 (17), 89 (36), 77 (5). UV $\lambda_{max}^{CH_3CN}$ nm (log ε): 297 (3.46). IR: 3057, 1753, 1626, 1603, 1480, 1459, 1372, 1254, 1218, 1190, 986, 770, 753, 694 $cm^{-1}$. $^1$H-NMR δ: 2.36 (3H, s, $CH_3$), 4.01 (2H, s, 4-$H_2$), 7.20 (1H, t, *J*=7.6 Hz, 6-H), 7.30—7.50 (5H, m, Ar-H), 7.69 (1H, d, *J*=7.8 Hz, 8-H), 7.94 (2H, m, 2′, 6′-H). $^{13}$C-NMR δ: 20.9 ($CH_3$), 30.6 (C-4), 110.5 (C-8), 124.6 (C-6), 125.7 (C-5), 126.9 (C-2′, 6′), 127.9 (C-4′), 128.0 (C-7), 128.1 (C-3), 128.6 (C-3′, 5′), 132.3 (C-1′), 133.1 (C-4a), 135.4 (C-3a), 140.6 (C-8a), 145.1 (C-2), 167.4 (C=O). *Anal.* Calcd for $C_{18}H_{14}N_2O_2$: C, 74.47; H, 4.86; N, 9.65. Found: C, 74.73; H, 4.56; N, 9.61. b) A mixture of 3-hydroxy-2-phenyl-3*H*-pyrazolo[1,5-*a*]indole (**7**, 275 mg, 1.11 mmol), acetic anhydride (0.21 ml, 2.23 mmol) and DMAP (136 mg, 1.11 mmol) in dry $CH_2Cl_2$ (10 ml) was stirred at r.t. for 2 h, then poured into 1 M HCl containing ice. Extraction with ether and usual work-up yielded the acetate **6** (293 mg, 91%).

**3-Hydroxy-2-phenyl-4*H*-pyrazolo[1,5-*a*]indole (5)** A solution of the acetate **6** (4.06 g, 14.0 mmol) in 2% KOH in MeOH (100 ml) was stirred at 0—5 °C for 0.5 h. After confirming the disappearance of the ester on TLC, the reaction mixture was acidified with 1 M HCl (pH 3), and the precipitates were collected to give **5** (3.31 g, 95%), mp 240.0—242.0 °C (dec.) (from acetone). MS *m/z*: 248 ($M^+$, 84), 149 (32), 145 (17), 144 (15), 117 (100), 116 (25), 104 (27), 90 (15), 89 (28), 81 (56), 77 (15). UV $\lambda_{max}^{CH_3CN}$ nm (log ε): 311 (4.06). IR: 3033 (br), 1622, 1602, 1469, 1411, 1393, 1304, 1292, 1279, 1244, 1138, 1091, 989, 772, 746, 696 $cm^{-1}$. $^1$H-NMR ($d_6$-DMSO) δ: 3.96 (2H, s, 4-$H_2$), 7.20 (1H, t, *J*=7.4 Hz, 6-H), 7.28 (1H, tt, *J*=7.4, 1.2 Hz, 4′-H), 7.42 (3H, m, Ar-H), 7.56 (2H, m, 5,8-H), 8.06 (2H, m, 2′,6′-H), 9.34 (1H, s, OH). $^{13}$C-NMR ($d_6$-DMSO) δ: 27.8 (C-4), 109.2 (C-8), 123.8 (C-6), 125.5 (C-2′, 6′), 126.3 (C-5), 126.7 (C-4′), 127.8 (C-7), 128.2 (C-3′, 5′), 129.7 (C-3), 133.4 (C-4a, 1′), 134.7 (C-3a), 139.9 (C-8a), 142.3 (C-2). *Anal.* Calcd for $C_{16}H_{12}N_2O$: C, 77.40; H, 4.87; N, 11.29. Found: C, 77.35; H, 5.10, N, 11.23.

**3-Hydroxy-2-phenyl-3*H*-pyrazolo[1,5-*a*]indole (7)** a) $NaBH_4$–$CeCl_3$. The ketone **2** (1.520 g, 6.17 mmol) and $CeCl_3 \cdot 7H_2O$ (2.300 g, 6.17 mmol) were dissolved in a mixture of MeOH and $CH_2Cl_2$ (1:1, 140 ml) and the solution was cooled at −20 °C under an argon atmosphere. To this solution, $NaBH_4$ (234 mg, 6.19 mmol) was added and the resulting mixture was stirred for 30 min. After evaporation of the solvent, the residue, which showed a single spot on TLC, was recrystallized from ethyl acetate–pentane to give the alcohol **7** (1.472 g, 96%). A trace of the 4*H*-isomer **5** was detected in the mother liquor of recrystallization on TLC. **7**, yellow needles, mp 148.0—149.0 and 240.0—242.0 °C (from ethyl acetate–pentane). MS *m/z*: 248 ($M^+$, 98), 219 (6), 145 (52), 144 (47), 117 (100), 104 (83), 89 (43), 77 (20). IR: 3361, 3060, 1618, 1486, 1441, 1304, 1219, 1153, 1044, 963, 791, 730, 688 $cm^{-1}$. UV $\lambda_{max}^{CH_3CN}$ nm (log ε): 219 (4.10), 279 (3.76), 362 (3.84). $^1$H-NMR δ: 2.28 (1H, d, *J*=10.0 Hz, OH), 5.87 (1H, dd, *J*=10.0, 1.5 Hz, 3-H), 6.61 (1H, br s, 4-H), 7.12 (1H, td, *J*=7.5, 1.1 Hz, 6-H), 7.29 (1H, td, *J*=7.5, 1.0 Hz, 7-H), 7.45 (3H, m, 3′,4′,5′-H), 7.58 (1H, d, *J*=7.5 Hz, 5-H), 7.66 (1H, d, *J*=7.5 Hz, 8-H), 8.03 (2H, m, 2′,6′-H). $^{13}$C-NMR δ: 70.7 (C-3), 98.5 (C-4), 109.7 (C-8), 120.7 (C-6), 121.9 (C-5), 123.8 (C-7), 127.2 (C-2′,6′), 128.8 (C-3′,5′), 130.1 (C-1′), 130.4 (C-4a), 130.5 (C-8a), 130.6 (C-4′), 136.9 (C-3a), 163.4 (C-2). *Anal.* Calcd for $C_{16}H_{12}N_2O$: C, 77.40; H, 4.87; N, 11.29. Found: C, 77.38; H, 4.59; N, 11.34. b) $NaBH_4$–$CaCl_2$. b) A solution of **2** (246 mg, 1.0 mmol) and $CaCl_2$ (222 mg, 2.0 mmol) in a mixture of MeOH and $CH_2Cl_2$ (1:1, 30 ml) was prepared and cooled to 0 °C. After addition of $NaBH_4$ (38 mg, 1.0 mmol), the solution was stirred for 1 h, then concentrated *in vacuo*. The residue was dissolved in $CH_2Cl_2$ and water and the organic layer was separated. The crude product obtained by the usual procedure was purified by flash column chromatography to give the 3*H*-isomer **7** (201 mg, 81%) and the 4*H*-isomer **5** (36 mg, 14%).

**3-Hydroxy-2-phenyl-[3-$^2$H]-3*H*-pyrazolo[1,5-*a*]indole (D-7)** Reduction of the ketone **2** (246 mg, 1.00 mmol) with $NaBD_4$ (42 mg, 1.0 mmol) and anhydrous $CeCl_3$ (246 mg, 1.0 mmol) in a mixture of dry $CH_2Cl_2$ (15 ml) and $CH_3OD$ (5 ml) as described above gave **D-7** (213 mg, 85%) (deuterium incorporation: 91% from MS) and the phenolic product **5** (17 mg, 6%) containing 16% deuterium from MS. **D-7**, mp 148.0—150.0 °C and 242—245 °C (dec.) (from ethyl acetate). MS *m/z*: 249 ($M^+$, 100), 248 (10), 220 (10), 146 (44), 144 (51), 118 (82), 105 (59), 89 (33), 77 (14). $^1$H-NMR δ:2.26 (1H, br s, OH), 6.58 (1H, s, 4-H), 7.11 (1H, td, *J*=7.7, 1.0 Hz, 6-H), 7.28 (1H, td, *J*=7.7, 1.0 Hz, 7-H), 7.43 (3H, m, 3′,4′,5′-H), 7.57 (1H, d, *J*=7.7 Hz, 5-H), 7.65 (1H, d, *J*=7.7 Hz, 8-H), 8.06 (2H, m, 2′,6′-H). $^{13}$C-NMR δ: 70.7 (C-3), 98.5 (C-4), 109.7 (C-8), 120.7 (C-6), 121.9 (C-5), 123.8 (C-7), 127.2 (C-2′, 6′), 128.8 (C-3′, 5′), 130.1 (C-1′), 130.4 (C-4a), 130.5 (C-8a), 130.6 (C-4′), 136.8 (C-3a), 163.3 (C-2).

**3-Acetoxy-2-phenyl-3*H*-pyrazolo[1,5-*a*]indole (8)** The alcohol **7** (133 mg, 0.54 mmol) and acetic anhydride (0.10 ml, 1.06 mmol) were dissolved in $CH_2Cl_2$ (5 ml) and cooled at 0 °C. To this solution DMAP (3 mg, 0.02 mmol) was added and the reaction mixture was stirred at the same temperature for 0.5 h. The solution was poured into 1 M HCl containing ice, and extracted with ether to give, after chromatography, the acetates **8** (123 mg, 79%) and **6** (20 mg, 13%). **8**, pale yellow needle, mp 144.0—145.0 °C (from ethyl acetate–pentane). MS *m/z*: 290 ($M^+$, 27), 248 (100), 231 (44), 219 (6), 145 (37), 144 (17), 128 (10), 117 (63), 104 (33), 101 (14), 89 (25), 77 (28). UV $\lambda_{max}^{CH_3CN}$ nm (log ε): 218 (3.88), 280 (3.52), 365 (3.57). IR: 3059, 1745, 1738, 1619, 1450, 1441, 1299, 1231, 1217, 1045, 1034, 796, 734, 692 $cm^{-1}$. $^1$H-NMR δ: 2.15 (3H, s, $COCH_3$), 6.65 (1H, dd, *J*=1.5, 0.7 Hz, 4-H), 6.76 (1H, d, *J*=1.5 Hz, 3-H), 7.13 (1H, td, *J*=7.8, 1.1 Hz, 6-H), 7.32 (1H, td, *J*=7.8, 1.1 Hz, 7-H), 7.47 (3H, m, 3′,4′,5′-H), 7.60 (1H, d, *J*=7.8 Hz, 5-H), 7.70 (1H, dd, *J*=7.8, 0.7 Hz, 8-H), 7.88 (2H, m, 2′,6′-H). $^{13}$C-NMR δ: 20.9 ($CH_3$), 69.7 (C-3), 101.2 (C-4), 109.7 (C-8), 120.8 (C-6), 122.1 (C-5), 124.2 (C-7), 126.9 (C-2′, 6′), 129.0 (C-3′, 5′), 130.0 (C-1′), 130.4 (C-4a), 130.6 (C-4′, 8a), 134.0 (C-3a), 159.9 (C-2), 170.2 (C=O). *Anal.* Calcd for $C_{18}H_{14}N_2O_2$: C, 74.47; H, 4.86; N, 9.65. Found: C, 74.54; H, 4.65; N, 9.67.

**3-Acetoxy-2-phenyl-[3-$^2H_1$]-3*H*-pyrazolo[1,5-*a*]indole (D-8)** The deuterated alcohol **D-7** (249 mg, 1.00 mmol) in dry $CH_2Cl_2$ (10 ml) was treated with acetic anhydride (0.20 ml, 2.12 mmol) in the presence of DMAP (6 mg, 0.05 mmol) at 0—5 °C for 30 min. The usual work-up as described above yielded the acetates **D-8** (246 mg, 84%) (deuterium incorporation: 98% from MS) and **6** (27 mg, 9%) (deuterium incorporation: 23% from MS). **D-8**, yellow needles, mp 142.0—143.0 °C (from ethyl acetate–pentane). MS *m/z*: 291 ($M^+$, 34), 290 (0.5), 249 (100), 232 (52), 220 (9), 146 (26), 118 (41), 117 (28), 105 (24), 89 (14), 77 (21). $^1$H-NMR δ: 2.14 (3H, s, $COCH_3$), 6.65 (1H, d, *J*=1.0 Hz, 4-H), 7.13 (1H, td, *J*=8.1, 1.0 Hz, 6-H), 7.32 (1H, td, *J*=8.1, 1.1 Hz, 7-H), 7.47 (3H, m, 3′,4′,5′-H), 7.60 (1H, d, *J*=8.1 Hz, 5-H), 7.69 (1H, dd, *J*=8.1, 1.0 Hz, 8-H), 7.88 (2H, m, 2′,6′-H). $^{13}$C-NMR δ: 20.8 ($CH_3$), 101.2 (C-4), 109.7 (C-8), 120.8 (C-6), 122.1 (C-5), 124.1 (C-7), 126.8 (C-2′, 6′), 128.9 (C-3′, 5′), 130.0 (C-1′), 130.4 (C-4a), 130.6 (C-4′, 8a), 133.9 (C-3a), 159.8 (C-2), 170.2 (C=O). The C-3 signal was not detected.

**3-Hydroxy-3-methyl-2-phenyl-3*H*-pyrazolo[1,5-*a*]indole (9) and 3-Hydroxy-4-methyl-2-phenyl-4*H*-pyrazolo[1,5-*a*]indole (10)** a) A solution of 3 M methylmagnesium bromide in ether (0.50 ml, 1.5 mmol) was added to a solution of the conjugated ketone **2** (246 mg, 1.0 mmol) in dry THF (20 ml) at −50 °C under an argon atmosphere and the solution was stirred at the same temperature for 15 min. The reaction was quenched with aqueous ammonium chloride and the solution was neutralized with sodium carbonate then extracted with ether. Flash column chromatography of the crude product afforded **9** (162 mg, 61%) and **10** (79 mg, 30%). **9**, mp 128.5—129.0 °C (from ethanol). MS *m/z*: 262 ($M^+$, 15), 247 (4), 144 (6), 45 (100). IR: 3521, 3366, 3182, 3061, 2975, 2810, 1617, 1536, 1443, 1301, 1163, 1106, 769, 740, 695 $cm^{-1}$. $^1$H-NMR δ: 1.81 (3H, s, $CH_3$), 2.70 (1H, s, OH), 6.45 (1H, s, 4-H), 7.12 (1H, td, *J*=7.6, 1.0 Hz, 6-H), 7.28 (1H, td, *J*=7.6, 1.0 Hz, 7-H), 7.42 (3H, m, 3′,4′,5′-H), 7.56 (1H, d, *J*=7.6 Hz, 5-H), 7.67 (1H, d, *J*=7.6 Hz, 8-H), 8.14 (2H, m, 2′,6′-H). $^{13}$C-NMR δ: 25.6 ($CH_3$), 78.7 (C-3), 95.4 (C-4), 109.7 (C-8), 120.6 (C-6), 121.8 (C-5), 123.5 (C-7), 127.3 (C-2′, 6′), 128.7 (C-3′, 5′), 129.8 (C-1′), 130.2 (C-4a), 130.3 (C-4′, 8a), 141.9 (C-3a),

165.9 (C-2). *Anal.* Calcd for $C_{17}H_{14}H_2O$: C, 77.84; H, 5.38; N, 10.68. Found: C, 77.94; H, 5.54; N, 10.76. **10**, readily colored while standing, mp 175.0–176.0 °C (from ethyl acetate–pentane). MS *m/z*: 262 ($M^+$, 100), 247 (57), 159 (26), 144 (22), 130 (56), 116 (11), 104 (31). IR: 3065 (br), 2969, 2693, 1624, 1603, 1587, 1473, 1392, 1306, 1242, 752, 695 $cm^{-1}$. $^1$H-NMR $\delta$: 1.53 (3H, d, $J$=7.3 Hz, $CH_3$), 4.03 (1H, q, $J$=7.3 Hz, 4-H), 5.33 (1H, br s, OH), 7.15 (1H, td, $J$=7.5, 1.0 Hz, 6-H), 7.24—7.46 (5H, m, Ar-H), 7.61 (1H, d, $J$=7.6 Hz, 8-H), 7.93 (2H, m, 2′,6′-H). $^{13}$C-NMR $\delta$: 16.7 ($CH_3$), 35.0 (C-4), 110.2 (C-8), 124.3 (C-6), 124.6 (C-5), 126.8 (C-2′, 6′), 127.7 (C-4′), 128.1 (C-7, 3), 128.8 (C-3′, 5′), 132.6 (C-1′), 133.8 (C-4a), 136.4 (C-3a), 139.0 (C-8a), 144.7 (C-2). 3-Acetoxy-4-methyl-2-phenyl-4*H*-[1,5-*a*]indole (**11**), oil. MS *m/z*: 304 ($M^+$, 13), 262 (100), 247 (27), 130 (45), 104 (22), 77 (29). HRMS: Calcd for $C_{19}H_{16}N_2O_2$: 304.1211. Found $M^+$: 304.1269. IR: 3061, 2972, 2932, 1761, 1626, 1602, 1476, 1458, 1444, 1370, 1305, 1246, 1194, 751, 696 $cm^{-1}$. $^1$H-NMR $\delta$: 1.49 (3H, d, $J$=7.3 Hz, 4-$CH_3$), 2.37 (3H, s, $COCH_3$), 4.26 (1H, q, $J$=7.3 Hz, 4-H), 7.21 (1H, t, $J$=7.7 Hz, 6-H), 7.29—7.49 (5H, m, Ar-H), 7.66 (1H, d, $J$=7.6 Hz, 8-H), 7.90 (2H, m, 2′,6′-H). $^{13}$C-NMR $\delta$: 16.8 (4-$CH_3$), 20.8 ($COCH_3$), 37.0 (C-4), 110.4 (C-8), 124.5 (C-5), 124.7 (C-6), 126.9 (C-2′, 6′), 127.9 (C-4′, 3), 128.1 (C-7), 128.6 (C-3′, 5′), 132.3 (C-1′), 138.9 (C-4a), 139.7 (C-3a), 140.5 (C-8a), 145.6 (C-2), 167.8 (C=O). b) A solution of 1.17 M MeLi in ether (4 ml, 4.68 mmol) was added to a suspension of CuI (453 mg, 2.38 mmol) in dry $CH_2Cl_2$ (20 ml) at 0 °C in an argon atmosphere and the solution was stirred for 10 min, then cooled to −30 °C. To this cuprate solution, a solution of **2** (246 mg, 1.00 mmol) in dry $CH_2Cl_2$ (5 ml) was added and the resulting mixture was stirred at −30 °C for 30 min. The reaction was quenched with 1 M HCl and the solution was extracted with ethyl acetate. The extracts were washed with brine and dried. Flash column chromatography (petroleum ether–ethyl acetate, 1 : 4) of the crude product yielded **10** (224 mg, 86%).

**Acid-Catalyzed Isomerization of the 3*H*-Isomers** In an atmosphere of dry nitrogen the 3*H*-isomer (0.2 mmol), anhydrous $CH_2Cl_2$ (1 ml) and 1.0 M AcOD solution in $CH_2Cl_2$ (1 ml, 1.0 mmol) were placed in a round bottomed flask and the resulting solution was stirred at r.t. for the period indicated in Table II. The reaction progress was monitored by TLC (petroleum ether–ethyl acetate, 1 : 1). The precipitates, when formed, were collected, washed with water and dried to give the phenolic 4*H*-isomer. The reaction solution was diluted with $CH_2Cl_2$, washed with saturated brine and dried over anhydrous $MgSO_4$. After filtration, the filtrate was evaporated to give the ester product.

**Base-Catalyzed Isomerization of the 3*H*-Isomers** The 3*H*-isomer (0.2 mmol) and DMAP (0.2 mmol) were dissolved in a solution of anhydrous $CH_2Cl_2$–$CH_3OD$ (2 : 1, 3 ml) and the solution was stirred at r.t. The reaction was monitored by TLC (silica gel, petroleum ether–ethyl acetate, 1 : 1) every 30 min for the alcohol and every 10 min for the ester. When the starting material had disappeared, the solution was acidified to pH 5 by adding 1 M HCl. The precipitates, when formed, were collected to give the phenolic 4*H*-isomer. The solution was diluted with $CH_2Cl_2$, washed with brine and dried over $MgSO_4$. The crude product thus obtained was purified by flash column chromatography to give the acetate of the 4*H*-isomer. 3-Acetoxy-2-phenyl-[4-$^2H_1$]-4*H*-pyrazolo[1,5-*a*]indole (D-**6**, 52 mg, 100%) (96% deuteration from MS), colorless crystals, mp 98.0—99.0 °C (from ethyl acetate). MS *m/z*: 292 ($M^+$+1, 2.32), 291 ($M^+$, 12), 290 (0.5), 249 (79), 146 (13), 145 (19), 118 (100), 117 (83), 104 (16), 91 (19), 90 (64), 89 (29), 77 (9), 76 (7). $^1$H-NMR $\delta$: 2.36 (3H, s, $CH_3$), 4.00 (1H, br s, 4-H), 7.20 (1H, td, $J$=7.6, 1.0 Hz, 5-H), 7.30—7.50 (5H, m, Ar-H), 7.69 (1H, d, $J$=7.8 Hz, 8-H), 7.93 (2H, m, 2′,6′-H). $^{13}$C-NMR $\delta$: 20.9 ($CH_3$), 30.3 (C-4, with triplet splitting), 110.5 (C-8), 124.6 (C-6), 125.7 (C-5), 126.9 (C-2′, 6′), 127.9 (C-4′), 128.0 (C-7), 128.1 (C-3), 128.6 (C-3′, 5′), 132.3 (C-1′), 133.1 (C-4a), 135,4 (C-3a), 140.6 (C-8a), 145.1 (C-2), 167.4 (C=O).

**Effect of Base Concentration in Isomerization of the 3*H*-Isomer (7)** The 3*H*-isomer **7** (14 mg, 0.56 mmol) and 1,1,2,2-tetrachloroethane (9.5 mg, 0.06 mmol) as an internal standard were added to $CDCl_3$ (0.7 ml) in an NMR tube. In this solution, the following amount of DMAP was dissolved: solution A (DMAP 0.7 mg, 0.1 eq), B (DMAP 3.5 mg, 0.5 eq), and C (DMAP 6.9 mg, 1.0 eq). The $^1$H-NMR spectra of these solution were measured at 25±2 °C. The integration of 4-$H_2$ ($\delta$ 3.96, s) of the 4*H*-isomer **5** was not reliable due to the close proximity of a small water signal, so that the decreases of the 3-H ($\delta$ 5.87, dd) and 4-H ($\delta$ 6.61, s) signals of the 3*H*-isomer **7** were recorded using an internal reference signal ($\delta$ 5.93 ppm). No isomerization was observed in the absence of base after reaction for 3 h. The results of the reactions (time/remaining content of **7**) were as follows: solution A: 8 min/96%, 1 h/76%, 2 h/66%, 3 h/57%; B: 13 min/90%, 1 h/67%, 2 h/46%, 3 h/40%; C: 7 min/77%, 1 h/23%, 2 h/0%.

**4-Chloro-3-methyl-4*H*-pyrazolo[1,5-*a*]indole (18)** A solution of the alcohol **9** (110 mg, 0.42 mmol) in dry $CH_2Cl_2$ (5 ml) was cooled in an ice-bath, and to this solution, triethylamine (0.18 ml, 1.29 mmol) and mesyl chloride (0.05 ml, 0.65 mmol) were added. The resulting solution was kept at r.t. for 2 h, then poured into ice-water and extracted with ether. The extracts were washed, dried, and evaporated. The crude product was flash-chromatographed (petroleum ether–ethyl acetate, 95 : 5) to give **18** (92 mg, 78%), yellow crystals, mp 87.0—88.0 °C (from ethanol). MS *m/z*: 282 ($M^+$+2, 7), 280 ($M^+$, 22), 245 (100), 142 (35), 115 (25), 89 (6), 77 (7). IR: 3058, 2958, 1623, 1599, 1476, 1459, 1302, 1235, 770, 748, 695 $cm^{-1}$. $^1$H-NMR $\delta$: 2.37 (1H, d, $J$=0.7 Hz, $CH_3$, singlet when irradiated at $\delta$ 5.90), 5.90 (1H, br s, 4-H), 7.21 (1H, td, $J$=7.7, 0.7 Hz, 6-H), 7.32—7.50 (4H, m, Ar-H), 7.58 (2H, m, 5,8-H), 7.73 (2H, m, 2′,6′-H). $^{13}$C-NMR $\delta$: 9.3 ($CH_3$), 48.1 (C-4), 110.5 (C-8), 112.4 (C-3), 125.0 (C-6), 126.5 (C-5), 127.7 (C-2′, 6′), 127.9 (C-4′), 128.5 (C-3′, 5′), 130.5 (C-7), 133.5 (C-1′), 135.0 (C-4a), 139.5 (C-8a), 143.3 (C-3a), 155.6 (C-2). *Anal.* Calcd for $C_{17}H_{13}ClN_2$: C, 72.72; H, 4.67; N, 9.98. Found: C, 72.97; H, 4.76; N, 9.78.

**3-Hydroxy-4-(1-hydroxypropyl)-2-phenyl-4*H*-pyrazolo[1,5-*a*]indole (20)** The 3*H*-isomer **7** (103 mg, 0.41 mmol) and propionaldehyde (0.05 ml, 0.69 mmol) were dissolved in dry $CH_2Cl_2$ (7 ml) under dry argon and the solution was cooled to −50 °C. To this solution, borontrifluoride etherate (0.06 ml, 0.49 mmol) was added under effective stirring and the solution was kept at the same temperature for 30 min. After quenching with water, the solution was extracted with ether. The crude product was purified by flash column chromatography (petroleum ether–ethyl acetate, 85 : 15) to give **20** (109 mg, 85%), a white amorphous solid. MS *m/z*: 306 ($M^+$, 24%), 248 (100), 219 (11), 145 (42), 117 (54), 116 (14), 115 (14), 104 (61), 89 (20), 77 (7), 59 (6). HRMS: Calcd for $C_{19}H_{18}N_2O_2$: 306.1366. Found $M^+$: 306.1362. IR: 3300, 3064, 2962, 1625, 1607, 1472, 1394, 1307, 1239, 1088, 964, 770, 754, 694 $cm^{-1}$. $^1$H-NMR $\delta$: 0.79 (3H, t, $J$=7.2 Hz, $CH_2CH_3$), 1.02 (2H, m, $CH_2CH_3$), 3.22 (1H, br s, Et-CHOH), 4.42 (1H, m, Et-CHOH), 4.50 (1H, d, $J$=5.1 Hz, 4-H), 6.63 (1H, br s, 3-OH), 7.13 (1H, td, $J$=7.5, 1.0 Hz, 6-H), 7.24—7.48 (5H, m, Ar-H), 7.63 (1H, d, $J$=7.8 Hz, 8-H), 8.12 (2H, m, 2′,6′-H). $^{13}$C-NMR $\delta$: 10.1 (C-12), 24.1 (C-11), 47.3 (C-4), 75.6 (C-10), 110.5 (C-8), 124.1 (C-6), 125.1 (C-5), 126.2 (C-2′, 6′), 127.3 (C-4′), 128.5 (C-3′, 5′), 128.7 (C-7), 131.4 (C-3), 133.1 (C-1′), 133.3 (C-4a), 135.5 (C-3a), 141.0 (C-8a), 142.9 (C-2).

**3-Hydroxy-4-hydroxymethyl-2-phenyl-4*H*-pyrazolo[1,5-*a*]indole (21)** Into a solution of the 3*H*-isomer **7** (248 mg, 1.00 mmol) in dry $CH_2Cl_2$ (20 ml) cooled to −40 °C was introduced a gentle stream of dry argon containing formaldehyde gas, which was generated by heating paraformaldehyde (300 mg, 10 mmol) at 200 °C.[14] After completion of the introduction, trifluoroborane etherate (0.13 ml, 1.06 mmol) was added to the solution and the reaction was continued at the same temperature for 10 min. The usual work-up and chromatographic purification (petroleum ether–ethyl acetate, 3 : 1) yielded **21** (212 mg, 76%), a white amorphous solid. MS *m/z*: 278 ($M^+$, 41), 260 (7), 248 (28), 247 (100), 219 (9), 145 (10), 144 (18), 143 (12), 129 (10), 117 (16), 116 (30), 115 (16), 104 (28), 89 (22), 77 (9). HRMS: Calcd for $C_{17}H_{14}N_2O_2$: 278.1055. Found $M^+$: 278.1062. IR: 3197, 3049, 2914, 1625, 1603, 1472, 1389, 1233, 1059, 747, 696 $cm^{-1}$. $^1$H-NMR (DMSO-$d_6$) $\delta$: 3.73 (1H, m, CHHOH, dd, $J$=10.3, 6.8 Hz after $D_2O$ exchange), 4.12 (1H, m, CHHOH, dd, $J$=10.3, 5.1 Hz after $D_2O$ exchange), 4.27 (1H, dd, $J$=6.8, 5.1 Hz, 4-H), 5.14 (1H, br s, $CH_2OH$), 7.19 (1H, td, $J$=7.5, 1.2 Hz, 6-H), 7.28 (1H, tt, $J$=7.3, 1.3 Hz, 4′-H), 7.36—7.47 (3H, m, Ar-H), 7.51 (1H, d, $J$=7.3 Hz, 8-H), 7.64 (1H, d, $J$=7.5 Hz, 5-H), 8.04 (2H, m, 2′,6′-H), 8.99 (1H, br s, 3-OH). $^{13}$C-NMR (DMSO-$d_6$) $\delta$: 43.2 (C-4), 61.2 (C-10), 109.0 (C-8), 123.8 (C-6), 125.5 (C-2′, 6′), 126.2 (C-5), 126.8 (C-4′), 128.1 (C-7), 128.2 (C-3′, 5′), 131.5 (C-3), 133.3 (C-1′), 135.2 (C-4a), 136.3 (C-3a), 139.7 (C-8a), 142.6 (C-2).

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