[Chem. Pharm. Bull. 34(9)3588—3594(1986)]

Reaction of 2-Methyl-4-phenyl-2,3-dihydro-1*H*-pyrazolo[2,3,4-*de*][1,5]-naphthyridine 2-Oxides with Acetic Anhydrides: Polonovski Reaction *versus* Mesomeric Betaine Formation

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(Received January 13, 1986)

Treatment of 2-methyl-4-phenyl-2,3-dihydro-1*H*-pyrazolo[2,3,4-*de*][1,5]naphthyridine 2-oxide (**10a**) with acetic anhydride and triethylamine or trifluoroacetic anhydride (TFAA) in the presence of dimethyl acetylenedicarboxylate (DMAD) gave the Polonovski reaction products **11**—**14** as the major products. The 3,4-diphenyl derivative **10b**, when treated with acetic anhydride and triethylamine either in the presence or the absence of DMAD, gave only the *O*-acetylhydroxylamine **17**, while treatment of the same *N*-oxide **10b** with TFAA in the presence of DMAD at −20 °C afforded the expected cycloadduct **22** as the major product.

Keywords——pyrazolo[1,5-*a*]pyridine; pyridine *N*-imide; amine *N*-oxide; heterocyclic mesomeric betaine; *O*-mesitylenesulfonylhydroxylamine; 1,3-dipolar cycloaddition; Polonovski reaction; pleiadiene analogue

The chemistry of heterocyclic mesomeric betaines has received considerable attention in recent years.[1] We have previously reported the synthesis and 1,3-dipolar cycloaddition reaction of such a mesomeric betaine **2**.[2] As a continuation of our work in this field, we have examined the reaction of 2-methyl-2,3-dihydro-4-phenyl-1*H*-pyrazolo[2,3,4-*de*][1,5]-naphthyridine 2-oxides (**10**) with acetic anhydride and trifluoroacetic anhydride (TFAA), in the hope that the closely related betaines **4** might be generated. Here we wish to report results obtained with the *N*-oxides **10a** and **10b**.

The synthetic route used for the preparation of the *N*-oxides **10a** and **10b** is outlined in Chart 2. 1,3-Dipolar cycloaddition of the *N*-aminopyridinium salt **6** with 3-phenyl-2-propynal (R=H) in the presence of potassium carbonate in acetonitrile gave the pyrazolo[1,5-*a*]pyridines **7a** (26%) and **8a** (12%) after separation by column chromatography. Structural differentiation of the two isomers can be readily made by ^{1}H-nuclear magnetic resonance (^{1}H-NMR) spectroscopy (see Experimental).[3] Deprotection of **7a** with 30% hydrogen bromide–acetic acid solution followed by treatment with formaldehyde and sodium cyanoborohydride

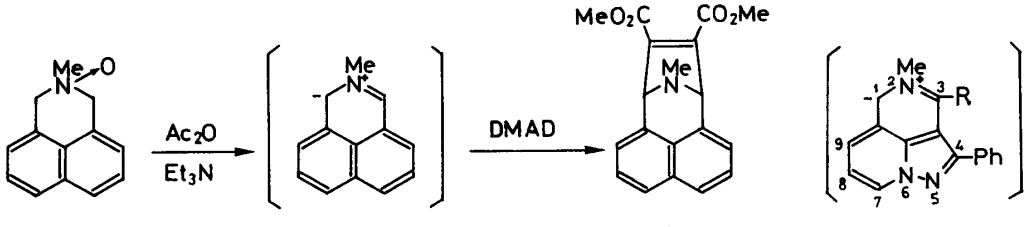

Chart 1

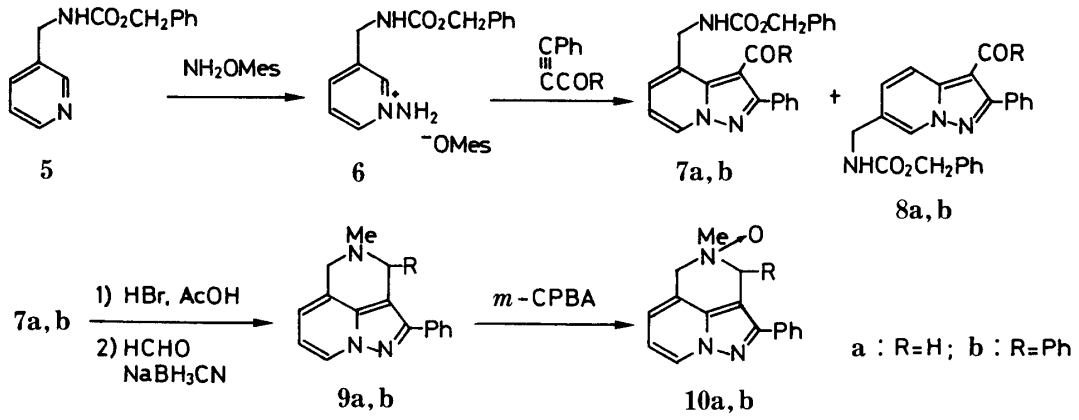

Chart 2

gave the tricyclic amine **9a** in 86% yield (from **7a**). Similarly, the tricyclic amine **9b** was prepared starting with the *N*-aminopyridinium salt **6** and 1,3-diphenyl-2-propyn-1-one (R = Ph). Oxidation of the amine **9a** with *m*-chloroperbenzoic aicd (*m*-CPBA) gave the desired *N*-oxide **10a**. Similar oxidation of the amine **9b** gave the corresponding *N*-oxide **10b** as a mixture of two stereoisomers.[4] These *N*-oxides **10a**, **b** were unstable in air and were used for the next reaction without further purification.

Treatment of the *N*-oxide **10a** with acetic anhydride and triethylamine in the presence of dimethyl acetylenedicarboxylate (DMAD) at $-10\,^{\circ}C$[2] gave an inseparable mixture of the Polonovski reaction products, **11** and **12** (69% total yield).[5,6] When the same *N*-oxide **10a** was allowed to react with TFAA in the presence of DMAD in methylene chloride at $-20\,^{\circ}C$, again the ring-opening products **13** (24%) and **14** (31%) were obtained as the major products. Structural differentiation between the isomeric pair, **13** and **14**, was made on the basis of the infrared (IR) carbonyl absorption; the absorption of the formyl group in the 3-formyl derivative **13** should appear at lower frequency than that in the 4-formyl derivative **14** because of the vinylogous amide structure in the former[3b] (1665 cm^{-1} for **13** *versus* 1690 cm^{-1} for **14**).

Apparently the Polonovski reaction is favored over the formation of the betaine **4a**. This result is in sharp contrast to the case of the *N*-oxide **1**, which gave only the cycloadduct **3** on treatment with acetic anhydride and triethylamine in the presence of DMAD.[2] This contrasting behavior of **10a** may be attributed, at least in part, to the ring strain resulting from the fusion of the five-membered ring, which may cause destabilization of **4a**.

We next examined the behavior of the 3,4-diphenyl derivative **10b**, because stabilization

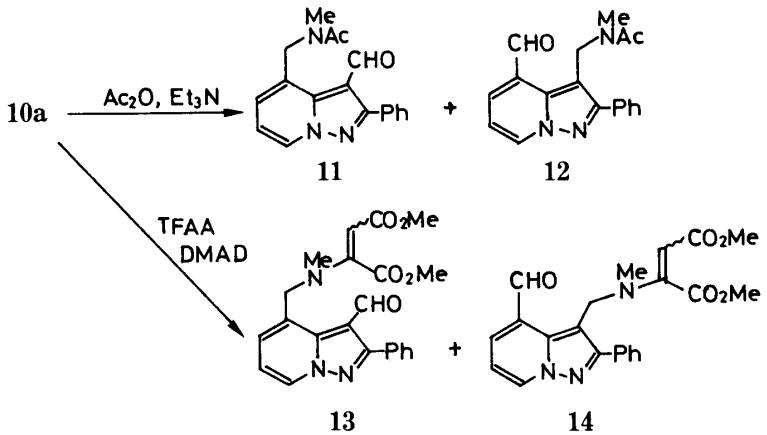

Chart 3

of the betaine **4b** by the phenyl group was expected. The *N*-oxide **10b**, however, when treated with acetic anhydride and triethylamine in the presence of DMAD at 0 °C, was found to give the *O*-acetylhydroxylamine **17** in 70% yield[6]; the expected cycloadduct was not detected in the reaction mixture. The structure of **17** was deduced from the following spectroscopic and chemical evidence. The IR spectrum (in $CHCl_3$) showed a strong carbonyl absorption at 1760 cm^{-1} and a hydroxyl stretching band at 3300 cm^{-1}. The NMR spectrum showed a broad singlet at δ 1.80 (3H, $OCOCH_3$), a singlet at δ 2.61 (3H, NCH_3), a broad singlet at δ 3.42 (2H, $ArCH_2N$), a broad signal between δ 6.1 and 6.4 (1H, OH), and a doublet at δ 6.18 (1H, J= 10 Hz, ArCHOH). Hydrolysis of **17** with 10% sodium hydroxide provided the hydroxylamine **18**, which gave positive tests with Tolens' reagent and triphenyltetrazolium chloride solution. Furthermore, treatment of **17** with chloroform containing 0.2% hydrogen chloride at room temperature resulted in the extrusion of benzaldehyde (identified by gas-liquid chromatography) to give **19** in quantitative yield.[7]

A posible mechanistic interpretation of the formation of **17** from **10b** involves an initial *O*-acetylation of **10b**. This step is followed by ring opening to give a resonance-stabilized carbenium ion intermediate **15**, which leads to the diacetate **16**. Hydrolysis of **16** during work-up would give **17**.

On the other hand, when the *N*-oxide **10b** was treated with TFAA at −20 °C in the

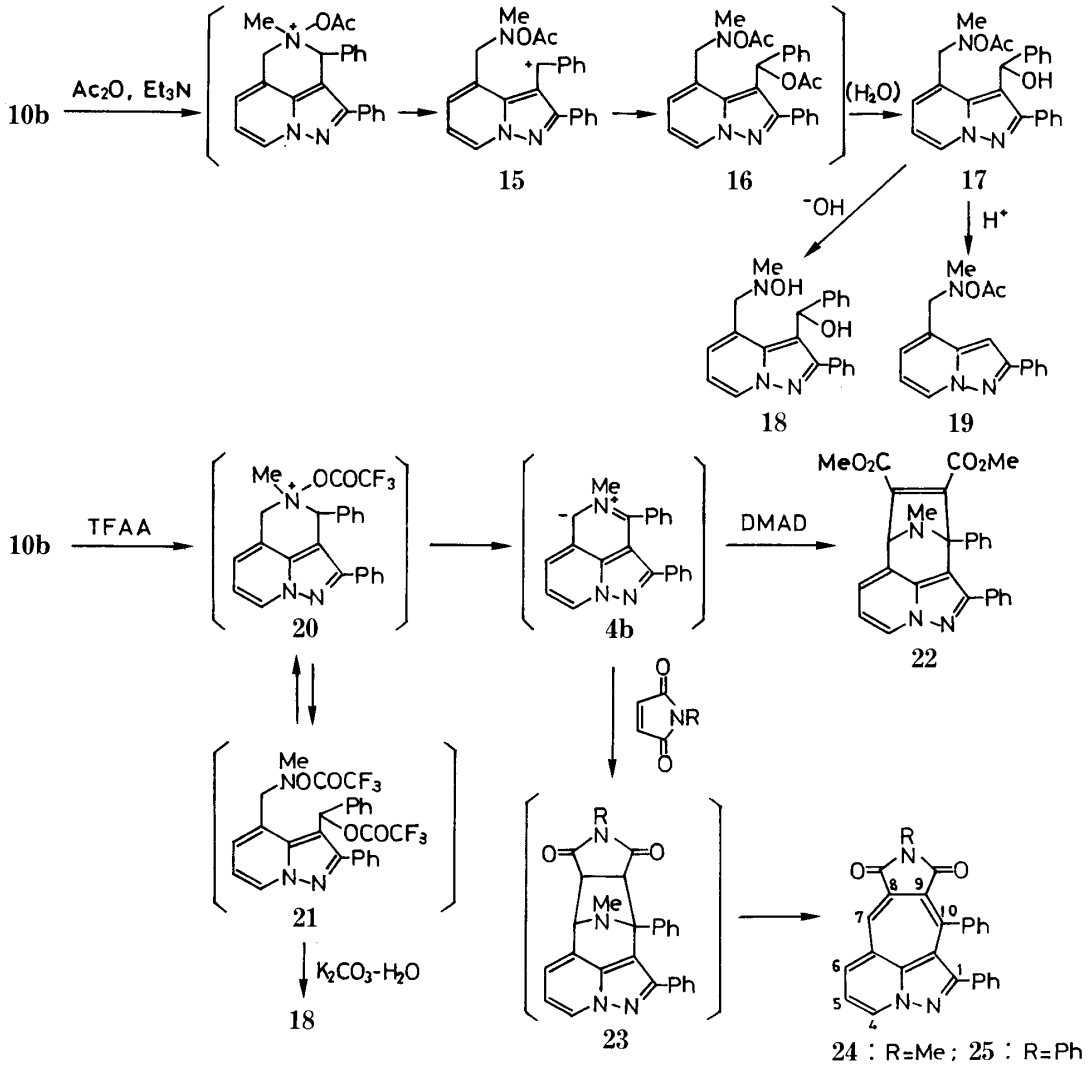

Chart 4

presence of DMAD, the expected cycloadduct **22** was obtained as the major product (33%), whose structure was assigned on the basis of the spectroscopic evidence (see Experimental). When this reaction was followed by thin layer chromatography (TLC), the formation of an unstable product was observed at the early stage of the reaction. Although all attempts to isolate this product were unsuccessful because of the lability of the product in air, the crude reaction mixture obtained from the reaction of **10b** with TFAA in methylene chloride at 0 °C was treated with aqueous potassium carbonate to give the hydroxylamine **18** in 55% yield. This fact, together with the finding that treatment of **10b** with acetic anhydride and triethylamine gave the *O*-acetylhydroxylamine **17**, suggests that this unstable product has the structure **21**.

The yield of the cycloadduct **22** was improved to 43% by the following procedure[8]: after **10b** was treated with TFAA in methylene chloride at 0 °C, the solvent was replaced with chlorobenzene[9] and the mixture was refluxed in the presence of DMAD. The remainder of the crude product was resinous. Interestingly, use of *N*-methyl- or *N*-phenylmaleimide in place of DMAD gave directly the corresponding pleiadiene analogue **24** (29%) or **25** (44%) as green crystals. Apparently the initial adduct **23** is thermally unstable and eliminates methylamine under the reaction conditions.

These results can be rationalized in terms of the intermediacy of **20** and **21**, which are in equilibrium under the reaction conditions. The intermediate **20** may then generate the mesomeric betaine **4b** which gives the cycloadducts **22**, **24**, and **25**. This view was supported by the fact that the hydroxylamine **18**, when refluxed in the presence of TFAA and DMAD in toluene, gave **22** (checked by TLC).

In summary, the present work has revealed that a new heterocyclic mesomeric betaine **4b** was generated *in situ* by treatment of the *N*-oxide **10b** with TFAA, but in the case of the *N*-oxide **10a**, the Polonovski reaction competes well with the betaine formation reaction.

Experimental[10]

3-[*N*-(Benzyloxycarbonyl)aminomethyl]pyridine (5)——Benzyl chloroformate (41.5 g, 0.24 mol) in $CHCl_3$ (85 ml) and 10% aqueous NaOH solution (92 ml) was added to a solution of 3-(aminomethyl)pyridine (25 g, 0.23 mol) in water (90 ml) under ice-cooling and stirring. The mixture was stirred at room temperature overnight. The $CHCl_3$ layer was separated and the aqueous layer was extracted with $CHCl_3$. The combined extract was reextracted with 10% HCl. The aqueous layer was washed with $CHCl_3$, then neutralized with solid K_2CO_3, and extracted with $CHCl_3$. The extract was dried ($MgSO_4$) and concentrated. The residual solid was recrystallized from benzene to give **5** (38.0 g, 68%), mp 72 °C. IR (KCl): 3180 (NH), 1720 (C=O) cm^{-1}. NMR ($CDCl_3$) δ: 4.38 (2H, d, J=6 Hz, $ArCH_2N$), 5.12 (2H, s, OCH_2Ph), 5.30 (1H, br s, NH), 7.23 (1H, dd, J=8, 5 Hz, H-5), 7.35 (5H, s, Ph), 7.62 (1H, br d, J=8 Hz, H-4), 8.50 (1H, dd, J=5, 2 Hz, H-6), 8.53 (1H, d, J=2 Hz, H-2). *Anal.* Calcd for $C_{14}H_{14}N_2O_2$: C, 69.40; H, 5.83; N, 11.56. Found: C, 69.47; H, 5.58; N, 11.52.

1-Amino-3-[*N*-(benzyloxycarbonyl)aminomethyl]pyridinium Mesitylenesulfonate (6)——A solution of *O*-mesitylenesulfonylhydroxylamine (MSH)[11] (21.5 g, 75% assay, 75 mmol) in CH_2Cl_2 (100 ml) was added dropwise to an ice-cooled solution of **5** (18.0 g, 74 mmol) in CH_2Cl_2 (150 ml) with stirring. The mixture was stirred at room temperature for 1 h, ether was added, and the precipitated crystals were collected and recrystallized from ethanol to give **6** (30.8 g, 91%), mp 139—140.5 °C. *Anal.* Calcd for $C_{23}H_{27}N_3O_5S$: C, 60.38; H, 5.95; N, 9.18. Found: C, 60.55; H, 5.96; N, 9.08.

4-[*N*-(Benzyloxycarbonyl)aminomethyl]-2-phenylpyrazolo[1,5-*a*]pyridine-3-carbaldehyde (7a) and 6-[*N*-(Benzyloxycarbonyl)aminomethyl]-2-phenylpyrazolo[1,5-*a*]pyridine-3-carbaldehyde (8a)——A suspension of K_2CO_3 (4.14 g, 0.03 mol) and **6** (4.60 g, 0.01 mol) in CH_3CN (100 ml) was stirred for 15 min, and then 3-phenyl-2-propynal (1.40 g, 11 mmol) was added. The reaction mixture was stirred at room temperature overnight. The insoluble material was filtered off and the filtrate was concentrated *in vacuo*. The residue was chromatographed on silica gel. Elution with benzene containing gradually increasing amounts of AcOEt gave **7a** (0.2 g, 26%) and **8a** (0.09 g, 12%).

Compound **7a**: mp 148—149 °C (from MeOH). IR ($CHCl_3$): 3400 (NH), 1660 (C=O) cm^{-1}. NMR ($CDCl_3$) δ: 4.77 (2H, d, J=7 Hz, $PhCH_2N$), 5.03 (2H, s, OCH_2Ph), 6.23 (1H, br t, J=7 Hz, NH), 7.07 (1H, t, J=7 Hz, H-6), 7.29 (5H, s, Ph), 7.5—7.8 (5H, m, Ph), 7.67 (1H, br d, J=7 Hz, H-5), 8.53 (1H, br d, J=7 Hz, H-7), 9.84 (1H, s, CHO). *Anal.* Calcd for $C_{23}H_{19}N_3O_3$: C, 71.67; H, 4.97; N, 10.90. Found: C, 71.94; H, 4.91; N, 10.93.

Compound **8a**: mp 133—134 °C (from MeOH). IR ($CHCl_3$): 3300 (NH), 1720 (C=O), 1660 (C=O) cm^{-1}. NMR ($CDCl_3$) δ: 4.44 (2H, d, J=6.5 Hz, $PhCH_2N$), 5.14 (2H, s, OCH_2Ph), 5.36 (1H, br s, NH), 7.33 (5H, s, Ph), 7.4—7.6, 7.7—7.8 (6H, m, Ph, H-5), 8.34 (1H, br d, J=9 Hz, H-4), 8.51 (1H, s, H-7), 10.40 (1H, s, CHO). *Anal.* Calcd for $C_{23}H_{19}N_3O_3$: C, 71.67; H, 4.97; N, 10.90. Found: C, 71.68; H, 4.83; N, 10.86.

3-Benzoyl-4-[*N*-(benzyloxycarbonyl)aminomethyl]-2-phenylpyrazolo[1,5-*a*]pyridine (7b) and 3-Benzoyl-6-[*N*-(benzyloxycarbonyl)aminomethyl]-2-phenylpyrazolo[1,5-*a*]pyridine (8b)——By using a similar procedure to that described above for the preparation of **7a** and **8a**, **7b** (5.8 g, 43%) and **8b** (1.6 g, 12%) were obtained from **6** (13.5 g, 0.03 mol) and 1,3-diphenyl-2-propyn-1-one (6.3 g, 0.03 mol).

Compound **7b**: mp 152—153 °C (from AcOEt). IR ($CHCl_3$): 3275 (NH), 1710 (C=O), 1640 (C=O) cm^{-1}. NMR ($CDCl_3$) δ: 4.49 (2H, d, J=7 Hz, $PhCH_2N$), 5.03 (2H, s, OCH_2Ph), 6.28 (1H, t, J=7 Hz, NH), 6.95 (1H, t, J=7 Hz, H-6), 7.1—7.4, 7.6—7.7 (19H, m, Ph), 7.48 (1H, br d, J=7 Hz, H-5), 8.52 (1H, dd, J=7, 1 Hz, H-7). *Anal.* Calcd for $C_{29}H_{23}N_3O_3$: C, 75.47; H, 5.02; N, 9.11. Found: C, 75.57; H, 5.03; N, 9.10.

Compound **8b**: mp 150—151 °C (from AcOEt). IR ($CHCl_3$): 3225 (NH), 1720 (C=O), 1640 (C=O) cm^{-1}. NMR ($CDCl_3$) δ: 4.44 (2H, d, J=6.5 Hz, $PhCH_2N$), 5.14 (2H, s, OCH_2Ph), 5.30 (1H, br s, NH), 7.1—7.2 (5H, m, Ph), 7.3—7.4, 7.5—7.6 (6H, m, Ph, H-5), 7.96 (1H, br d, J=9 Hz, H-4), 8.51 (1H, s, H-7). *Anal.* Calcd for $C_{29}H_{23}N_3O_3$: C, 75.47; H, 5.02; N, 9.11. Found: C, 75.56; H, 4.85; N, 9.03.

2-Methyl-4-phenyl-2,3-dihydro-1*H*-pyrazolo[2,3,4-*de*][1,5]naphthyridine (9a)——A mixture of **7a** (1.90 g, 5 mmol) and 30% HBr in AcOH (5.4 ml, 20 mmol) was allowed to stand at room temperature overnight with occasional agitation. The precipitated crystals were collected, washed with ether and suspended in MeOH (50 ml). An aqueous 10% K_2CO_3 solution was added to the suspension until the pH became 7, then $NaBH_3CN$ (314 mg, 5 mmol) was added and the reaction mixture was stirred at room temperature for 3 h. A 37% aqueous solution of HCHO (1.2 ml, 15 mmol) was added to the stirred solution. After 15 min, the solvent was distilled off *in vacuo* and the residue was dissolved in H_2O (10 ml). The solution was extracted with $CHCl_3$ and the extract was washed with brine, dried ($MgSO_4$), and concentrated. The residue was chromatographed [silica gel; benzene–AcOEt (20 : 3)] to give **9a** (1.1 g, 86%) as a powder. NMR ($CDCl_3$) δ: 2.62 (3H, s, NCH_3), 3.82 (2H, s, H-1), 4.10 (2H, s, H-3), 6.65 (1H, t, J=7 Hz, H-8), 6.74 (1H, dd, J=7, 1 Hz, H-9), 7.3—7.5, 7.7—7.9 (5H, m, Ph), 8.24 (1H, dd, J=7, 1 Hz, H-7). It formed the picrate, mp 196—199 °C (from CH_3CN). *Anal.* Calcd for $C_{22}H_{18}N_6O_7$: C, 55.23, H, 3.79; N, 17.57. Found: C, 55.47; H, 3.84; N, 17.47.

2-Methyl-3,4-diphenyl-2,3-dihydro-1*H*-pyrazolo[2,3,4-*de*][1,5]naphthyridine (9b)——By using a similar procedure to that described above for the preparation of **9a**, **9b** (1.6 g, 76%) was obtained from **7b** (3.0 g, 6.5 mmol), mp 171—172 °C (from MeOH). NMR ($CDCl_3$) δ: 2.42 (3H, s, NCH_3), 3.60, 3.82 (1H each, ABq, J=16 Hz, H-1), 5.27 (1H, s, H-3), 6.74 (1H, t, J=7 Hz, H-8), 6.80 (1H, br d, J=7 Hz, H-9), 7.2—7.4, 7.7—7.8 (10H, m, 2 × Ph), 8.35 (1H, d, J=7 Hz, H-7). *Anal.* Calcd for $C_{22}H_{19}N_3$: C, 81.20; H, 5.89; N, 12.91. Found: C, 81.11; H, 5.80; N, 12.97.

2-Methyl-4-phenyl-2,3-dihydro-1*H*-pyrazolo[2,3,4-*de*][1,5]naphthyridine 2-Oxide (10a)——*m*-CPBA (798 mg, 85% assay, 3.8 mmol) was added to a cooled solution of **9a** (890 mg, 3.6 mmol) in CH_2Cl_2 (35 ml) and the mixture was stirred at room temperature overnight, then extracted successively with 3% Na_2SO_3, saturated $NaHCO_3$, and H_2O. The aqueous extracts were combined and washed with CH_2Cl_2. The aqueous layer was concentrated *in vacuo*, and the residue was extracted with EtOH. The extract was concentrated to give a syrup, which was dissolved in $CHCl_3$. The extract was dried ($MgSO_4$) and concentrated to give **10a** (638 mg, 67%); mp 117—123 °C (dec.) (from CH_2Cl_2–ether). NMR ($CDCl_3$) δ: 3.20 (3H, s, NCH_3), 4.60, 4.84 (1H each, ABq, J=15 Hz, H-1), 4.95, 5.09 [1H each, ABq with a further small splitting (J=1 Hz) of the higher doublet, J=15 Hz, H-3], 6.83 (1H, t, J=7 Hz, H-8), 6.99 (1H, dd, J=7, 1 Hz, H-9), 7.3—7.6, 7.7—7.8 (5H, m, Ph), 8.38 (1H, d, J=7 Hz, H-7). Since this compound was unstable, the crude product was used for the next step without further purification.

2-Methyl-3,4-diphenyl-2,3-dihydro-1*H*-pyrazolo[2,3,4-*de*][1,5]naphthyridine 2-Oxide (10b)——*m*-CPBA (0.80 g, 85% assay, 3.9 mmol) was added to a solution of **9b** (1.15 g, 3.5 mmol) in CH_2Cl_2 (35 ml) and the mixture was stirred at room temperature overnight, then washed successively with 3% Na_2SO_3, aqueous $NaHCO_3$, and H_2O. The organic solution was dried (Na_2SO_4), and the solvent was evaporated off. The residue was dissolved in a small amount of CH_2Cl_2, and ether was added to the solution. The precipitated solid was collected to give **10b** (630 mg, 53%), which was shown to be a mixture of two diastereoisomers. A portion of the mixture was subjected to preparative TLC [silica gel: $CHCl_3$–MeOH (20 : 1)] to give two products in a ratio of 4 : 1.

The major isomer of **10b**: mp 107—110 °C (dec.) (from CH_2Cl_2–ether). NMR ($CDCl_3$) δ: 3.24 (3H, s, NCH_3), 4.22, 4.59 (1H each, ABq, J=16 Hz, H-1), 5.65 (1H, s, H-3), 6.90 (1H, t, J=7 Hz, H-8), 7.03 (1H, br d, J=7 Hz, H-9), 7.2—7.6 (10H, m, 2 × Ph), 8.45 (1H, d, J=7 Hz, H-7).

The minor isomer of **10b**: mp 89—91 °C (dec.) (from benzene). NMR ($CDCl_3$) δ: 3.23 (3H, s, NCH_3), 4.45, 4.75 (1H each, ABq, J=14 Hz, H-1), 5.92 (1H, s, H-3), 6.86 (1H, t, J=7 Hz, H-8), 7.04 (1H, br d, J=7 Hz, H-9), 7.2—7.6 (10H, m, 2 × Ph), 8.43 (1H, d, J=7 Hz, H-7).

Since **10b** was unstable, the crude mixture was used directly for the next reaction.

Reaction of 10a with Acetic Anhydride in the Presence of DMAD——The *N*-oxide **10a** (88 mg, 0.33 mmol) was added to a solution of DMAD (94 mg, 0.66 mmol) and triethylamine (0.09 ml) in acetic anhydride (4 ml) at −10 °C. The mixture was stirred at −10 °C for 80 min, then the acetic anhydride was evaporated off below 50 °C *in vacuo* and

the residue was diluted with H_2O and extracted with $CHCl_3$. The extract was dried ($MgSO_4$) and concentrated. The residue was subjected to preparative TLC [silica gel; benzene–AcOEt (1 : 1)] to give an inseparable mixture of 4-(*N*-acetyl-*N*-methylamino)methyl-2-phenylpyrazolo[1,5-*a*]pyridine-3-carbaldehyde (**11**) and 3-(*N*-acetyl-*N*-methylamino)methyl-2-phenylpyrazolo[1,5-*a*]pyridine-4-carbaldehyde (**12**) (68 mg, 69%) as a pale yellow powder. IR ($CHCl_3$): 1685 (C=O), 1640 (C=O) cm^{-1}. NMR ($CDCl_3$) δ: 1.90, 1.95 (3H, 2 : 1, s, $COCH_3$), 2.53, 2.54 (3H, 2 : 1, s, NCH_3), 5.06, 5.13 (2H, 1 : 2, s, $ArCH_2N$), 6.87, 6.94 (1H, 2 : 1, t, J=7 Hz, H-6), 7.3—7.6 (5H, m,Ph), 7.74, 7.75 (1H, 2 : 1, br d, J=7 Hz, H-5), 8.59, 8.63 (1H, 2 : 1, br d, J=7 Hz, H-7), 9.90, 10.08 (1H, 1 : 2, s, CHO). *Anal.* Calcd for $C_{18}H_{17}N_3O_2$: C, 70.34; H, 5.58; N, 13.67. Found: C, 70.22; H, 5.49; N, 13.57.

Reaction of 10a with TFAA in the Presence of DMAD——The *N*-oxide **10a** (133 mg, 0.5 mmol) was added to a solution of DMAD (143 mg, 1 mmol) in TFAA (5 ml) at −20 °C. The mixture was stirred at −20 °C for 2.5 h and left at room temperature overnight. Excess TFAA was evaporated off *in vacuo* below 30 °C and the residue was dissolved in H_2O (6 ml). The solution was neutralized with solid K_2CO_3 and extracted with $CHCl_3$. The extract was washed with brine, dried ($MgSO_4$), and concentrated. The residue was chromatographed [silica gel: benzene–AcOEt (20 : 3)] to give dimethyl *N*-methyl-*N*-(3-formyl-2-phenylpyrazolo[2,3-*a*]pyrid-4-ylmethyl)amino-2-butenedioate (**13**) (48 mg, 24%), and dimethyl *N*-methyl-*N*-(4-formyl-2-phenylpyrazolo[2,3-*a*]pyrid-3-ylmethyl)amino-2-butenedioate (**14**) (64 mg, 31%).

Compound **13**: mp 163—164.5 °C (from MeOH). IR ($CHCl_3$): 1740 (C=O), 1690 (C=O), 1665 (C=O) cm^{-1} NMR ($CDCl_3$) δ: 2.96 (3H, s, NCH_3), 3.63, 3.92 (3H each, 2 × s, 2 × OCH_3), 4.68 (1H, s, vinylic H), 5.16 (2H, s, $ArCH_2N$), 7.10 (1H, t, J=7 Hz, H-6), 7.36 (1H, dd, J=6, 1 Hz, H-5), 7.4—7.7 (5H, m, Ph), 8.51 (1H, dd, J=7, 1 Hz, H-7), 9.88 (1H, s, CHO). MS *m/z* (rel. int., %): 407 (M^+, 10), 375 (3), 348 (6), 305 (2), 235 (100). *Anal.* Calcd for $C_{22}H_{21}N_3O_5$: C, 64.85; H, 5.20; N, 10.31. Found: C, 64.94; H, 5.04; N, 10.33.

Compound **14**: mp 156—157 °C (from MeOH). IR ($CHCl_3$): 1740 (C=O), 1690 (C=O) cm^{-1}. NMR ($CDCl_3$) δ: 2.57 (3H, s, NCH_3), 3.64, 3.88 (3H each, 2 × s, 2 × OCH_3), 4.76 (1H, s, vinylic H), 4.78 (2H, s, $ArCH_2N$), 7.01 (1H, t, J=7 Hz, H-6), 7.4—7.7 (5H, m, Ph), 7.84 (1H, dd, J=7, 2 Hz, H-5), 8.72 (1H, s, dd, J=7, 2 Hz, H-7), 10.04 (1H, s, CHO). MS *m/z* (rel. int., %): 407 (M^+, 18), 369 (9), 346 (24), 345 (17), 333 (7), 316 (12), 305 (12), 266 (6), 262 (6), 234 (100). *Anal.* Calcd for $C_{22}H_{21}N_3O_5$: C, 64.85; H, 5.20; N, 10.31. Found: C, 64.91; H, 5.29; N, 10.24.

4-(*N*-Acetoxy-*N*-methylamino)methyl-2-phenylpyrazolo[1,5-*a*]pyridine-3-(α-phenyl)methanol (17)——Compound **10b** (250 mg, 0.7 mmol) was added to an ice-cooled solution of triethylamine (0.1 ml, 0.7 mmol) and acetic anhydride (7 ml), and the solution was stirred at 0 °C for 1.5 h. Excess acetic anhydride was evaporated off below 40 °C and the residue was dissolved in H_2O (4 ml). The solution was neutralized with solid K_2CO_3 and extracted with $CHCl_3$. The extract was washed with brine, dried ($MgSO_4$), and concentrated. The residue was recrystallized from benzene–*n*-hexane to give **17** (207 mg, 70%): mp 157—164 °C (dec.). IR ($CHCl_3$): 3300 (OH), 1760 (C=O) cm^{-1}. NMR ($CDCl_3$) δ: 1.80 (3H, br s, $COCH_3$), 2.61 (3H, s, NCH_3), 3.42 (2H, br s, $ArCH_2N$), 6.1—6.4 (1H, br, OH), 6.18 (1H, d, J=10 Hz, ArCHOH), 6.68 (1H, t, J=7 Hz, H-6), 6.95 (1H, br d, J=7 Hz, H-5), 7.1—7.5, 7.65—7.75 (10H, m, 2 × Ph), 8.50 (1H, dd, J=7, 1 Hz, H-7). *Anal.* Calcd for $C_{24}H_{23}N_3O_3$: C, 71.80; H, 5.78; N, 10.47. Found: C, 71.70; H, 5.80; N, 10.38.

4-(*N*-Hydroxy-*N*-methylamino)methyl-2-phenylpyrazolo[1,5-*a*]pyridine-3-(α-phenyl)methanol (18)——(a) From **17**: A suspension of **17** (76 mg, 0.2 mmol) in 10% NaOH (3 ml) was stirred at room temperature for 5 h and the separated crystals were collected (52 mg). The mother liquor was saturated with NaCl, extracted with CH_2Cl_2, and dried (Na_2SO_4). Evaporation of the solvent gave additional crystals (15 mg). The crystals were combined and purified by chromatography (silica gel: $CHCl_3$) to give **18** (43 mg, 63%): mp 190—199 °C (from CH_2Cl_2). IR (Nujol): 3100 (OH) cm^{-1}. NMR ($CDCl_3$) δ: 1.60 (2H, br s, 2 × OH), 2.43 (3H, s, NCH_3), 3.20 (2H, m, $ArCH_2N$), 6.10 (1H, s, ArCHOH), 6.72 (1H, t, J=7 Hz, H-6), 6.94 (1H, br d, J=7 Hz, H-5), 7.2—7.5, 7.6—7.7 (10H, m, 2 × Ph), 8.51 (1H, br d, J=7 Hz, H-7). *Anal.* Calcd for $C_{22}H_{21}N_3O_2 \cdot 1/2H_2O$: C, 71.72; H, 6.02; N, 11.41. Found: C, 71.43; H, 5.98; N, 11.19.

(b) From **10b**: An ice-cooled solution of the *N*-oxide **10b** (300 mg, 0.9 mmol) in dry CH_2Cl_2 (9 ml) and TFAA (0.74 ml, 5.4 mmol) was stirred for 4 h and then 10% aqueous K_2CO_3 solution was added to adjust the pH to 8. The mixture was allowed to stand at room temperature for 2 d and work-up as described above gave **18** (50 mg, 54%): mp 190—199 °C.

4-(*N*-Acetoxy-*N*-methylamino)methyl-2-phenylpyrazolo[1,5-*a*]pyridine (19)——A solution of **17** (101 mg, 0.25 mmol) in $CHCl_3$ (5 ml) containing 0.2% HCl was allowed to stand at room temperature for 4 h. The solvent was evaporated off *in vacuo* to give a syrup, which was purified by preparative TLC [silica gel: benzene–AcOEt (5 : 1)] to give an oil, which was distilled at bp 109—116 °C (0.75 mmHg) (bath temperature) to give **19** (65 mg, 86%). IR ($CHCl_3$): 1755 (C=O) cm^{-1}. NMR ($CDCl_3$) δ: 1.94 (3H, s, $COCH_3$), 2.85 (3H, s, NCH_3), 4.18 (2H, s, $ArCH_2N$), 6.67 (1H, t, J=7 Hz, H-6), 7.01 (1H, s, H-3), 7.09 (1H, br d, J=7 Hz, H-5), 7.2—7.5, 7.9—8.0 (5H, m, Ph), 8.38 (1H, br d, J=7 Hz, H-7). Exact MS *m/z*: Calcd for $C_{17}H_{17}N_3O_2$: 295.1321. Found: 295.1318.

Dimethyl 6,9-Imino-10-methyl-1,9-diphenyl-6,9-dihydro-2,2a-diazabenz[*c*,*d*]azulene-7,8-dicarboxylate (22)——(a) By using a similar procedure to that described for the reaction of **10a** with TFAA, the *N*-oxide **10b** (34 mg, 0.1 mmol) was treated with TFAA (1.5 ml) in the presence of DMAD (0.025 ml, 0.2 mmol). Work-up gave **22** (15 mg, 33%): mp 182—183.5 °C (from isopropanol). IR (KCl): 1720 (C=O) cm^{-1}. NMR ($CDCl_3$) δ: 1.78 (3H, s, NCH_3),

3.72, 3.75 (3H each, 2 × s, 2 × OCH_3), 5.08 (1H, s, H-7), 6.90 (1H, t, J=7 Hz, H-5), 7.0—7.4, 7.5—7.6 (11H, m, H-6 and 2 × Ph), 8.44 (1H, dd, J=7, 1 Hz, H-4). *Anal.* Calcd for $C_{28}H_{23}N_3O_4$: C, 72.25; H, 4.98; N, 9.03. Found: C, 72.37; H, 5.09; N, 8.96.

(b) TFAA (0.04 ml, 0.3 mmol) was added to an ice-cooled solution of **10b** (34 mg, 0.1 mmol) in dry CH_2Cl_2 with stirring. The mixture was stirred for 5 h at the same temperature, then chlorobenzene (3 ml) and DMAD (0.025 ml, 0.2 mmol) were added, and the mixture was refluxed for 1 h, during which time CH_2Cl_2 and the excess of TFAA were blown off under a stream of argon. Chlorobenzene was evaporated off *in vacuo*, and the residue was subjected to preparative TLC [silica gel; benzene–AcOEt (5 : 1)] to give **22** (20 mg, 43%).

***N*-Methyl-1,10-diphenylcyclohepta[*hi*]pyrazolo[1,5-*a*]pyridine-8,9-dicarboximide (24)**——TFAA (0.04 ml, 0.3 mmol) was added to an ice-cooled solution of **10b** (34 mg, 0.1 mmol) in CH_2CH_2 (5 ml) with stirring. The mixture was stirred at the same temperature for 30 min, then toluene (8 ml) and *N*-methylmaleimide (11.3 mg, 0.1 mmol) were added and the mixture was refluxed for 1 h, during which time CH_2Cl_2 and the excess TFAA were blown off under a stream of argon. Toluene was evaporated off *in vacuo* and the residue was purified by preparative TLC [silica gel; benzene–AcOEt (5 : 1)] to give **24** (12 mg, 29%): mp above 250 °C (dec.) (from CH_2Cl_2–isopropanol) as green crystals. IR (Nujol): 1745 (C=O), 1695 (C=O) cm^{-1}. UV $\lambda_{max}^{CHCl_3}$ nm (log ε): 320 (3.95), 335 (3.94), 372 (4.18), 389 (4.33), 410 (4.30), 500 (2.78), 540 (2.87), 585 (2.81), 640 (2.57). NMR ($CDCl_3$) δ: 2.86 (3H, s, NCH_3), 6.19 (1H, dd, J=7, 1.5 Hz, H-6), 6.26 (1H, t, J=7 Hz, H-5), 6.43 (1H, s, H-7), 6.6—7.0 (10H, m, 2 × Ph), 7.53 (1H, dd, J=7, 1.5 Hz, H-4). *Anal.* Calcd for $C_{26}H_{17}N_3O_2$: C, 77.40; H, 4.25; N, 10.42. Found: C, 77.16; H, 4.13; N, 10.35.

1,10,*N*-Triphenylcyclohepta[*hi*]pyrazolo[1,5-*a*]pyridine-8,9-dicarboximide (25)——By using a similar procedure to that described for the preparation of **24**, **25** (21 mg, 44%) was obtained from **10b** (34 mg, 0.1 mmol) and *N*-phenylmaleimide (17 mg, 0.1 mmol): mp above 250 °C (from CH_2Cl_2–isopropanol) as green crystals. IR (Nujol): 1745 (C=O), 1695 (C=O) cm^{-1}. UV $\lambda_{max}^{CHCl_3}$ nm (log ε): 320 (3.88), 370 sh (3.88), 390 (3.95), 410 (3.91), 507 sh (2.44), 547 (2.51), 650 (2.06). NMR ($CDCl_3$) δ: 6.18 (1H, dd, J=7, 1.5 Hz, H-6), 6.25 (1H, t, J=7 Hz, H-5), 6.50 (1H, s, H-7), 6.7—7.0 (10H, m, 2 × Ph), 7.1—7.4 (5H, m, Ph), 7.54 (1H, dd, J=7, 1.5 Hz, H-4). *Anal.* Calcd for $C_{31}H_{19}N_3O_2$: C, 79.98; H, 4.11; N, 9.03. Found: C, 79.87; H, 3.80; N, 8.87.

Acknowledgement The authors thank Mrs. T. Minematsu and Mr. Z. Morita for the measurements of the NMR and mass spectra, respectively.

References and Notes

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