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TOTAL SYNTHESIS OF 13- AND 14-AZAEQUILENINES VIA HETEROCYCLOADDITION

W. A. ZUNNEBELD[1] and W. N. SPECKAMP*
Laboratory for Organic Chemistry, University of Amsterdam, Nieuwe Achtergracht 129, Amsterdam, The Netherlands

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Abstract—Benzo-[f]-quinolines and benzo-[f]-isoquinolines were prepared via heterocycloaddition of N-butyloxycarbonylmethylenetoluene sulfonamide to a vinyl dihydronaphthalene. Structural assignments were based on PMR and mass spectral analysis. 13- and 14-aza-equilenines have been obtained via standard procedures starting from the respective adducts.

INTRODUCTION

An attractive and frequently used method for the synthesis of polynuclear carbocyclic systems is the $4\pi_s + 2\pi_s$ cycloaddition. While the synthetic utility of this method has been demonstrated abundantly over a period of more than 40 years, the complementary heterocyclic procedure in which the dienophile component has the imine structure still awaits development of its intrinsic potential as a general procedure for heterocyclic synthesis.[2] In this communication some observations on the recently described[3] N-alkyloxycarbonyl-methylene sulfonamides **1** are reported.

Condensation of **1** with 1-vinyl-6-methoxy-3,4-dihydronaphthalene (**2**) at 0° gave a 3:1 mixture of positional isomers **3a** and **3b** in quantitative yield. Upon carrying out the reaction at room temperature, however, in addition to **3a** and **3b** the isomerized adducts **4a** and **4b** were also found, although the combined yield of adducts was considerably lower.

Most likely at higher temperature the acid catalyzed isomerization of the C_1–C_{10b} double bond in the initially formed cycloadducts and the dimerization of diene **2** are both competing processes. Small impurities in the imine, such as its hydrated form, serve as the acid catalyst for both side reactions as was convincingly demonstrated in the following way: stirring a mixture of **3a** and **3b** overnight in presence of the sulfonamide **5** gave a mixture of **3a**, **3b**, **4a** and **4b**. Furthermore dimerization of **2** occurred to an appreciable extent after addition of **5** $BuOOC-\underset{OH}{\overset{H}{C}}-\overset{H}{N}-SO_2ArCH_3$ at r.t. to a solution of **2** in benzene of about the same concentration as used in the cycloaddition process.

As separation of the adducts **3a** and **3b** proved tedious, the crude mixture was treated with sodium ethoxide in ethanol during which process elimination of the sulfinic acid[3] residue took place. Hydrolysis of the disproportionation sensitive dihydropyridine esters (*vide infra*) gave a mixture of pyridine carboxylic acids which could be readily separated via acidification to $p_H < 1$ affording the acid **6b** as a crystalline solid. When the remaining solution was made less acidic $-p_H \approx 5$—the acid **6a** crystallized. Alternatively, separation could be effected via fractional crystallization from methanol, isomer **6a** being virtually insoluble. Esterification of the respective acids (CH_2N_2/CH_3OH[4] or Ag_2O/C_2H_5I[5] inhomogeneously) gave the corresponding methyl and ethyl esters **7** and **8**.

Structural proofs for the pyridine carboxylic acids **6a** and **6b** and the corresponding esters **7a** and **7b** were based on the examination of PMR and mass spectral data. In the PMR spectrum the pyridine protons of **6a** form an AB quartet (CF_3COOH; $J_{H_1H_2} = 6{\cdot}5$ Hz) while for **6b** and AB quartet (CF_3COOH; $J_{H_1H_2} = 8{\cdot}5$ Hz) was found. The corresponding ester **7a** showed also an AB quartet for H_1 and H_2 ($CDCl_3$; δH_1 7·59, δH_2 8·50 $J_{H_1H_2} = 5{\cdot}0$ Hz). For **7b** H_1 and H_2 were observed as a singlet ($CDCl_3$; δH_1H_2 7·95) which upon change of solvent again gave an AB quartet (C_6D_6; $J_{H_1H_2} = 8{\cdot}0$ Hz). The observed J-values are in accord with the expected substitution pattern.[6]

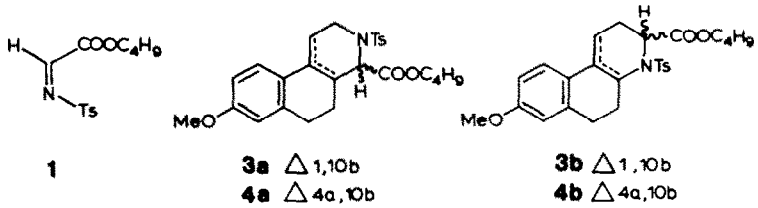
In addition the mass spectra of both **7a** and **8a** showed a characteristic fragmentation pattern which is summarized in Scheme 1. Due to the proximity of an α-CH_2 substituent, hydrogen transfer to the CO group is taking place thus inducing a series of consecutive fragmentations all for which appropriate metastable peaks were found. The mass spectra of esters **7b** and **8b** showed exclusively the well-documented ortho fragmentation,[7] Scheme 2, which resulted in the formation of a stable $m/e = 211$ fragment.

Via routine methods the esters **7b** and **8a** were converted to the corresponding hydroxypropionates **10a** and **10b**; however, attempts to hydrogenate the pyridine ring selectively were unsuccessful.

The formation of both types of adducts **3a** and **3b** could be interpreted in terms of absence of major electronic effects in the transition state. On the other hand, both the diene[8] as well as the imine[9] have been shown to add in a regioselective manner. Formation of a major amount of the expected adduct **3a** is in accord with predictions based upon the latter behaviour. A slight reversal in the mode of addition can be understood if steric factors, viz. a hindrance of the C_5-methylene and the ester function are operative. It can be demonstrated[10] that the importance of this factor is greatly determined by the size of the carbon substituent in the imine which in turn effectively governs the direction of addition.

A second point of interest is found in a comparison of the yields of adducts **3a** + **3b** and the amount of pyridine carboxylic acids **6a** + **6b** the latter never exceeding 50% of the starting material thus pointing to the aforementioned

*To whom all inquiries should be directed.

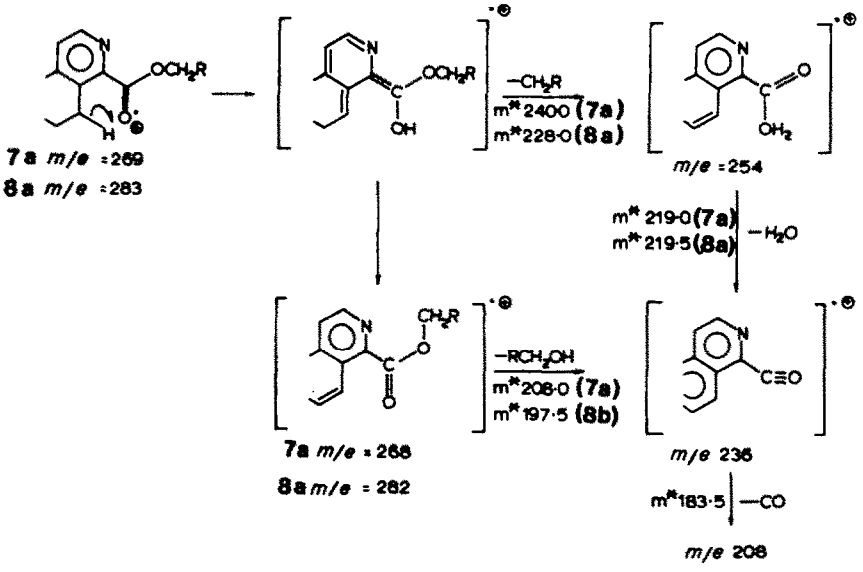


1 **3a** △1,10b; **4a** △4a,10b **3b** △1,10b; **4b** △4a,10b

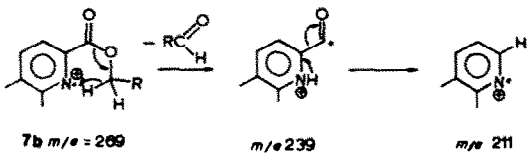
6a R=COOH; **7a** R=COOMe; **8a** R=COOEt; **9a** R=C(=O)–CH$_2$COOEt; **10a** R=C(OH)H–CH$_2$COOEt

6b R=COOH; **7b** R=COOMe; **8b** R=COOEt; **9b** R=C(=O)–CH$_2$COOMe; **10b** R=C(OH)H–CH$_2$COOMe

11 R=H; **12** R=Me **13**



Scheme 1



Scheme 2

disproportionation of the initially formed dihydropyridines. A chemical proof for this process to occur is taken from the isolation of the amino acid **11** from the reaction mixture although its yield did not account for the remaining half of adduct material. Presumably other decomposition pathways and/or air oxidation may also play a role in the aromatization.

During the treatment of **6a** with CH_2N_2 a crystalline material was formed which upon consideration of its

spectral characteristics was assigned the betaine structure **13**. Corroborative evidence was obtained via its $NaBH_4$ reduction to amino acid **12** which possessed spectral data similar in all respects to those obtained from the unsubstituted parent compound **11**.

LAH reduction of the mixture of **3a** + **3b** gave in nearly quantitative yield a mixture of the corresponding alcohols; separation of it proved to be tedious* and while other approaches to this type of system were more convenient this route was not further pursued.

Benzo[f]quinolines and benzo[f]isoquinolines. To obtain the aza-aromatic systems **15a** and **15b** dehydrogenation of esters **7a** and **8b** was carried out. Although **8b** was smoothly converted into the corresponding ester **15b** upon oxidation with SeO_2/dioxane,[11] dehydrogenation of **7a** under a variety of circumstances gave mixtures of decarboxylated product **13a** and ester **15a**. The difficulty in obtaining the aromatized system is also indicated in similar dihydrophenanthrene derivatives.[12] An alternative route was found in the reaction of **7a** with two eqiv. of N-bromosuccinimide[13] which afforded quantitatively the bromo-ester **14a** which in turn was smoothly debrominated via hydrogenation (Pd/C–HOAc)[14] to **15a**. Evidently **14a** is formed via aromatic bromination, bromine being formed upon HBr-induced decomposition of NBS.

Both esters were converted to the corresponding condensation products **16a** and **16b** in the usual manner which upon hydrogenation (Pt–HOAc/75°/100 atm) gave the 13- and 14-aza-equilenines **17** and **19**. In order to facilitate the interpretation of its PMR spectrum **17** was acetylated to the acetoxy-steroid **18** obtained as a single stereoisomer. The available PMR data—$J_{NCH\text{-}CHO}$ = 4·5 Hz—do not permit a rigid conclusion on the stereochemistry of the compound.

The presently described method can be considered as an attractive pathway for the synthesis of polycondensed heterocyclics. Further information about the scope and limitations of the method is given in accompanying papers.

EXPERIMENTAL

M.ps are not corrected. IR spectra were taken on a Unicam SP-200 as KBr tablets. The NMR spectra were determined on a Varian HA-100 in $CDCl_3$, unless otherwise stated, with TMS as internal standard, δ values are given in ppm. Mass spectra were obtained on an AEI mass-spectrometer type MS 9-H. The UV spectra were measured on a Cary-14 in EtOH.

N - (*Butyloxycarbonylmethylene*) - p - *toluene sulfonamide* **1**. N - sulfinyl - *p* - toluene sulfonamide (70 g) and butyl glyoxylate (freshly distilled over P_2O_5 42 g) in 100 ml benzene were refluxed until evolution of SO_2 ceased. Imine-% in general 80–90% (PMR analysis). The soln was used as such in the cycloaddition, or the crude imine was taken up in a different solvent after removal of benzene. It is necessary to operate under exclusion of moisture.

1-*Vinyl*-6-*methoxy*-3,4-*dihydronaphthalene* (**2**). Obtained via the procedure of Nazarov,[15] yield: 78%; b.p. 110–113°/0·1 mm n_D^{20} = 1·591.

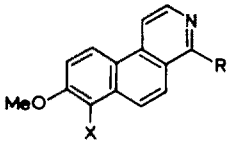
Addition of **1** *to* **2**. To a soln of **1** (18·3 g) in 35 ml benzene was slowly added **2** (12·0 g) under ice cooling. After stirring overnight at 5°, 35 ml ether were added and the organic soln washed with KOH (5%), H_2O and sat NaCl aq. The remaining oil obtained in almost quantitative yield consisted of a mixture of **3a** and **3b**. Via chromatography over Al_2O_3, the mixture could be purified although some isomerization to **4a** and **4b** could not be avoided. IR ($CHCl_3$): 1730 (C=O), 1340 and 1160 (SO_2) cm^{-1}; PMR δ ($CDCl_3$): 5·7–6·2(m) $\underline{H}_1$; 7·34 (d, J = 8·5 c/s) $\underline{H}_{10}$, 7·23 (d) and 7·72 (d) tosyl.

Isomerization of **3a** *and* **3b**. The oily mixture (0·35 g) was refluxed for 3 hr in HOAc (3 ml). $CHCl_3$ was added and the soln extracted with KOH (5%), H_2O and sat NaCl aq. Evaporation of the solvent afforded an oily mixture of **4a** and **4b**; IR ($CHCl_3$): 1725 (C=O), 1340 and 1160 (SO_2) cm^{-1}; PMR δ ($CDCl_3$): 7·04 (d, J = 8·5 c/s) $\underline{H}_{10}$, 7·23 (d) and 7·66 (d) tosyl.

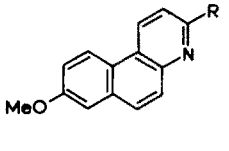
4 - *Carboxy* - 8 - *methoxy* - 5,6 - *dihydro-benzo(f)isoquinoline* **6a** *and* 3 - *carboxy* - 8 - *methoxy* - 5,6 - *dihydro-benzo(f)quinoline* **6b**. Compounds **3a** + **4a** (54 g) in 60 ml EtOH was slowly added to a soln of Na (7·2 g) in 160 ml EtOH during which a finely divided ppt was formed. After stirring for 3 days at r.t. the soln was refluxed (3 hr) and 10 ml H_2O added. Removal of the solvent afforded a residue which was dissolved in 100 ml H_2O and extracted with ether.

Procedure A. Acidification of the aqueous fraction with conc. HCl till P_H = 5 and extraction with $CHCl_3$ afforded an oily residue which was dissolved in acetone. Gradually a mixture of **6a** and **6b** crystallized, Yield *ca* 14·0 g (45%). Separation was accomplished via repeated MeOH extraction of the solid leaving almost pure **6a**, yield: 9·3 g; m.p. 218–220° (HCl aq dil) yellow needles. UV: λ_{max}^{EtOH}: 349 (28·200) nm; PMR δ (CF_3COOH): δ 2·9–3·9 (m) 4$\underline{H}$; 4·05 (s) O$\underline{CH}_3$; 7·15 (m) 2Ar$\underline{H}$; 8·02 (d, J = 8·5 c/s) $\underline{H}_{10}$; 8·39 (d, J = 6·5 c/s) $\underline{H}_1$; 8·68 (d, J = 6·5 c/s) $\underline{H}_2$. (Found: C, 70·7; H, 5·0; O, 18·7; N, 5·4. Calc. for $C_{15}H_{13}O_3N$ (255·3): C, 70·58; H, 5·13; O, 18·80; N, 5·49%). From the MeOH extract 3·0 g of **6b** was obtained. Crystallization HCl aq (dil) afforded **6b** . HCl m.p. 186–187° (subl) PMR δ (CF_3COOH): 3·1–3·9 (m) 4H; 4·05 (s) O$\underline{CH}_3$; 7·15 (m) 2ArH; 7·97 (d, J = 8·5 c/s) $\underline{H}_{10}$; 8·58 (d, J = 8·5 c/s) $\underline{H}_2$; 8·91 (d,

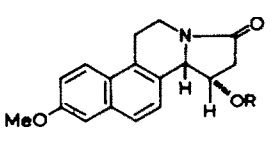
*Separation can be effected—albeit with great loss of material—via treatment of the mixture with phenylisocyanate.



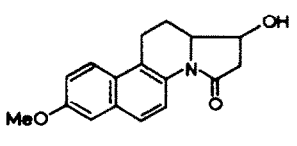
13a X = H R = H
14a X = Br R = COOEt
15a X = H R = COOEt
16a X = H R = C(=O)—CH_2COOEt



15b R = COOEt
16b R = C(=O)—CH_2COOEt



17 R = H
18 R = Ac



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J = 8·5 c/s) H_1. (Found: C, 61·7; H, 5·0; O, 16·4; N, 4·7; Cl, 12·2. Calc. for $C_{15}H_{14}O_3NCl$ (291·8): C, 61·74; H, 4·84; O, 16·45; N, 4·80; Cl, 12·15%).

Procedure B. The aqueous soln of **6a + 6b** was acidified till $P_H < 1$ upon which **6b**. HCl crystallized. Then **6a** was obtained as indicated under A, yields of **6a** and **6b** were somewhat less as found under A.

4 - *Carbomethoxy* - 8 - *methoxy* - 5,6 - *dihydro-benzo(f)isoquinoline* **7a** *and* N - *methyl* - 8 - *methoxy* - 5,6 - *dihydro-benzo(f)isoquinolinium* - 4 - *carboxylate* **13**. To a suspension of **6a** (1·7 g) in 7 ml MeOH an ether soln of CH_2N_2 was added (excess) at 0°. After standing overnight **13** was filtered off as a solid and recrystallized from H_2O; m.p. 190–192°, yield: 0·54 g (30%); PMR δ (CF_3COOH): 3·13 (s) 4H; 4·01 (s) OCH_3; 4·40 (s) N–CH_3; 7·1 (m) 2ArH; 8·0 (d, J = 8·5 c/s) H_{10}; 8·17 (d, J = 7 c/s) H_1; 8·50 (d, J = 7·0 c/s) H_2. (Found: C, 71·4; H, 5·8; O, 17·8; N, 5·3. Calc. for $C_{16}H_{15}NO_3$ (269·3): C, 71·36; H, 5·61; O, 17·82; N, 5·20%). The filtrate afforded **7a**, 1·17 g (65%); m.p. 97–98° (EtOH). UV: λ_{max}^{EtOH}: 293·5 (15·700) and 313·5 (16·200) nm; PMR δ ($CDCl_3$): 2·6–3·4 (m) 4H; 3·82 (s) OCH_3; 3·98 (s) $OOCH_3$; 6·85 (m) 2ArH; 7·65 (d) H_{10}; 7·59 (d, J = 5 c/s) H_1 and 8·52 (d, J = 5 c/s) H_2. (Found: C, 71·3; H, 5·7; O, 17·9; N, 5·3. Calc. for $C_{16}H_{15}O_3N$ (269·3): C, 71·36; H, 5·61; O, 17·82, N, 5·20%).

3 - *Carbomethoxy* - 8 - *methoxy* - 5,6 - *dihydro-benzo(f)quinoline* **7b**. Prepared as **7a**, yield: 62%, m.p. 127–128° (EtOH). UV: λ_{max}^{EtOH}: 330 (22·800) nm; PMR δ ($CDCl_3$): 2·7–3·3 (m) 4H; 3·81 (s) OCH_3; 3·97 (s) $OOCH_3$; 6·83 (m) 2ArH; 7·62 (d) H_{10}; 7·96 (s) $H_1 + H_2$. (Found: C, 71·2; H, 5·7; O, 17·8; N, 5·1. Calc. for $C_{16}H_{15}O_3N$ (269·3): C, 71·36; H, 5·61; O, 17·82; N, 5·20%).

4 - *Carbethoxy* - 8 - *methoxy* - 5,6 - *dihydro-benzo(f)isoquinoline* **8a**. Compound **1a** (2·0 g) Ag_2O (2·0 g) and EtI (4·0 g) in 20 ml xylene were refluxed for 1 hr. Evaporation of the solvent after filtration afforded 1·85 g of **2a** as an oil, m.p. 66–67° (ether). UV: λ_{max}^{EtOH}: 293·5 (15·400) and 313 (15·900) nm; PMR δ ($CDCl_3$): 7·58 (d, J = 5·0 c/s) H_1 and 8·52 (d, J = 5·0 c/s) H_2. (Found: C, 72·1; H, 6·1; O, 17·1; N, 4·9. Calc. for $C_{17}H_{17}O_3N$ (283·3): C, 72·06; H, 6·05; O, 16·94; N, 4·94%).

3 - *Carbethoxy* - 8 - *methoxy* - 5,6 - *dihydro-benzo(f)quinoline* **8b**. Prepared as **8a**, yield: 90%, m.p. 96–97° (ether). UV: λ_{max}^{EtOH}: 329·5 (24·300) nm; PMR δ ($CDCl_3$): 7·95 (s) $H_1 + H_2$; δ (C_6D_6): 7·47 (d, J = 8 c/s) H_2; 8·56 (d, J = 8 c/s) H_2. (Found: C, 72·2; H, 6·1; O, 17·0; N, 4·8. Calc. for $C_{17}H_{17}O_3N$ (283·3): C, 72·06; H, 6·05; O, 16·94; N, 4·94%).

Ethyl [8 - *methoxy* - 5,6 - *dihydro-benzo(f)isoquinolinoyl* - 4] - *acetate* **9a**. Compound **8a** (1·0 g) EtOAc (0·55 g) and NaH (0·20 g; 50% dispersed in oil) in 30 ml THF were refluxed for 18 hr. After addition of 50 ml H_2O, 0·6 g HOAc and 60 ml EtOAc the organic layer was separated and repeatedly washed with NaCl aq (sat). Evaporation yielded 1·1 g of an oil (87%) which could be used without purification in the next step, m.p. 71·5–73·5° (EtOH); UV: λ_{max}^{EtOH}: 260·5 (14·600), 292·5 (15·700) and 318 (11·000) nm; PMR δ $CDCl_3$): 1·23 (t) CH_3; 2·5–3·5 (m) 4H; 3·82 (s) OCH_3; 4·18 (q) OCH_2; 4·19 (s) $COCH_2$; 6·85 (m) 2ArH; 7·63 (d) H_{10}; 7·59 (d, J = 5 c/s) H_2; 8·47 (d, J = 5 c/s) H_2. (Found: C, 70·0; H, 6·0; O, 19·8; N, 4·4. Calc. for $C_{19}H_{19}O_4N$ (325·3): C, 70·14; H, 5·89; O, 19·67; N, 4·31%).

Methyl - [8 - *methoxy* - 5,6 - *dihydro-benzo(f)quinolinoyl* - 3] - *acetate* **9b**. Compound **7b** (1·00 g) and MeOAc (0·60 g) in 13 ml C_6H_6 were added to a refluxing suspension of NaOEt (0·35 g) in 7 ml C_6H_6. The pink soln was refluxed for 6 hr and after standing overnight the crude Na-salt of **9b** crystallized. After filtration the salt was treated with HOAc, $CHCl_3$ and water. Work-up in the usual way afforded 0·90 g of **9b** as an oil, m.p. 100–102° (EtOH); UV: λ_{max}^{EtOH}: 237·5 (9·500) and 342·5 (24·000) nm; PMR δ ($CDCl_3$): 3·01 (s) 4H; 3·73 (s) $OOCH_3$; 3·82 (s) OCH_3; 4·19 (s) $COCH_2$; 6·85 (m) 2ArH; 7·62 (d) H_{10}; 7·93 (s) $H_1 + H_2$. (Found: C, 69·4; H, 5·5; O, 20·4; N, 4·5. Calc. for $C_{18}H_{17}O_4N$ (311·3): C, 69·44; H, 5·50; O, 20·56; N, 4·50%).

Hydrogenation of **9a** *and* **9b**. The keto-ester (0·264 g) in 10 ml HOAc was hydrogenated over PtO_2 (0·03 g) in a Parr apparatus at r.t. After filtration of the catalyst and evaporation of the solvent the residue was dissolved in $CHCl_3$. Work-up afforded the OH-derivative in almost quantitative yield as an oil. **10a**: PMR δ ($CDCl_3$): 3·83 (s) OCH_3; 4·19 (q) OCH_2; 5·43 (t) CHOH; 7·46 (d, J = 5 c/s) H_1; 8·42 (d, J = 5 c/s) H_2. **10b**: PMR δ ($CDCl_3$): 3·70 (s) $OOCH_3$; 3·82 (s) OCH_3; 5·17 (t) CHOH; 7·25 (d, J = 8 c/s) H_2; 7·87 (d, J = 8 c/s) H_1.

4 - *Carboxy* - 8 - *methoxy* - 1,2,3,4,5,6 - *hexahydro-benzo(f)isoquinoline* **11**. Obtained as an almost insoluble solid in varying amounts in the hydrolysis of **3a + 4a**. After acidifying the alkaline water soln till $p_H = 5$ and $CHCl_3$ extraction **11** crystallized and was filtered off, m.p. 235–237° (AcOH); UV: λ_{max}^{EtOH}: 277·5 (16·800) nm; PMR δ (CF_3COOH): 2·3–3·2 (m) 6H; 3·6–4·2 (m) N–CH_2; 4·02 (s) OCH_3; 5·00 (s) N–CH–COOH; 6·95 (m) 2ArH; 7·3 (d) H_{10}; 8·0 $NH_2^{\oplus}$. (Found: C, 69·3; H, 6·7; O, 18·7; N, 5·6. Calc. for $C_{13}H_{17}O_3N$ (259·3): C, 69·48; H, 6·61; O, 18·51; N, 5·40%). The N-Me derivative **12** was obtained upon $NaBH_4$ reduction of **13**. Upon stirring 0·48 g of **13** with 0·50 g of $NaBH_4$ in 30 ml of H_2O overnight, acidification and $CHCl_3$ extraction 0·45 g of **12** were obtained, m.p. 158–162° ($CHCl_3$–EtOH); UV: λ_{max}^{EtOH}: 277 (15·200) nm; PMR δ ($CDCl_3$): 2·95 (s) NCH_3; 3·75 (s) OCH_3; 2·0–4·0 (m) 6H; 4·2 (broad s) N–CH 6·4–7·1 (m) 3ArH; 8·85 (s) COOH.

8 - *Methoxy-benzo(f)isoquinoline* **13a**. Upon refluxing **8a** (0·85 g) and 10% Pd/C (1·0 g) in 25 ml diglyme for 5 days, **13a** (0·60 g) was obtained, m.p. 119-125° (EtOH–Et_2O), UV: λ_{max}^{EtOH}: 255·5 (54·000), 262·5 (60·100), 292 (12·700) and 302 (1·100) nm; PMR δ ($CDCl_3$): 3·87 (s) OCH_3; 7·18 (m) $H_7 + H_9$; 7·61 (s) $H_3 + H_6$; 8·12 (d, J = 6 c/s) H_1; 8·36 (d) H_{10}; 8·61 (d, J = 6 c/s) H_2; 9·10 (s) H_4. (Found: C, 80·2; H, 5·4. Calc. for $C_{14}H_{11}ON$ (209·2): C, 80·36; H, 5·30%).

4 - *Carbethoxy* - 7 - *bromo* - 8 - *methoxy-benzo(f)isoquinoline* **14a**. Compound **8a** (2·60 g) NBS (3·65 g) and a catalytic amount of Bz_2O_2 in 65 ml CCl_4 were refluxed for 2 hr during which Br_2 was evolved. After addition of 130 ml $CHCl_3$ the soln was washed with KOH aq (5%). Evaporation gave 3·3 g of material, m.p. 185–187° (acetone); UV: λ_{max}^{EtOH}: 228·5 (33·800) and 276·5 (37·000); PMR δ ($CDCl_3$): 1·52 (t) CH_3; 3·99 (s) OCH_3; 4·60 (q) OCH_2; 7·18 (d, J = 9 c/s) H_9; 8·17 (d, J = 9·5 c/s) H_6; 8·25 (d, J = 5·5 c/s) H_1; 8·35 (d, J = 9 c/s) H_{10}; 8·49 (d, J = 9·5 c/s) H_5; 8·70 (d, J = 5·5 c/s) H_2.

4 - *Carbethoxy* - 8 - *methoxy-benzo(f)isoquinoline* **15a**. Compound **14a** (1·51 g) NEt_3, (0·60 g) 10% Pd/C (0·50 g) in 40 ml AcOH was hydrogenated in a Parr apparatus at r.t. for 12 hr. After filtration of the catalyst and removal of the solvent, the residue was taken up in C_6H_6 and washed with KOH aq (5%). The crude product was chromatographed over Al_2O_3 (eluted with C_6H_6–$CHCl_3$) to yield 0·84 g of **15a**, m.p. 118·5–119·5° (EtOH); UV: λ_{max}^{EtOH}: 223 (26·100) and 268 (43·000) nm; PMR δ ($CDCl_3$): 1·52 (t) CH_3; 3·89 (s) OCH_3; 4·60 (q) OCH_2; 7·19 (m) 2ArH; 7·65 (d, J = 9 c/s) H_6; 8·28 (d, J = 5·5 c/s) H_1; 8·35 (d) H_{10}; 8·43 (d, J = 9 c/s) H_5; 8·69 (d, J = 5·5 c/s) H_2. (Found: C, 72·5; H, 5·6; O, 17·1; N, 4·9. Calc. for $C_{17}H_{15}O_3N$ (281·3): C, 72·58; H, 5·37; O, 17·06; N, 4·98%).

3 - *Carbethoxy* - 8 - *methoxy-benzo(f)quinoline* **15b**. Compound **8b** (1·47 g) and SeO_2 (2·25 g) in 50 ml dioxane were refluxed for 16 hr. After filtration the solvent was evaporated and the residue dissolved in $CHCl_3$. The soln was thoroughly washed with KOH aq (3%), yield: 1·40 g, m.p. 156–158° (EtOH), Lit.[16] 157–158°; UV: λ_{max}^{EtOH}: 230·5 (27·300); 243·5 (24·400); 274 (33·200); 319 (11·200); 346·5 (6·300) and 365 (5·500) nm; PMR δ ($CDCl_3$): 1·48 (t) CH_3; 3·88 (s) OCH_3; 4·55 (q) OCH_2; 7·18 (m) 2ArH; 7·77 (d, J = 9 c/s) H_6; 8·07 (d, J = 9 c/s) H_5; 8·15 (d, J = 8·5 c/s) H_2; 8·32 (d) H_{10}; 8·73 (d, J = 8·5 c/s) H_1. (Found: C, 72·3; H, 5·5; O, 17·1; N, 5·1. Calc. for $C_{17}H_{15}O_3N$ (281·3): C, 72·58; H, 5·37; O, 17·06; N, 4·98%).

Ethyl [8 - *methoxy-benzo(f)isoquinolinoyl* - 4] - *acetate* **16a**. Prepared as **9a** from **15a** (0·85 g) EtOAc (0·55 g), NaH (0·20 g; 50% dispersion in oil) in 25 ml THF, yield: 0·91 g, m.p. 154–156° (C_6H_6). New crystals were formed during the melting process which melted again from 250–260°; UV: λ_{max}^{EtOH}: 226 (25·600), 251 (28·300), 267 (27·600) and 284·5 (24·500) nm; PMR δ ($CDCl_3$): 4·35 (s) $COCH_2$; 8·32 (d, J = 5·5 c/s) H_1; 8·62 (d, J = 5·5 c/s) H_2. (Found: C, 70·4; H, 5·3; O, 19·6; N. 4·3. Calc. for $C_{19}H_{17}O_4N$ (323·3): C, 70·57; H, 5·30; O, 19·79; N, 4·33%).

Ethyl [8 - *methoxy-benzo(f)quinolinoyl* - 3] - *acetate* **16b**. Prepared as **16a**, yield: 1·14 g, m.p. 97·5–100°; Lit.[16] 96–99°; UV: λ_{max}^{EtOH}: 231 (25·900), 248 (17·700), 277 (34·100), 332 (14·600) and 370 (6·600) nm; PMR δ ($CDCl_3$): 4·33 (s) $COCH_2$; 8·10 (d, J = 8·5 c/s) H_2; 8·72 (d, J = 8·5 c/s) H_1.

13 - *Aza* - 15 - *hydroxy* - 18 - *nor* - *equilenine methyl ether* **17**. Compound **16a** (0·90 g) and PtO_2 (0·10 g) in 45 ml AcOH were hydrogenated at 75°/110 at overnight. After removal of the catalyst and evaporation of the solvent the residue was dissolved in $CHCl_3$ and washed with KOH aq (5%), yield: 0·43 g, m.p. 194–198° (C_6H_6). UV: λ_{max}^{EtOH}: 236·5 (60·700), 256 (4·150), 265 (5·100), 275 (5·200), 285 (3·250), 319·5 (1·500) and 333·5 (1·900) nm. (Found: C, 71·9; H, 6·0; O, 17·1; N, 5·0. Calc. for $C_{17}H_{17}O_3N$ (283·3): C, 72·06; H, 6·05; O, 16·94; N, 4·94%).

13 - *Aza* - 15 - *acetoxy* - 18 - *nor-equilenine methyl ether* **18**. Compound **17** (0·22 g) was refluxed for 5 hr with excess Ac_2O. Work-up afforded 0·20 g of an oil, which was chromatographed over Florisil and eluted with $CHCl_3$, yield: 0·111 g, m.p. 160·5–163·5° (MeOH); PMR δ ($CDCl_3$): 2·20 (s) $OCCH_3$; 2·4–3·1 (m) 16-CH_2; 3·05–3·35 (m) 3H, 11-CH_2 + 12-CH; 3·91 (s) OCH_3; 4·50–4·68 (m) 12-CH; 4·95 (d, J = 4·5 c/s) 14-CH; 5·15-5·4 (m) CHOAc; 7·18 (m) 2ArH; 7·44 (d) H_6; 7·66 (d) H_7; 7·81 (d) H_1. (Found: C, 70·0; H, 5·9; O, 19·9; N, 4·1. Calc. for $C_{19}H_{19}O_4N$ (325·4): C, 70·14; H, 5·89; O, 19·67; N, 4·31%).

1,2,3,11,12,12a - *Hexahydro* - 1 - *hydroxy* - 8 - *methoxy* - 3 - *oxo benzo(f)pyrrolo[1.2-a]quinoline* **19**. Prepared as **17**, m.p. 237–240° (AcOH), Lit.[16] 236–237°; UV: λ_{max}^{EtOH}: 219 (20·700), 233·5 (23·300), 251 (51·000), 259·5 (44·800), 277·5 (10·800), 286·5 (13·600), 298 (11·800), 332·5 (2·500), 347·5 (2·600) nm; PMR δ (CF_3COOH): 4·07 (s) OCH_3; 4·15 (m) NCH; 4·65 (m) CHOH. (Found: C, 72·2; H, 6·1; O, 17·1; N, 5·1. Calc. for $C_{17}H_{17}O_3N$ (283·3): C, 72·06; H, 6·05; O, 16·94; N, 4·94%).

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REFERENCES

[1]Abstracted in part from the thesis of W. A. Zunnebeld, University of Amsterdam (1969).

[2]For some recent examples see: [a]M. Lora-Tamayo and R. Madronero, *1,4-Cycloaddition Reactions* p. 127. Hamer, Acad. Press (1967); [b]D. vor der Brück, R. Bühler and H. Plieninger, *Tetrahedron* **27**, 791 (1971); [c]J. M. Biehler and J. P. Fleury, *Ibid.* **27**, 3171 (1971); [d]D. Ben-Ishai and E. Goldstein, *Ibid.* **27**, 3119 (1971).

[3]R. Albrecht and G. Kresze, *Chem. Ber.* **98**, 1431 (1965).

[4]R. G. Jones and E. C. Kornfeld, *J. Am. Chem. Soc.* **73**, 107 (1951).

[5]H. Liliedahl, *Acta Chem. Scand.* **20**, 95 (1966).

[6]H. Suhr, *Anwendungen der kernmagnetischen Resonanz in der Organischen Chemie* p. 231. Springer-Verlag (1965).

[7]G. M. Clarke, R. Grigg and D. H. Williams, *J. Chem. Soc.* (B), 339 (1966).

[8]Z. G. Hajos, D. R. Parrish and M. W. Goldberg, *J. Org. Chem.* **30**, 1213 (1965).

[9]Ref. 3.

[10]W. N. Speckamp, W. A. Zunnebeld and R. P. Loven, *Tetrahedron* **31**, 1723 (1975).

[11]E. P. Burrows, A. Rosowsky and E. J. Modest, *J. Org. Chem.* **32**, 4090 (1967).

[12]S. G. Boots and W. S. Johnson, *J. Org. Chem.* **31**, 1285 (1966).

[13]R. Filler, *Chem. Rev.* **63**, 21 (1963).

[14]M. Wilchek, T. F. Spande, B. Witkop and G. W. A. Milne, *J. Am. Chem. Soc.* **89**, 3349 (1967).

[15]I. N. Nazarov, I. V. Torgov and G. P. Verkholerova, *Dokl. Akad. Nauk. S.S.S.R.* **112**, 1067 (1957); *Chem. Abstr.* **51**, 14647d (1957).

[16]E. R. H. Jones, *J. Chem. Soc.* 5907 (1964).