Ind-N-Alkylation of Rutaecarpine and Synthesis of Two Novel Related Heterocyclic Ring Systems: Indolo[1′,2′:3,4]pyrazo[1,2-*a*]quinazoline and Indolo[1′,2′:3,4][1,4]diazepino[1,2-*a*]quinazoline

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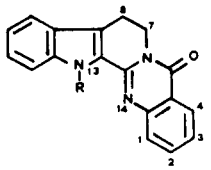
Received April 18, 1977

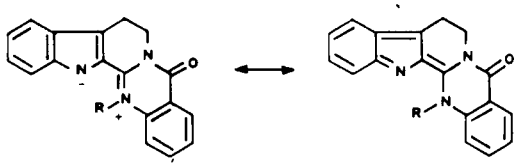
The failure to obtain the *N*-(13)alkylrutaecarpines (**1d,e,f**) by heating rutaecarpine (**1a**) with neat alkyl halides at 120° is discussed in comparison with the facile reaction with methyl iodide. In contrast, with alkyl halide-potassium carbonate in acetone, the corresponding *N*-(13)alkylrutaecarpines (**1d-l**) are obtained in good yield. By use of 1,3-diiodopropane and 1,2-dibromoethane, this reaction provides a facile route to **12a** and **13** which are derivatives of the heretofore unknown indolo[1′,2′:3,4]pyrazo[1,2-*a*]quinazoline and indolo[1′,2′:3,4][1,4]diazepino[1,2-*a*]quinazoline ring systems.

J. Heterocyclic Chem., 14, 839 (1977)

In our studies on the chemical behaviour of indolopyridoquinazoline alkaloids, *e.g.* rutaecarpine (**1a**) and its analogues, we have found (1) that a very effective *N*-(13)-methylation to **1b** was achieved by use of neat methyl iodide at 120° (method A) or by methyl iodide-potassium

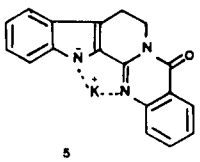


1a R = H
1b R = Me
1c R = Me-d_3
1d R = Et
1e R = n-Bu
1f R = i-Am
1g R = i Am. $\Delta^{7(8)}$
1h R = allyl
1i R = benzyl
1j R = β-phenetyl
1k R = CH_2-COOMe
1l R = $(CH_2)_2$—$NHEt_2Cl^-$
1m R = $(CH_2)_3$-I



3a R = Me **3b**
4a R = Et **4b**

carbonate in refluxing acetone (method B) (2). The direct methylation as in method A was thought to proceed through the reaction sequence depicted in Scheme I. This scheme was substantiated by i) the behaviour of **3** (1) with [$^2H_3$]-CH_3I under the same conditions or in refluxing chloroform to furnish **1c**; ii) the isolation of **2**, from the reaction mixture, albeit in small amount. The methylation with methyl iodide-potassium carbonate took place directly at N(13) on the resonance-stabilizes ambident anion which formed the ion pair **5** with the counterion: this



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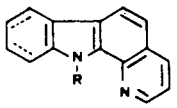
ion-pair was highly stabilized by strong chelation through the lone-pairs of N(13) and N(14). No evidence for the intermediacy of the *N*-(14)methosalt **3** was obtained by monitoring the reaction with an authentic sample of **3**, stable under these conditions.

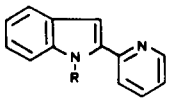
The stereo-electronic factors governing the above reactions were also found in the structurally similar compounds 7,8,9,10-tetrahydro-11*H*-pyrido[2,3-*a*]carbazole (**6a**), 11*H*-pyrido[2,3-*a*]carbazole (**7a**) and 2-(2′-pyridyl)-indole (**8a**). Compound **6a** was obtained by indolization of the 8-quinolylhydrazone of cyclohexanone (3), whereas **8a** was obtained *via* triethyl phosphite-induced reductive cyclization (4) of 2-*o*-nitrostyrylpyridine, together with the hitherto unknown 3,3′-biindole (**9**). Compounds **6a**, **7a** and **8a** behaved analogously to the indolopyridoquinazoline alkaloids forming the corresponding *ind-N*-methyl derivatives **6b**, **7b** and **8b** in acceptable yield under the conditions of either method A or B (see Experimental).

In the present work the reactions of rutaecarpine (**1a**) with some alkyl halide R-X where R > CH_3 and α,ω-alkyl

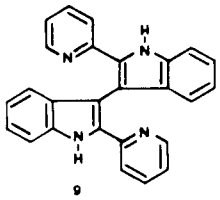


6a R = H tetrahydro
6b R = Me tetrahydro
7a R = H
7b R = M

dihalides X-R-X where R = -$(CH_2)_2$- and -$(CH_2)_3$- are discussed. In particular, with the alkyl dihalides we have obtained and characterized two new heterocyclic compounds **12a** and **13**: these derive from the hitherto unknown parent systems indolo[1′,2′:3,4]pyrazo[1,2-*a*]-quinazoline (**14**) and indolo[1′,2′:3,4][1,4]diazepino-[1,2-*a*]quinazoline (**15**).



8a R = H
8b R = Me



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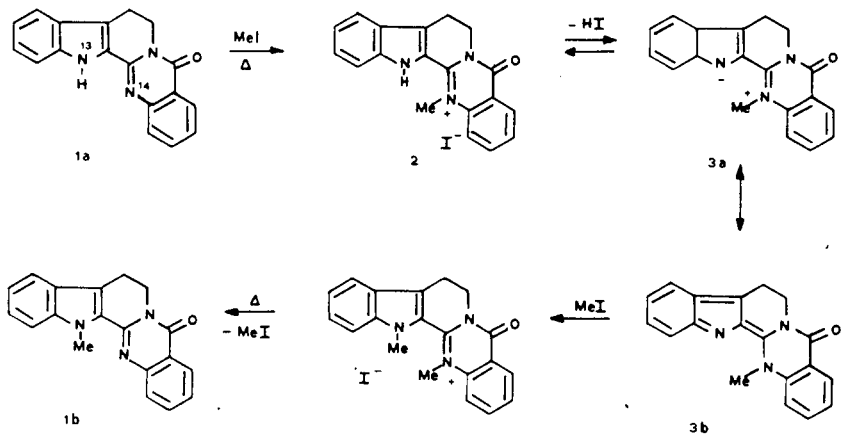
Scheme I

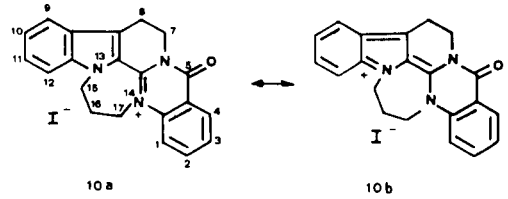


On heating **1a** with neat ethyl iodide, *n*-butyl iodide or isoamyl iodide at 120° no evidence for *ind*-*N*-alkylation was obtained: only in the case of ethyl iodide an elusive trace of **4** was detected by tlc, after base treatment of the reaction mixture. Compound **4** was identified by comparison with an authentic sample obtained from 1,2,3,4-tetrahydronorharman-1-one and *N*-ethylanthranilic acid methyl ester. This behaviour is nicely explained by analogy with the reaction Scheme I. The molecular model of **1a** shows, in fact, that N(13) and N(14) are very close. The initially formed intermediate similar to **3** is therefore rather crowded at N(13) hindering the access to this negatively charged site which lacks the reactivity as a nucleophile in S_N2 displacement reactions. This probably causes the striking difference between methyl iodide and larger primary alkyl halides in their reactions with **1a**.

This view has been strongly supported by a comparison of subsequent alkylation of **3** and **4** with several primary halides. While **3** was smoothly converted into **1b** in almost quantitative yield either with neat methyl iodide at 120° or with excess methyl iodide in refluxing chloroform (S_N2 displacement) (5), a base-induced β-elimination, instead, occured with ethyl iodide, *n*-butyl iodide and isoamyl iodide and the dehydroevodiamine hydroiodide **2** was the only isolated product. Furthermore, when β-elimination was not possible as for benzyl bromide and for bromoacetic acid methyl ester *N*-(13)alkyl derivatives **1i** and **1k**, respectively were isolated, albeit in very low yield. On the other hand, predictively, **1b** was obtained on refluxing **4** with neat methyl iodide at 120° or in chloroform solution but no alkylation products are detected by tlc on treatment of **4** with ethyl iodide and other halides. The overwhelming propensity for elimination *vs.* S_N displacement is well known as a consequence of steric hindrance at the nucleophilic centre (6).

In contrast, the alkylation of **1a** with methyl iodide-potassium carbonate in refluxing acetone with alkyl halides (ethyl iodide, *n*-butyl iodide, isoamyl iodide, allyl bromide, benzyl bromide, β-phenethyl bromide, bromoacetic acid methyl ester and β-diethylaminoethylchloride) furnished the corresponding *N*-(13)alkyl derivatives **1d-l** in good yield (60-96%). All new compounds gave satisfactory uv and ms spectral data (*vide* Experimental).

The alkylation of rutaecarpine has now been extended to some alkyl dihalides, in order to obtain products dialkylated at both N(13) and N(14). Rutaecarpine reacted readily with excess 1,3-diiodopropane in refluxing acetone in the presence of potassium carbonate providing the major product **1m** and a small amount of an additional compound **10**. The uv and ms data agree with those of a *N*-(13)-

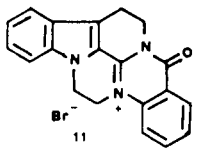


alkylrutaecarpine. The minor component **10** is a sparingly soluble yellow compound which exhibits ir bands (nujol) at 1710, 1610, 1600 and 1565 cm^{-1}. The carbonyl band at 1710 cm^{-1} occurs at higher energies than normally observed in the ir spectra of rutaecarpine derivatives. However, this value agrees with that of **1a** salts and **2**, where N(14) is quaternized (νCO at 1703-1709 cm^{-1}) (6).

Further supports for structure **10** come from uv data and from fading of the yellow colour upon treatment of the methanolic solution with sodium borohydride (6). The ^{1}H-nmr spectrum shows, *i.a.*, a complex signal for C(16)H_2 at δ 3.00, a triplet for C(8)H_2 at δ 3.50 (^{3}J 7.0 Hz) and a complex multiplet at δ 4.70 for the remaining methylene protons at C(7), C(15) and C(17). The close similarity of the C(15)H_2 and C(17)H_2 chemical shifts is explained by the contribution of the canonical resonance structure **10b**. Additional and more direct support for the structure **10** being it was a subsequent cyclization product from **1m**, was obtained as **10** was isolated under refluxing

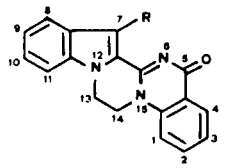
1m in acetone or better in dry DMF.

A comparative study of the behaviour of rutaecarpine with excess 1,2-dibromoethane under the above conditions has been carried out. The reaction proceeds to completion and affords **11** as traces and **12a** as the major product.



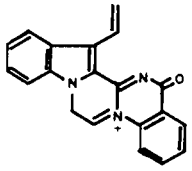
11

By analogy with **10** structure **11** is supported by the high frequency carbonyl band at 1708 cm^{-1}, by its uv spectrum and by the fading of the yellow solution under treatment with sodium borohydride. Structure **12a** assigned to the main product was based on analytical and spectral data. The molecular formula $C_{20}H_{15}N_3O$ was indicated by the combustion analysis. The ^{1}H-nmr spectrum consists of i) a multiplet between δ 4.70-5.10 due to the C(13) and C(14) methylene bridge: ii) an AB portion of ABX pattern at δ 6.05 ($^3J_{cis}$ 11.0 Hz, $^2J_{gem}$ 1.5 Hz) and 6.10 ($^3J_{trans}$ 17.0 Hz, $^2J_{gem}$ 1.5 Hz) for the C(17)H_2 of the vinyl moiety; iii) a doublet of doublets at δ 8.41 (^{3}J 8.0 Hz, ^{4}J 2.0 Hz) attributable to the C(4)*H* strongly deshielded by the neighbouring *peri* carbonyl group; and

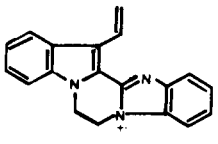


12a R = $C_{(16)}H{=}C_{(17)}H_2$
12b R = $C_{(16)}H_2{-}C_{(17)}H_3$

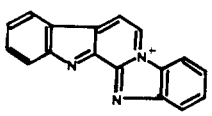
iv) a multiplet between δ 7.80-8.20 assigned to the remaining seven aromatic protons and to the C(16)*H* of the vinyl moiety. Furthermore, the lack of the deceptively simple triplets at *ca.* δ3.40 and 4.70 (^{3}J 7-8 Hz) ubiquitous in all the rutaecarpine derivatives and due to the methylene protons at C(7) and C(8), corroborated the structure **12a**. The mass spectrum of **12a** (EI, 70 eV, 160°) showed a strong molecular ion at m/e 313 (62%) in agreement with the molecular formula and peaks at m/e 312 (base peak), 285 and 257 were also evident. To these ions, in accord with the fragmentation pattern of a quinazolone system



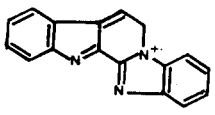
a, m/e 312



b, m/e 285



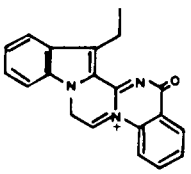
c, m/e 257



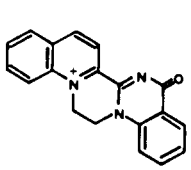
d, m/e 256

(7), were respectively assigned the structure **a**, **b**, **c** and **d**. The metastable peaks at m/e 311.0, 260.3 and 231.7 strongly support the transitions 313 → 312, 313 → 285 and 285 → 257, respectively. Catalytic hydrogenation (10% palladium/carbon, methanol) of the vinyl double bond in **12a** led to the dihydro derivative **12b**, supported by ms and ^{1}H nmr spectral data. In fact, the ^{1}H nmr spectrum revealed a A_3X_2 system for the C(16)H_2-C(17)H_3 at δ 1.46 and 3.35 (^{3}J 7.5 Hz) instead of the ABX system for the vinyl group in **12a**. The mass spectrum showed a molecular ion at m/e 315 (base peak) and peaks at m/e 314, 300 (M^+-Me), 287 (M^+-CO), 286 (M^+-CO-H) and 272 (M^+-Me-CO) were also present. By analogy with fragmentation pattern of **12a**, we attributed the structures **e**, **f**, **g**, **h** and **i** to these ions and the metastable peaks at m/e 313.0, 285.7 and 261.4 support the transitions 315 → 314, 315 → 300 and 315 → 286, respectively.

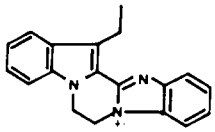
Compound **12a** was recovered in nearly quantitative yield on refluxing **11** in DMF and potassium carbonate. This gives additional support to the structure **12a** and indicates that it was formed *via* a β-elimination resulting



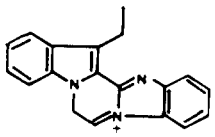
e, m/e 314



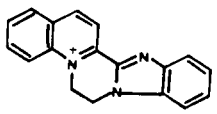
f, m/e 300



g, m/e 287



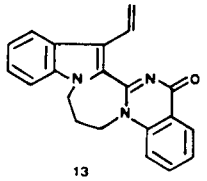
h, m/e 286



i, m/e 272

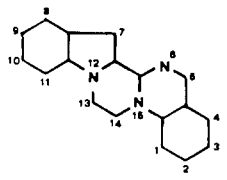
from the attack of the base on acidic C(7)H_2. It is noteworthy that *N*-(13)-2-bromoethylrutaecarpine was not detected by tlc under these conditions. This was due, of course, to the easy intramolecular cyclization to **11**.

The salt **10** behaved in the same way as **11** in refluxing DMF and potassium carbonate, giving rise to **13** in quantitative yield. On the other hand, **13** could be obtained directly from **1a** and 1,3-diiodopropane in refluxing DMF-potassium carbonate, being the structure of **13** based on the same spectroscopic considerations as for **12a**.

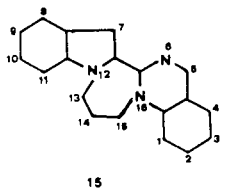


13

Work is in progress for a new approach to the new heterocyclic system **14** and **15** from which **12** and **13** were derived and for a better knowledge of their chemical and physicochemical properties.



14



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EXPERIMENTAL

All melting points are uncorrected. The chemical shift values (60MHz) are expressed in δ (ppm) relative to TMS as the internal standard, in the mixture deuteriochloroform + 20% trifluoroacetic acid used as solvent unless otherwise stated. All tlc analyses were performed on precoated glass plates of silica gel and uv light or iodine vapours for visualization.

General Procedure for the Alkylation of **1a**, **3**, **4**, **6a**, **7a** and **8a**.

Method A.

A suspension of the title compound (1.0 mmole) in neat alkyl halide (5 ml.) was sealed in a glass ampoule under nitrogen and kept at 120° for 10 hours. After cooling, the solvent was removed *in vacuo*, the residue treated with diethylamine (0.5 ml.) and taken up in chloroform. The product and/or unreacted material were recovered by preparative tlc, filtration through neutral alumina or silica gel. Identification of products was based on spectral analyses or was performed by direct comparison (tlc) with authentic samples. The spectral data and m.ps of the new compounds are written below and more details on reactions are listed in the Table.

Chromatographic eluents are for **1a** and *N*-(13)derivatives (benzene-ether, 1:1, E_1); for **3**, **4**, **10**, **11** (ethyl acetate-diethylamine, 93:7, E_2) and for **12** and **13** (chloroform-methanol, 9:1, E_3).

Method B.

To a solution of the title compound (2.0 mmoles) in dry acetone (20 ml.) was added a solution of alkyl halide (2.5 mmoles) in acetone followed by anhydrous potassium carbonate (4.0 mmoles). The resulting suspension was stirred under reflux for 8 hours. Water was then added and the product extracted with chloroform. Evaporation to dryness gave a material which was purified as above.

N-(13)Ethylrutaecarpine (**1d**).

This compound had m.p. 144-146° (ether) as colourless needles: λ max (Methanol): 277, 289, 328, 344, 361 nm: m/e 315 (M^+, 68%), 314 (100), 287 (M^+-28, 48), 286 (28), 157.5 (M^{2+}, 18); metastable peaks at m/e 285.7 (315 → 300), 285.0 (287 → 286), 261.5 (315 → 287).

Anal. Calcd. for $C_{20}H_{17}N_3O$: C, 76.17: H, 5.43; N, 13.33. Found: C, 76.34: H, 5.28; N, 13.19.

N-(13)-*n*-Butylrutaecarpine (**1e**).

This compound had m.p. 127-128° (ether) as colourless prisms: λ max (Methanol): 265 (sh), 276, 289, 329, 343, 361 nm; m/e 343 (M^+), 314 (M^+-C_2H_5), 300 (M^+-C_3H_7), 286, 257; metastable peaks at m/e 285.0 (287 → 286), 262.4 (343 → 300), 240.0 (343 → 287).

Anal. Calcd. for $C_{22}H_{21}N_3O$: C, 76.94: H, 6.16; N, 12.24. Found: C, 77.24; H, 6.31; N, 12.38.

N-(13)Isopentylrutaecarpine (**1f**).

This compound had m.p. 107-109° (diisopropyl ether) as colourless prisms; λ max (Methanol): 278, 289, 330, 344, 361 nm; m/e 357 (M^+, 38%), 315 (18), 314 (100), 301 (24), 300 (28), 288 (21), 287 (96), 286 (39); metastable peaks at m/e 299.0 (301 → 300), 285.0 (287 → 286), 253.8 (357 → 301), 252.1 (357 →

Table

Starting material	R-X	Method	Reaction product (%)	Starting material recovered (%)
1a	Et I	A	**4** (traces)	95
1a	*n*-Bu I, *i*-Am I Benzyl Br, Allyl Br	A		93
1a	Et I	B	**1d** (86)	11
1a	*n*-Bu I	B	**1e** (75)	20
1a	*i*-Am I	B (a)	**1f** (82)	15
1a	Allyl Br	B	**1h** (92)	5
1a	Benzyl Br	B	**1i** (96)	
1a	$Ph(CH_2)_2Br$	B	**1j** (61)	34
1a	MeO_2CCH_2Br	B	**1k** (94)	3
1a	$Et_2\overset{+}{H}N(CH_2)_2Cl\ Cl^-$	B	**1l** (75)	22
3	Et I, *n*-Bu I, *i*-Am I	A	**2** (15-25)	60-70
4	Me I	A (b)	**1b** (65)	23
4	Et I, *n*-Bu I, *i*-Am I	A		
6a	Me I	A	**6b** (55)	35
6a	Me I	B	**6b** (71)	22
7a	Me I	A	**7b** (63)	35
7a	Me I	B	**7b** (74)	24
8a	Me I	A	**8b** (62)	26
8a	Me I	B	**8b** (82)	15

(a) With undistilled *i*-Am I **1a** undergoes to iodine-promoted dehydrogenation and $\Delta^{7(8)}$-dehydro-*N*-(13)isopentylrutaecarpine was isolated in 52% yield (starting material recovered in 35%); m.p. 132-134° (diisopropyl ether) as pale yellow needles, λ max (Methanol) 251, 272, 284, 300 (sh), 334, 353, 373, 395 nm; m/e: 355 (M^+, 35%), 312 (M^+-C_3H_7, 41), 299 (M^+-C_4H_8, 19), 298 (24), 285 (M^+-C_5H_{10}, 100), 284 (19), 257 (18), 256 (26). Metastable peaks at m/e 297.0 (299 → 298), 251.8 (355 → 299), 228.8 (355 → 285). (b) Compound **1b** was also obtained by refluxing **4** with methyl iodide in chloroform solution (8 hours) in 72% yield (12% recovered starting material).

300), 230.7 (357 → 287).

Anal. Calcd. for $C_{23}H_{23}N_3O$: C, 77.28; H, 6.49; N, 11.76. Found: C, 77.19; H, 6.71; N, 11.78.

N-(13)Allylrutaecarpine (**1h**).

This compound had m.p. 129-131° (diisopropyl ether) as colourless needles; λ max (Methanol): 265 (sh), 276, 289, 329, 343, 361 nm; m/e 327 (M^+, 68), 326 (31), 312 (M^+-Me, 100), 300 (25), 287 (16), 286 (23), 163.5 (M^{2+}, 18); metastable peaks at m/e 325.0 (327 → 326), 297.6 (327 → 312).

Anal. Calcd. for $C_{21}H_{17}N_3O$: C, 77.04; H, 5.23; N, 12.84. Found: C, 77.33; H, 5.29; N, 13.04.

N-(13)Benzylrutaecarpine (**1i**).

This compound had m.p. 195-196° (ether) as pale yellow needles; λ max (Methanol): 278, 290, 328, 345, 362 nm; m/e 377 (M^+, 71%), 376 (16), 301 (24), 300 (M^+-C_6H_5, 100), 287 (7), 188.5 (M^{2+}, 12), 91 (40); metastable peaks at m/e 375.0 (377 → 376), 238.7 (377 → 300).

Anal. Calcd. for $C_{25}H_{19}N_3O$: C, 79.55; H, 5.07; N, 11.13. Found: C, 79.14; H, 4.97; N, 10.84.

N-(13)-β-Phenethylrutaecarpine (**1j**).

This compound had m.p. 153-155° (diisopropyl ether) as colourless needles; λ max (Methanol): 265 (sh), 276, 289, 329, 343, 361 nm; m/e 391 (M^+, 36%), 300 (M^+-C_7H_7, 98), 287 (M^+-C_8H_8, 100), 286 (60); metastable peaks at m/e 285.0 (287 → 286), 210.7 (391 → 297).

Anal. Calcd. for $C_{26}H_{21}N_3O$: C, 79.77; H, 5.41; N, 10.74. Found: C, 79.78; H, 5.78; N, 10.43.

N-(13)Carbomethoxymethylrutaecarpine (**1k**).

This compound had m.p. 189-191° (benzene) as fine colourless needles; λ max (Methanol): 265 (sh), 277, 291 (sh), 328, 343, 360 nm; m/e 359 (M^+, 48%), 328 (M^+-Me, 7), 300 (M^+-CO_2Me, 100), 259 (10); metastable peaks at m/e 299.7 (359 → 328), 250.7 (359 → 300).

Anal. Calcd. for $C_{21}H_{17}N_3O_3$: C, 70.18; H, 4.77; N, 11.69. Found: C, 70.02; H, 4.64; N, 11.91.

N-(13)Diethylaminoethylrutaecarpine Hydrochloride (**11**).

This compound had m.p. 245-246° (ethanol) as colourless needles; λ max (Methanol): 265 (sh), 277, 291, 329, 344, 361 nm; m/e 314 (5%), 300 (9), 287 (100), 100 (8), 99 (7), 86 (100).

Anal. Calcd. for $C_{24}H_{27}ClN_4O$: C, 68.15; H, 6.43; N, 13.24. Found: C, 68.32; H, 6.37; N, 13.09.

Synthesis of 8,14-Dihydro-14-ethylindolo[2′,3′:3,4]pyrido[2,1-*b*]-quinazolin-5(7*H*)one (**4**).

1,2,3,4-Tetrahydronorharman-1-one and *N*-ethylanthranilic acid methyl ester were refluxed in dry benzene in the presence of freshly distilled phosphorus oxychloride to afford pure **4** (68% yield), m.p. 183-185° dec. (benzene) as orange needles.

Anal. Calcd. for $C_{20}H_{17}N_3O$: C, 76.17; H, 5.43; N, 13.33. Found: C, 76.20; H, 5.25; N, 13.41.

Compound **4** Hydrochloride.

This compound had m.p. 205-207° dec. (ethanolic hydrogen chloride as yellow needles.

7,8,9,10-Tetrahydro-11*H*-pyrido[2,3-*a*]carbazole (**6a**).

This compound was obtained by indolization of the 8-quinolylhydrazone of cyclohexanone, according to Clemo (3), plates, m.p. 151° (ethyl acetate) [lit. (3) 151-152°].

11*H*-Pyrido[2,3-*a*]carbazole (**7a**).

Dehydrogenation of **6a** with 10% palladium-charcoal in boiling *p*-cymene gave **7a** (67% yield) as colourless needles, m.p. 170° (ethanol) [lit. (3) 169°]; λ max (ethanol) 243, 292 and 330 nm.

Synthesis of 2-(2′-Pyridyl)indole (**8a**).

2-(*o*-Nitrostyryl)pyridine (prepared according to Ruggli (8) (425 mg.) was suspended in triethylphosphite (20 ml.) and heated to reflux under nitrogen for 2 hours. The dark red solution was evaporated at 40° under reduced pressure (0.02 mm Hg) to give a viscous oil which was chromatographed on Woelm neutral alumina (grade III). Elution with benzene gave sequentially **8a** (290 mg.) and 2,2′-di(2-pyridyl)-3,3′-biindole (**9**) (65 mg.). Compound **8a** was obtained as colourless needles from light petroleum-benzene, m.p. 154° [lit. (9) 152°]; ^{1}H nmr (DMSO-d_6): 6.90-7.70 (6H, m), 7.84 [1H, dt, $^3J_{3',4'} \simeq {}^3J_{4',5'}$ 8.0 Hz, ^4J 2.0 Hz, C(4′)-*H*], 7.97 [1H, dt, ^3J 8.0 Hz, ^4J 2.0 Hz, C(4)-*H*], 8.62 [1H, dd, ^3J 5.0 Hz, ^4J 2.0 Hz, C(6′)-*H*], 11.62 (1H, br s, N*H*); m/e (170°) 194 (M^+, 100%), 167 (13), 140 (7), 139 (8), 90 (7), 89 (8), 78 (7), 63 (6).

2,2′-Di(2-pyridyl)3,3′-biindole (**9**).

This compound was obtained as colourless needles, m.p. 315-318° (benzene); λ max (Methanol): 211, 232 and 317 nm; ^{1}H nmr (DMSO-d_6): 6.70-7.70 (14H, m), 8.62 [1H, dd, ^3J 5.0 Hz, ^4J 2.0 Hz, C(6′)-*H*], 11.82 (1H, br s, N*H*); m/e (170°) 386 (M^+, 100%), 309, 282, 280, 195, 194, 78.

Anal. Calcd. for $C_{26}H_{18}N_4$: C, 80.80; H, 4.70; N, 14.50. Found: C, 80.95; H, 4.61; N, 14.44.

11-Methyl-7,8,9,10-tetrahydro-11*H*-pyrido[2,3-*a*]carbazole (**6b**).

This compound was obtained as colourless plates, m.p. 96° (Ethanol); λ max (Methanol): 227 and 276 nm; m/e (90°) 236 (M^+), 235, 208 (M^+-C_2H_4), 181, 167, 118, 103.

Anal. Calcd. for $C_{16}H_{16}N_2$: C, 81.32; H, 6.83; N, 16.86. Found: C, 81.53; H, 6.95; N, 11.51.

11-Methyl-11*H*-pyrido[2,3-*a*]carbazole (**7b**).

This compound was obtained as pale yellow needles, m.p. 110° (ethanol).

1-Methyl-2-(2′-pyridyl)indole (**8b**).

This compound had m.p. 88° (light petroleum-benzene) as tan crystals, [lit. (10) 90-91°]; λ max (Ethanol): 205, 219 and 313 nm.

Reaction of Rutaecarpine (**1a**) with 1,3-Diiodopropane in Acetone and Potassium Carbonate.

To a solution of **1a** (200 mg.) in dry acetone (150 ml.), anhydrous potassium carbonate (1.0 g.) and 1,3-diiodopropane (5 ml.) were added. The mixture was stirred and refluxed for 4 hours. Tlc (E_2) showed the absence of the starting material and the presence of two major spots. The most mobile component was isolated by silica gel chromatography (light petroleum-benzene, 1:1) and identified as *N*-(13)-(3-iodopropyl)rutaecarpine (**1m**) (180 mg.), m.p. 285° dec. darkening at 120°, as colourless needles (benzene), positive Beilstein test; λ max (Methanol): 265 (sh), 277, 290, 329, 344 and 361 nm; m/e (120°) 455 (M^+, 69%), 328 (M^+-I, 100), 327 (94), 326 (46), 312 (100), 300 (63), 287 (M^+-C_3H_4, 40), 286 (41); metastable peaks at m/e 325.0 (327 → 326), 285.0 (287 → 286), 236.5 (455 → 328).

The second component of the reaction mixture which migrated close to the base line gave a negative Beilstein test and was identified as **10** (75 mg.), m.p. 293° dec., as yellow needles (methanol); λ max (Methanol): 252, 300 (sh), 315, 366 nm; ν max (nujol): 1710, 1610, 1600, 1565 cm^{-1}; ^{1}H nmr: 3.00 [2H, t, ^3J 7.0 Hz,

C(16)H_2], 3.50 [2H, t, ^{3}J 7.0 Hz, C(8)H_2], 4.70 (6H, m), 7.20-8.20 (7H, m, aromatic protons), 8.40 [1H, dd, ^{3}J 8.0 Hz, ^{4}J 2.0 Hz, C(4)-H].

Anal. Calcd. for $C_{21}H_{17}N_3O$: C, 77.04; H, 5.23; N, 12.84. Found: C, 76.98; H, 5.41; N, 12.90.

Cyclization of **1m** into **10**.

By refluxing a solution of **1m** (50 mg.) in dry DMF (5 ml.) for 3.5 hours and trituration of the residue with dry ether yielded **10** (26 mg.), homogeneous by tlc (E_2).

Reaction of Rutaecarpine with 1,3-Diiodopropane in DMF and Potassium Carbonate.

Rutaecarpine (100 mg.) in dry DMF (25 ml.) and potassium carbonate (1.0 g.) were refluxed for 4 hours in the presence of excess 1,3-diiodopropane (10 ml.). The cooled suspension was filtered and evaporated at 0.1 mm Hg to afford a brown residue. Filtration over silica gel with chloroform-methanol, 99:1 gave pure **13** (89 mg.) as pale yellow needles, m.p. 212° (benzene): ν max (Chloroform): 1649, 1610, 1600, 1520 cm^{-1}; m/e (160°) 327 (M^+, 100%), 298 (89), 285 (12), 270 (10), 163.5 (M^{2+}, 5); metastable peaks at m/e 325.0 (327 → 326), 297.0 (299 → 298). Compound **13** was also obtained by refluxing **1m** for 5 hours or **10** in dry DMF and potassium carbonate for 3.5 hours in 68% and 72% yield, respectively.

Reaction of **1a** with 1,2-Dibromoethane in Acetone and Potassium Carbonate.

To a solution of **1a** (200 mg.) in acetone (100 ml.), 1,2-dibromoethane (20 ml.) and potassium carbonate (1.0 g.) were added. Only after 2 hours, tlc (E_2) revealed mainly the presence of two new components (R_f 0.20 and 0.34). The reaction mixture was filtered and evaporated to yield a yellow solid. A portion of the residue (100 mg.) was chromatographed on neutral alumina (grade II) and elution with benzene-chloroform mixtures gave **12a** (86 mg.), m.p. above 300° (benzene), negative Beilstein test; λ max (Methanol): 253, 311 and 361 nm (log ϵ 4.36, 4.11 and 4.50); ν max (Chloroform): 1645, 1610, 1600, 1520 cm^{-1}; ν max (Potassium bromide): 1630, 1600, 1523 cm^{-1}; ^{1}H nmr: 4.70-5.10 [4H, m, C(13)H_2 and C(14)H_2], 6.05 (1H, AB part of ABX system, $^3J_{cis}$ 11.0 Hz, $^2J_{gem}$ 1.5 Hz) and 6.10 (AB part of ABX system, $^3J_{trans}$ 17.0 Hz, $^2J_{gem}$ 1.5 Hz), 7.80-8.20 (8H, m), 8.41 [1H, dd, ^{3}J 8.0 Hz, ^{4}J 2.0 Hz, C(4)H]; m/e (160°) 313 (M^+, 62%), 312 (100), 285 (M^+-28, 17), 257 (10), 256 (9), 167 (6), 156.5 (M^{2+}, 7); metastable peaks at m/e 311.0 (313 → 312), 260.3 (313 → 285), 231.7 (285 → 257).

Anal. Calcd. for $C_{20}H_{15}N_3O$: C, 76.67; H, 4.79; N, 13.42. Found: C, 76.71; H, 4.81; N, 13.29.

The second portion of the mixture was fractioned by preparative tlc (E_2) and a few mg. of the slower-moving component was isolated. This amorphous material exhibited ir (nujol) carbonyl band at 1708 cm^{-1} and uv maxima (Methanol) at 248, 295, 308 and 361 nm and its deep yellow colour faded by treatment with sodium borohydride in 95% methanol. These evidences and the conversion of this compound into **12a** in nearly quantitative yield by refluxing in DMF (5 hours) in the presence of potassium carbonate indicate for it the structure **11**.

Catalytic Hydrogenation of **12a** to **12b**.

To the fluorescent solution of **12a** (50 mg.) in methanol (25 ml.) was added 10% palladium-carbon (25 mg.) and the mixture was stirred under a hydrogen atmosphere for 1 hour. The catalyst was then filtered off through Celite 535 and washed with chloroform. Concentration *in vacuo* of the combined colourless filtrate and washings afforded a solid. Crystallization from methanol gave pure **12b** (45 mg.) as colourless plates, m.p. 294-295° (sinterring at 260°); λ max (Methanol): 241 (sh), 252, 309 (sh), 318, 346 nm (log ϵ 4.25, 4.28, 4.37); ν max (Potassium bromide): 1630, 1605, 1520 cm^{-1}; ν max (Chloroform): 1645, 1610, 1600, 1520 cm^{-1}; ^{1}H nmr: 1.46 (3H, t, ^{3}J 7.5 Hz, CH_3-CH$_2$), 3.35 (2H, q, ^{3}J 7.5 Hz, CH$_3$-CH_2), 4.20-5.10 [4H, m, N(13)-CH_2-CH_2-N(14)], 7.80-8.20 (7H, m, aromatic protons), 8.48 [1H, dd, ^{3}J 8.0 Hz, ^{4}J 2.0 Hz, C(4)H]; m/e (150°) 315 (M^+, 100%), 314 (29), 300 (23), 287 (15), 286 (42), 272 (10), 257 (4), 168 (4), 143 (5); metastable peaks at m/e 313.0 (315 → 314), 285.7 (315 → 300), 261.4 (315 → 286).

Anal. Calcd. for $C_{20}H_{17}N_3O$: C, 76.17; H, 5.43; N, 13.33. Found: C, 76.45; H, 5.57; N, 13.46.

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