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METHYLENE-INDOLINES, INDOLENINES AND INDOLENINIUMS, XXII (1) THE FISCHER INDOLIZATION OF SOME SUBSTITUTED CYCLOPENTANONES.

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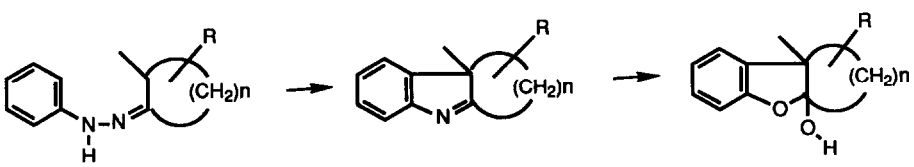
Abstract : When submitted to the acidic conditions of the Fischer indolization reaction, the phenylhydrazone of 2,5-dimethylcyclopentanone **1** did not give the expected indolenine **1c**, but carbinolamines **1d**. Depending on the substitution pattern of the aromatic ring, or that of the cyclopentanone, dimers **3j, 4j**, ketone **3e**, or compounds **5m** and **5n** resulting from the cleavage of the cyclopentane ring were obtained $NaBH_3CN$ reduction of the reaction mixture mainly gave indolines such as **1f**.

Some time ago, we reported[2] on the easy "nitrous acid deamination" of indolenines **B** (n=4) (resulting from the Fischer annulation of cyclohexanone-phenylhydrazones **A** to cyclohexano-benzofurans **C** (n=4) (scheme 1). The reaction was developed from the idea that indolenines **B** are equivalent to anilinoketones

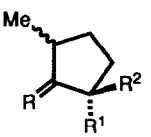
In view of the synthesis of marine sesquiterpenes of the aplysine series[3] we investigated the same sequence starting from substituted cyclopentanones (n=3). While the Fischer cyclization of the phenylhydrazones of α-unsubstituted cyclopentanones is well documented[4], results related to α-substituted cyclopentanones are scarce in the literature and formation of indolenines has only been claimed in a very few instances, albeit in low, or unspecified yields.[5,6,7]



scheme 1

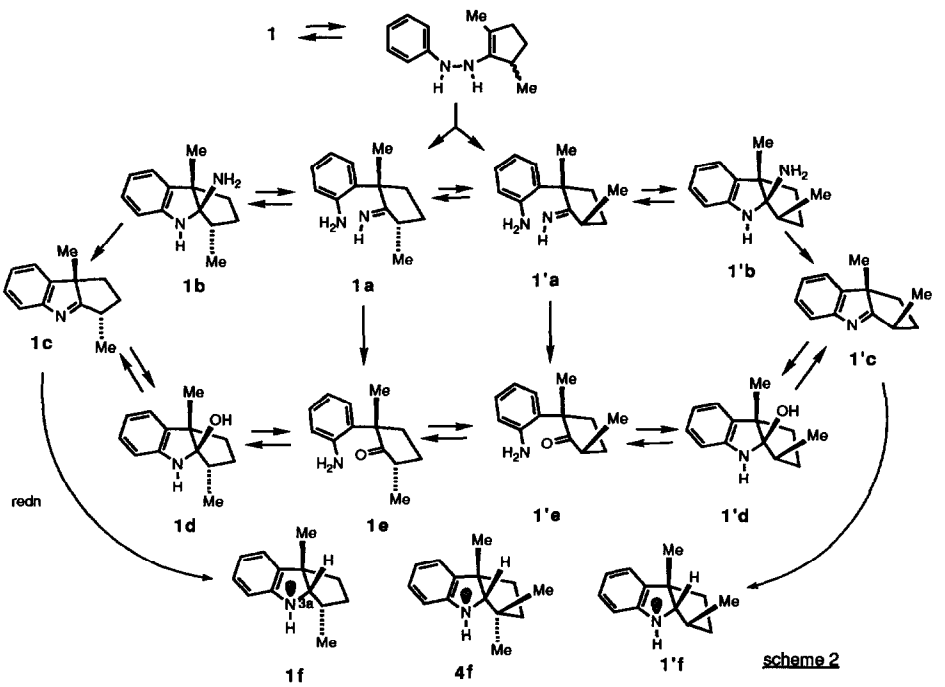
The present work is an account of attempts of Fischer indolization of arylhydrazones **1-5**. These compounds were prepared from 2,5-dimethyl-[8], 2,2,5-trimethyl-[9] cyclopentanone and from methyl-2,5-dimethylcyclopentanone-2-carboxylate[10], respectively, by heating with an arylhydrazine in refluxing ethanol containing a catalytic amount of AcOH. The resulting arylhydrazones began to decompose under attempted purification, and therefore the isolated crude materials were immediately heated in

concentrated acetic acid under argon for 1.5 h. After dilution with water, the reaction mixture was made alkaline and further extracted with methylene chloride The formed derivatives where then isolated after repeated centrifugal tlc.



	R^1	R^2	R
1	H	Me	N-NH-Ph
2	H	Me	N-NH-Ph(*m*-Me)
3	Me	Me	N-NH-Ph
4	Me	Me	N-NH-Ph(*m*-Me)
5	Me	COOMe	N-NH-Ph

When starting from 2,5-dimethylcyclopentanone, a compound was isolated (50%), whose structure deduced from the NMR and mass spectral data best fitted with a 1 1 mixture of diastereoisomeric carbinolamines **1d** and **1'd** (scheme 2) : the UV spectrum was indolinic; the mass spectrum exhibited a molecular peak at m/z 203 (24 %) and the base peak (100%) at m/z 147, which could result from a conceivably easy fragmentation to 3-methyloxindole. All peaks in the ^{13}C NMR spectrum could be attributed (figure 2) and the ^1H NMR spectrum was in agreement with the structure (figure 1) However an easy dimerization upon standing was deduced from the occurrence of some higher m/z ions in the mass spectrum 370 (0.2%; M - H_2O), 315(0 2%), 314(0.2) and 217(7%) and of some absorption in the IR carbonyl



scheme 2

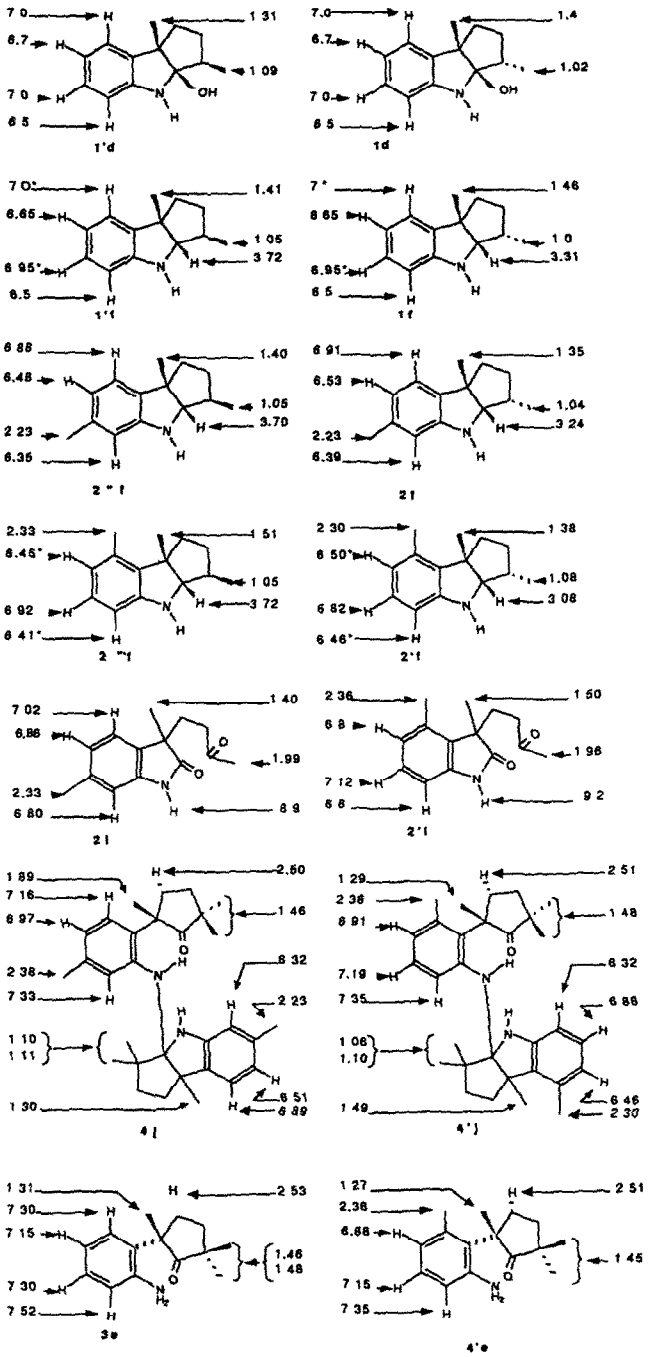


Figure 1: ^{1}H NMR data.

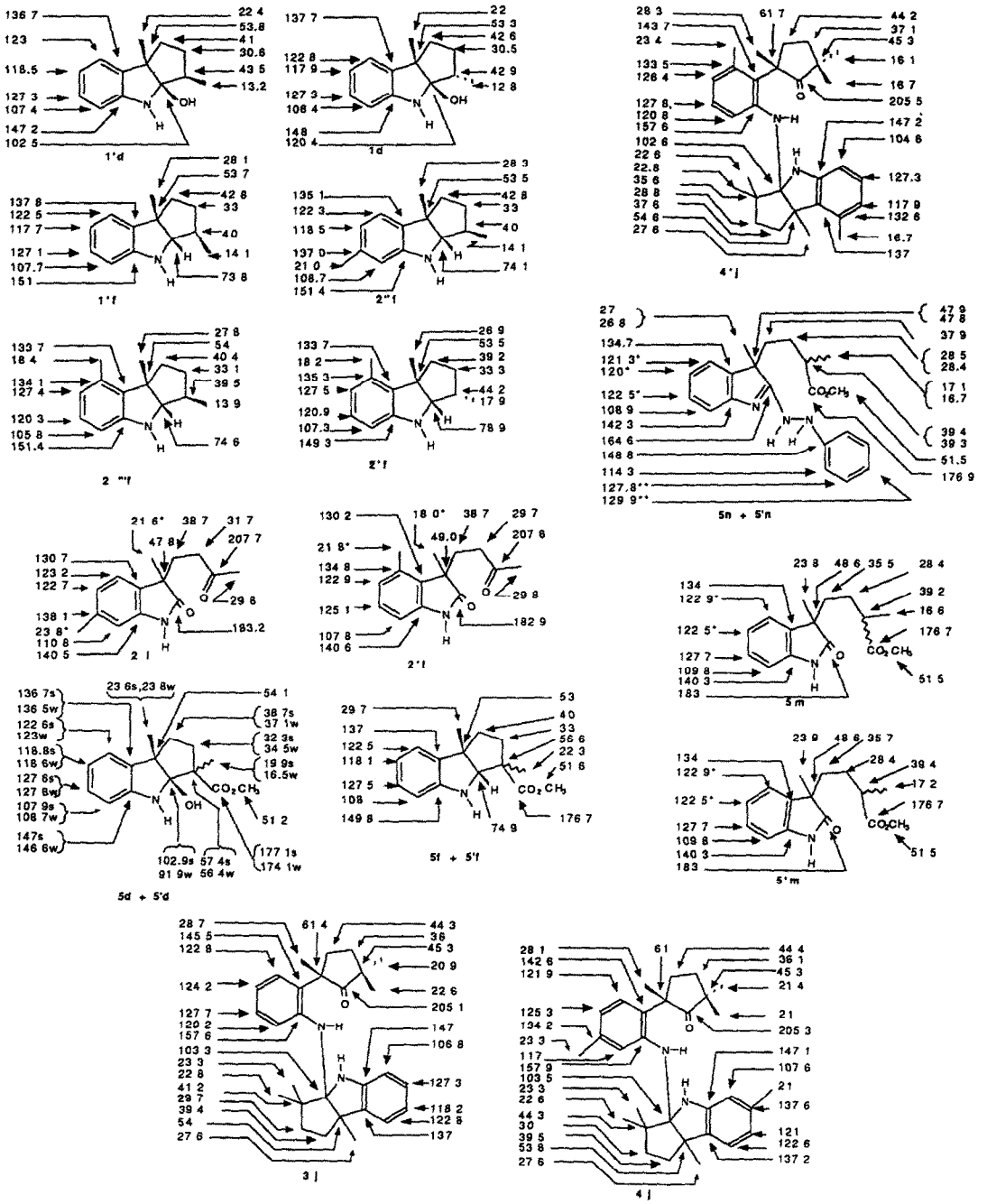
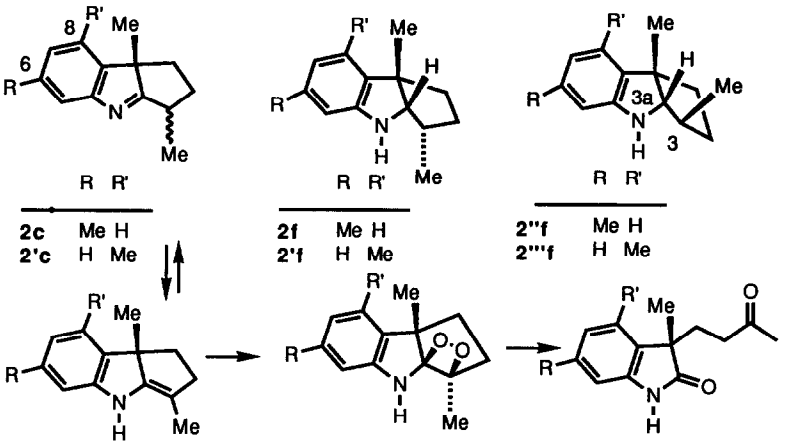


Figure 2 ^{13}C NMR data

region at 1710, 1700 and 1680 cm-1. In chloroform solution, this extra carbonyl absorption disappeared and no CO signal was detectable in the ^{13}C NMR spectrum. Therefore **1d** and **1'd** appeared to be monomeric, at least in this solvent. In the presence of silica, the initial 1:1 mixture of diastereoisomers equilibrated to a 1·5 mixture. The major isomer is thought to be **1'd**, which suffers less steric hindrance than **1d**.

Two paths may be envisioned to account for the formation of carbinolamines **1d** and **1'd**. This depends on the precursor from which ammonia is eliminated either the bicyclic imines **1a,1'a**, or the tricyclic aminals **1b,1'b** *via* indolenines **1c,1'c**. Some arguments support the latter hypothesis.[9]The fact that the equilibrium (in favor of **1'd**) was not immediately reached in the presence of water could imply that **1d** would result from addition of water on the (protonated) **1c**, rather than on **1a**,**1'a**, which would lead to the more easily interconvertible **1e** and **1'e**. When the reaction of phenylhydrazone **1** in acetic acid was immediately followed by *in situ* reduction with an excess $NaBH_3CN$, the sole indoline **1'f** was formed, with no trace of **1f**. On the contrary, when the reaction was performed in ethanolic HCl, both products **1f** and **1'f** were obtained in a 2:1 ratio The structure of **1'f** rests on its indolinic UV spectrum, on its mass spectrum (m/z 187.15, 52%, $M^{\cdot+}$ (C_{13} H_{17} N) , 158, 51 %; 144, 96%, 131, 45 %, 130, 100%), and on its ^{13}C NMR spectrum The question of the C(3) stereochemistry of **1f** and of **1'f** cannot be completely answered; NOE experiments gave no decisive results Finally, the most striking spectroscopical difference between **1f** and **1'f** was the 0.4 ppm downfield shift of the C(3a)-H NMR signal (3 72 in **1'f** *vs* 3 31 in **1f**), which was indicative of a small modification in the necessarily *cis* orientation of the C(3a)-H bond and the nitrogen pair. If this were not the case a stereoelectronical interaction would develop with the substituent at C(3), *i.e.* Me and H, for **1f** and **1'f**. In **1f**, the vicinity of C(3)-Me and N(4)-H distorts the fused system, so that C(3a)-H no longer completely eclipses the nitrogen pair (upfield signal at 3 31 ppm). The C(3a)-H signal of the congested compound **4f** appears at a nearly identical position (3.25 ppm). Thus, a shielded signal for C(3a)-H must be associated with a *cis* relationship between C(3a)-H and the bulkiest substituent at C(3) (scheme 2). This result implies the intermediacy of the (protonated) targeted indolenines **1c** and **1'c** in acidic medium Of interest is the striking structural relationship of **1d,1'd** and **1f** with a part-structure of the indole alkaloids tuboxenine and vindolinine, in which epimerization of the secondary methyl group has been reported [11]

In sharp contrast with these results (scheme 3), upon heating of the *m*-tolylhydrazone of 2,5-dimethylcyclopentanone **2** in concentrated acetic acid, six products were formed in low yields . two dimers, whose structures were not fully elucidated, but which apparently arose from C-C bonding between the aromatic rings, the two regioisomeric indolines **2"f** and **2'"f**, the structures of which compared with that of **1'f**, especially in terms of orientation of the C(3a)-H bond (δ H(3) = 3 70 and 3 72 ppm, respectively), and the two regioisomeric oxindolic methylketones **2 I** and **2' I**, whose structures were easily deduced from their spectral data. The reason why the presence of the additional aromatic methyl group modifies to such an extent the course of the reaction is not obvious. All four observed monomers appear to result, either from reduction (by hydrazine), or from oxidation (during work up, through a dioxetane) of each of the regioisomers **2c** and **2'c** As *m*-tolylphenylhydrazine had been prepared by $SnCl_2$ reduction of the corresponding nitrosamine, traces of Sn derivatives may have catalyzed this oxidation, and the aromatic dimerization as well.



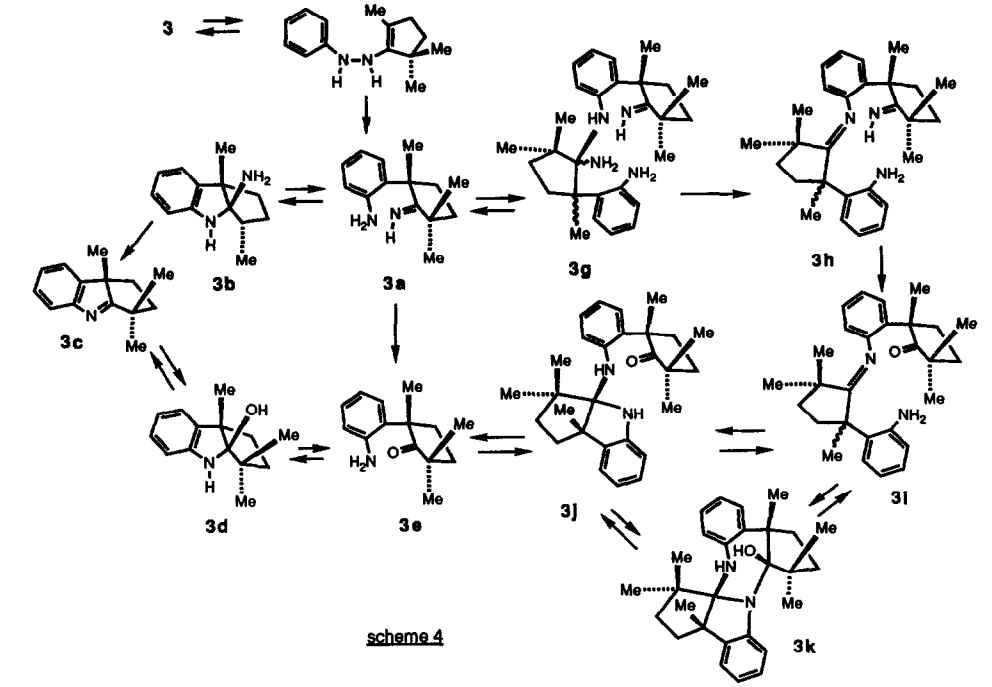
scheme 3

When the Fischer cyclization of **2** was immediately followed by $NaBH_3CN$ reduction (AcOH, 0°C, 2h), the four possible isomeric indolines **2f, 2'f, 2"f** and **2"'f** resulted. Their total yield after isolation was 35% (cyclization in AcOH), 41% (cyclization in 10% ethanolic H_2SO_4) and 48% (cyclization in 30% ethanolic HCl). In all three runs, the ratio of the (*rel*)-3α-methyl (**2f** + **2'f**) to the 3β-methyl derivatives (**2"f** + **2"'f**) was roughly 3:7, and the ratio of the 6-substituted isomers (**2f** + **2"f**) to the 8-substituted ones (**2'f** + **2"'f**) was slightly in favor of the 6-substituted series, as previously reported [12]

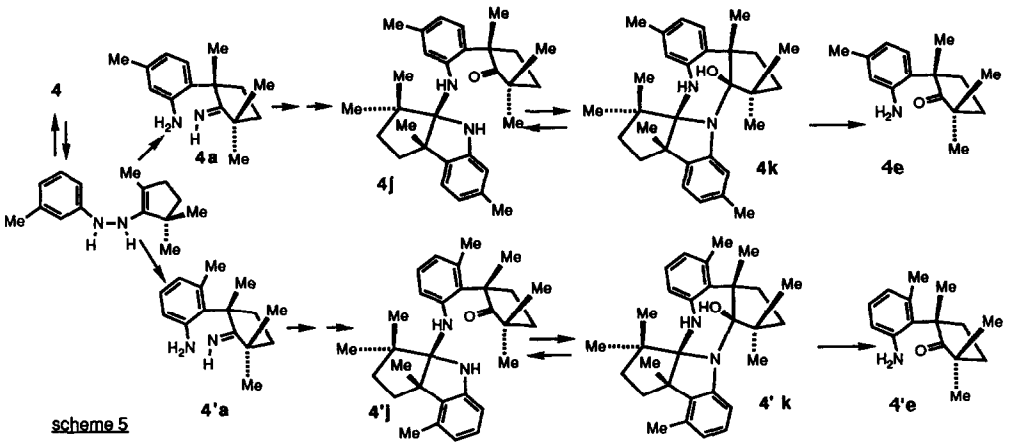
When starting from 2,2,5-trimethylcyclopentanone, heating of its phenylhydrazone **3** in acetic acid followed by aqueous workup and separation afforded dimer **3j** (58%) (scheme 4) Similarly (scheme 5), the *m*-tolylhydrazone **4** gave the symmetrical regioisomeric dimers **4j** (30 %) and **4'j** (28%) (as can be unambiguously deduced from the ^1H and ^{13}C NMR spectra) As no crossed dimer was found in the latter experiment, dimerization occured after separation of the monomers

The dimeric character of compounds **3j, 4j** and **4'j** appeared clearly from their UV, mass and NMR spectra For instance, although the molecular peak was not detected in the MS of **3j,** a series of fragments up to m/z 385 ($M^{\cdot+}$-31) was seen. Moreover, the complementary ions m/z 199 (35%, *cf* **3c**) and 217 (19%, *cf* **3d** or **3e**) were of high diagnostic value The base peak in the spectrum was at m/z 184 (199-15), in agreement with the easy loss of the angular methyl group in species **3c** under electron impact The six methyl groups appeared as six different signals on the ^1H and ^{13}C NMR spectra, and the eight aromatic carbons as eight different signals as well. The carbonyl group was responsible for an IR absorption at 1710 cm^{-1}, and for a 205 ppm signal on the ^{13}C NMR spectrum (figure 2) while the (indolinic) carbon C(3a) bearing the geminal diamino group was at 103.3 ppm

Of interest is the fact that each of the regioisomeric (racemic) dimers **4j** and **4'j** was present as only one of two possible diastereoisomeric pairs of monomers This might involve the intermediacy of a species



scheme 4



scheme 5

like **4k** in the dimerization process The steric interactions in such a species would then preclude dimerization of two enantiomeric monomers of opposite configuration. Again, the initially formed **3a** may evolve into **3j** along two different paths involving species **3b-e.** In contrast with the cyclization of **1**, the supplementary crowding due to the gem-dimethyl group appears to disfavor intramolecular cyclization into **3b** *vs* **3d**. A possibility is that the isolated dimer originates from initial dimerization of **3a** into **3g**, and from this into **3h** and **3i**.

Upon standing for 2 hrs in methanol in the presence of silica, **3j** almost quantitatively generated the monomeric bicyclic ketone **3e**, which did not spontaneously cyclize into the tricyclic carbinolamine **3d**. The same transformation was observed to a lesser extent upon prolonged (5 h) standing of **3j** in $CDCl_3$ during recording of NMR spectra. The structure of **3e** was deduced from the m/z 217 molecular peak in its MS, and from the simplification of the 1H NMR spectrum . four aromatic protons between 7.1 and 7.6 ppm , two methylenes at 1.9-2 ppm and three methyl groups at 1.30, 1.47 and 1.49 ppm. The easy (irreversible?) isolation of **3e** from **3j** would then be in favour of the formation of **3j** through **3g**, rather than from **3e**.

An identical phenomenon was observed during measurement of the NMR spectra of dimers **4j** and **4'j**. Here, the regioisomer **4'j** appeared more prone to hydrolysis into the monomer (due to the additional slight steric interaction involving the aromatic methyl group) than **4j**, and ketone **4'e** could be characterized.

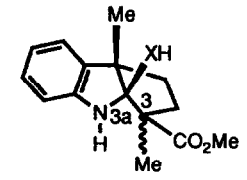
Upon indolization in AcOH, methyl-2,5-dimethylcyclohexanone-2-carboxylate yielded two pairs of unseparable diastereoisomers (scheme 6)· carbinolamines **5d, 5'd** (19%), and iminohydrazines **5n, 5'n** (15%), together with the stereoisomeric oxindoles **5m** (3%) and **5'm** (3%) (scheme 6) Carbinolamines **5d, 5'd**, indolinic UV spectrum, $M^{\cdot +}$ 261 (17%) exhibited in their MS a base peak at m/z 147 (3-methyloxindole). The ratio of isomers **5d**:**5'd** was 1:3 as seen from the methyl signals on the ^1H NMR spectrum · 1.40 and 1.31 ppm for the minor isomer, and 1 37 and 1.46 ppm for the major one All carbon atoms gave double signals in the ^{13}C NMR spectrum.

Compounds **5m, 5'm**, oxindolic UV spectrum, $M.^+$ 261, showed in their MS peaks corresponding to the progressive loss of the side chain : m/z 201-202 (14-7%, M-COOMe,H) 174 (5%), 160 (26%) and 146 (100%, 3-methylindole *minus* 1 mu. The ^1H NMR spectrum showed Me peaks at 1.07 (d) and 1.39 (s) ppm for one isomer, and at 1.09 (d) and 1 40 (s) ppm for the other, while the ^{13}C NMR spectrum exhibited 15 signals, which were in agreement with the structure (figure 2)

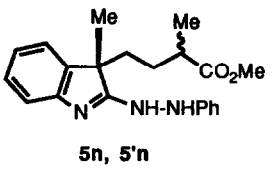
Iminohydrazines **5n, 5'n** had spectral features comparable with those of oxindoles **5m, 5'm** : UV, 205, 265 nm ; MS : M^+ 351 (19%) ; peaks at m/z 236 (complete loss of the side chain) and 77 (100%, benzenium ion), ^1H NMR, Me groups at 1.08/1.10 and 1.50/1 51 ppm in a 3 4 ratio ; ^{13}C NMR: 23 signals (figure 2).

Formation of carbinolamines **5d, 5'd** was similar to that of **1d, 1'd.** Cleavage of the 3,3a bond in the oxindoles obviously results from a retroaldol cleavage affecting **5d, 5'd**, and iminohydrazines **5n, 5'n** also result from a similar fragmentation affecting for instance **5p** and **5'p**. This reflects a competition between the addition of water and the addition of phenylhydrazine to an iminium at any stage of the reaction process Such additions of phenylhydrazines on indolenines have been reported[13,14,15] and are likely to occur during most of the Fischer syntheses of indolenines They are, however, reversible in most instances, which was not the case here, due to fragmentation

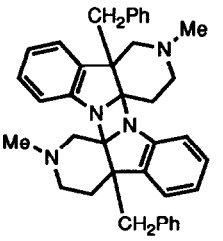
In situ reduction of the cyclization mixture with $NaBH_3CN$ gave the unaffected iminohydrazines **5n, 5'n** (25%) and indolines **5f, 5'f** (5%) (**5f:5f'**=5:1). The low frequency of the C=O band (1700 cm^{-1}), as well as the low field signal (3.8 ppm) of C(3a-H), favored the depicted structure **5f** for the major isomer. As no oxindoles **5m, 5'm** were present, it is inferred that these compounds do not result from hydrolysis of **5n, 5'n**, neither in acetic acid nor during the work up



5d, 5'd X = O
5p, 5'p X = N-NH-Ph
5f , 5'f XH = H



5n, 5'n



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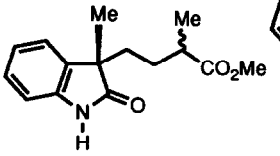
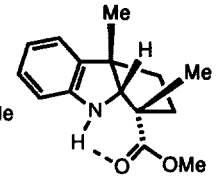


5m, 5'm



5 f

scheme 6

In conclusion, the Fischer cyclization of the phenylhydrazones of α,α'-disubstituted and trisubstituted cyclopentanones failed in every case to yield stable indolenines. When the related indoleninium ions, or their equivalents, are formed, they appear to be extremely prone to nucleophilic addition, either of water, or of phenylhydrazine, or through a dimerization process, to yield a *cis*-fused ring system

While less strained than the corresponding indoleniniums, the tricyclic carbinolamines resulting from water addition are themselves extremely sensitive to minor steric factors· whereas a (*rel*)-3β -Me appears to suffer more steric interactions than a (*rel*)-3α -Me, in the 3,3-dimethyl derivatives the steric interaction suffered by the non epimerisable (*rel*)-β - substituent is then overcome by opening of the pyrrole ring This observation, once again, underlines the equivalence of indolenines with anilinoketones.

Finally, it is apparent from the above results that each of the three monomeric or dimeric interconvertible species corresponding to **3d, 3e** and **3j** on scheme 4 are likely to be formed upon Fischer annulation of substituted cyclopentanones, while the structures of the isolated end products mainly hinge on steric factors. Regarding dimeric species, it may be noticed that no symmetrical dimer with a structure corresponding to compound **7**, recently described by Southwick following a different synthetic approach[16], was isolated.

From a preparative point of view, the yield of arylation of the cyclopentane nucleus was in most cases around 50%. Of special interest is the stereochemical control of three adjacent chiral centers on the cyclopentane ring in indoline **1f**.

EXPERIMENTAL

All commercially available products were purchased from Aldrich, and were used without purification; UV spectra were measured on a Varian 634 apparatus, IR spectra were recorded on a Beckman

Products	Type of chromato-graphy(eluant) *Relative polarity (1=less polar)*	Isolated yield % (x:y ratio if a mixture)	UV(MeOH) : λ max nm sh=shoulder	IR cm^{-1} . f=film soln=$CHCl_3$ solution w=weak	MS : M^+ (composition, intensity %) other peaks (intensity %)
1d +1'd	cc ($CHCl_3$)	50 (1:1)	207, 243, 295	f:3380,1710-1700-1680(w),1600	M^+ 203 1315($C_{13}H_{17}ON$, 24),185(18) 170(21),160(14),147(100),146(53),144-43(32)
2 l	cc (CH_2Cl_2) then tlc ($CHCl_2$-hexane 5.1) *1*	4 (*)	210, 250	f:3240,1710,1700,1620	M^+ 231($C_{14}H_{17}NO_2$, 36),161(49),160(100),142(15)
2' l	idem... *2*	4 (*)	210, 250, 280(sh)	f.3220,1700,1690,1600	M^+ 231($C_{14}H_{17}NO_2$, 30),174(8),161(54),160(100),142(14)
2" f	idem *3*	8 (*)		see Table II	
2'" f	idem... *4*	9 (*)		see Table II	
3 j	tlc (CH_2Cl_2)	58	270, 240, 298	soln:3660,3560,3450, 1710,1600,1580	No M^+ · 385(M-31,1),384(2),217 1457(19),199(35),185(13), 184 1134(100),171(13),160(17),147(85),146(40),144(40),143(37)
4 j	cc (CH_2Cl_2-MeOH 99:1) *1*	30	210, 247, 300	soln:3400,3320, 1710,1610,1580	No M^+ · 333(23),264(21),247(10),214(13),213(23),199(12) 198(54),162(13),161(44),160(46),159(42),158(100),157(23)
4' j	cc (CH_2Cl_2-MeOH 99:1) *2*	28	212, 248, 290	soln:3330,3280,1715 1700,1650,1580	No $M^{+\cdot}$ 443(M-1,2) ,424(21),313(10),312(10),287(15),247(13), 231(13),230(40),217(17),214(15),213(25),200(13),199(13), 198(50),162(33),161(100),158(58),157(44),144(27),130(15)
5d +5'd	cc (CH_2Cl_2-MeOH 99:1) *1*	*19 (1.3)*	*208,243,285*	*f.3360,1720,1710 1620*	M^+ 261($C_{15}H_{19}NO_3$, 17),201(26),200(19),184(13), 160(19),148(13),147(100),146(26),144(19)
5 n +5' n	*idem. . 2*	*15 (3·4)*	*205,265*	*f:3320,1740,1720 1680,1670,1660,1600*	M^+ 351($C_{21}H_{25}N_3O_2$, 19),236(42),184(13),145(51), 144(28),105(17),93(26),77(100)
5m	idem... *3*	3	208, 246, 280(sh)	f:3260,1720,1700	M^+ 261($C_{15}H_{19}NO_3$, 19),201(16),160(26),146(100), 130(15),128(25),117(14),115(32),91(11),77(14)
5'm	idem *4*	3	idem	idem	nearly identical with exception of 201(13),160(20)

(*) isolated yield lowered by successive centrifugal then thin layer chromatographies

Table I: Rearrangement products of arylhydrazones (^1H and ^{13}C NMR: see figures 1 and 2)

Products	Type of chromatography (solvant) Relative polarity (*1=less polar*)	Yield % (*method*)	UV(MeOH) λ max nm	IR cm^{-1} (film)	MS · M^{+}·(composition, intensity %) other peaks (intensity %)
1'f	tlc (CH_2Cl_2-hexane 4 1) *1*	35 (*A*)	208, 247, 302	3380, 1600	M^{+} 187($C_{13}H_{17}N$, 52),159(17),158(51),145(15),144(96), 143(12),132(31),131(45),130(100),77(28)
1f	" " *2*	3 (*B*)	"	3420, 1600	M^{+} 187($C_{13}H_{17}N$, 50), nearly superimposable with 1'f
2"f	tlc (CH_2Cl_2-hexane 3:1) *1*	13 (*A*) 18 (*B*) 14 (*C*)	218, 249, 302	3360, 1610	M^{+} 201.1502($C_{14}H_{19}N$, 75),188(22),173(20), 172 1119(100),159(15),158(98),146(36), 145(49),144 0812(49),115(13)
2"'f	" " *2*	11 (*A*) 16 (*B*) 13 (*C*)	219, 250, 300	3380, 1590	M^{+} 201.1508($C_{14}H_{19}N$, 70), nearly identical with 2"f with exception of 172(76) and 144(100)
2f	" " *3*	6 (*A*) 7 (*B*) 7 (*C*)	220, 245, 295	3380, 1590	M^{+} 201($C_{14}H_{19}N$, 80) nearly identical with 2"'f
2'f	" " *4*	5(*A*) 7 (*B*) 7 (*C*)	220, 245, 292	3380, 1590	M^{+} 201($C_{14}H_{19}N$, 60) nearly identical with 2"'f with exception of 172(39) and 146(80)
4f	tlc (CH_2Cl_2-hexane 4:1)	§	220, 248, 298	3400, 1600	M^{+} 215($C_{15}H_{21}N$, 60), 201(10),186(10),172(20), 158(45),146(100),144-45(65)
5f + 5'f	tlc (CH_2Cl_2-MeOH 99 :1)	5 (*A*) (5:1) mixture	207, 245, 298	3360, 1700, 1595	M^{+}· 245($C_{15}H_{19}NO_2$, 34),198(10), 170(10),145(48),144(100), 132(20),131(39),130(90),103(10),77(20)

§ This compound originates from 2,2,5-trimethylcyclopentanone present as a contaminant in 2,5-dimethylcyclopentanone

Table II : Physical data of indolines f (^1H and ^{13}C NMR : see figures 1 and 2)

Brücker AC 300 : HREIMS spectra (E=-70 eV) were obtained on a JEOL JMS D-300 spectrometer; Merck Kieselgel 60 PF_{254} was used for thin layer chromatography (tlc) or centrifugal chromatography (cc).

Preparation and rearrangement of arylhydrazones of 2,5-dimethyl-cyclopentanone, of 2, 2,5-trimethyl-cyclopentanone and methyl-5-methyl-cyclopentanone-2-carboxylate : general procedure :
(3-methyl-phenylhydrazine was prepared from *m*-toluidine[17])
* *Method A* : A mixture of arylhydrazine (1 mmol), ketone (1.1 mmol) and acetic acid (1 drop) in absolute ethanol (5 ml) was refluxed under nitrogen atmosphere until all the arylhydrazine was transformed into a mixture of two less polar products (hydrazones) (about 1 h). Ethanol was then thoroughly removed by distillation and 1 ml of glacial acetic acid was added. The mixture was heated at 100°C for 1 h, then diluted with water (20 ml), and made alkaline with K_2CO_3 up to pH 10 and extracted with CH_2Cl_2 (3 x 20 ml) The organic extracts were collected and washed with a saturated NaCl aqueous solution, then dried with $MgSO_4$, filtered, evaporated and chromatographed (see tables I and II).
* *Method B* : The ethanolic solution of phenylhydrazone was saturated with gazeous HCl, then refluxed for 1 5 h. The solvent was distilled; the residue was submitted to the above work-up.
* *Method C* : The ethanolic solution of phenylhydrazone was added with 97% H_2SO_4 (0.5ml/mmol) and refluxed for 1.5 h. Most of the ethanol was then distilled; the residue was diluted with a saturated Na_2CO_3 aqueous solution, and submitted to the usual work-up.

Preparation of ketone **3e** : On standing for 4 h in a CH_2Cl_2 suspension of silica, dimer **3j** partially gave ketone **3e** (**3j**:**3e** = 1:5, measured by ^1H NMR) ; Spectral data of the mixture, HREIMS : m/z (intensity %): no peaks over m/z 220 : 217.1457 (6) $C_{14}H_{19}NO$ (M^+ for **3e** , 199.1383 (31) $C_{14}H_{17}N$, 184.1134 (100) $C_{13}H_{14}N$; 161(17) $C_{10}H_{11}NO$, 147(26) ; 144(27) ; 143(29) , 130(12) , 115(14) ; 91(7); 77(10). IR ($CHCl_3$ soln.) 3410, 1705, 1600 and 1570 cm^{-1}. ^1H NMR : see Table I

Preparation of ketone **4'e** : On standing for 1.5 h in the presence of D_2O, a $CDCl_3$ solution of dimer **4'j** gave the nearly pure ketone **4'e**. IR ($CDCl_3$ soln) 1700, 1600 and 1580 cm^{-1} ; ^1H NMR : see Table I.

Preparation of indolines : $NaBH_3CN$ reduction of the rearrangement mixture of arylhydrazone : At the end of the above reaction (method A), the acetic acid solution was cooled at 0°C Then five molar equivalents of $NaBH_3CN$ were added portionwise within 1 h. Water was added, and the solution was made basic (pH=10) with K_2CO_3, and extracted as usual. If methods B or C were used, the ethanol was firstly removed (distillation), and replaced with 1-2 ml acetic acid/mmol. Then $NaBH_3CN$ was added as above (see table II for yields, and for physical data)

REFERENCES

1 Methylene-indolines, Indolenines and Indoleniniums, XXI, Laronze, J.Y.; Laronze, J.; Patigny, D., Lévy, J. *Tetrahedron Lett.* **1986**, *27* (4), 489.
2 . Lévy, J.; Sigaut, F. *Tetrahedron Lett.* **1983**, *24* (45), 4983.
Lévy, J ; Sigaut, F. *Tetrahedron Lett.* **1983**, *24* (45), 1987.
3 . Laronze, J.Y.; El Boukili, R.; Cartier, D.; Laronze, J., Lévy, J. *Tetrahedron Lett.* **1989**, *30* (17), 2229.
4 Robinson, B. "The Fisher Indole Synthesis", *J.Wiley*, New York **1982**.
5 Harradence, R.M.; Lion, F. *J.Proc.Roy.Soc.* **1939**, *73*, 14.
6 . Maeda, M.; Nakazaki, M. *Chem.Ind.* **1960**, 719.
7 . Kelly, A.M ; Mc Leod, D.H.; Parrick, J. *Can.J.Chem.* **1965**, *43*, 296.
8 Sisido, K.; Utimoto, K.; Isida, T. *J.Org Chem.* **1964**, *30*, 184.
9 . Dubois, J.E ; Fort, J.F. *Tetrahedron* **1972**, *28*, 1653.
10 Meyer, W.L.; Lobo, A.P., Marquis, E.T. *J.Org.Chem.* **1965**, *30*, 184.
11. Rasoanaivo, P. Ph.D.Thesis, Université de Paris Sud **1974**.
12. Baccolini, G., Marotta, E. *Tetrahedron* **1985**, *41*, 4620 and *loc.cit*
13 Nakaki, M.; Maeda, M. *Bull.Chem.Soc. Japan* **1962**, *35*, 1380.
14. Friesen, R.W., Vice, S.F.; Findlay, C.E.; Dimitrienko, G.I. *Tetrahedron Lett.* **1985**, *26* (2), 161.
15. Ohnuma, T ; Sekine, Y.; Ban, Y. *Israel J.Chem.* **1986**, *27*, 73
16. Southwick, P.L., Sullivan, D.S III, *Synthesis* **1986**, 731
17 Gilman, H *Org.Synth* Coll vol.*1* **1932**, 442