HETEROCYCLES. XII.[1] CHIRAL BENZO(c)PHENANTHRIDINES

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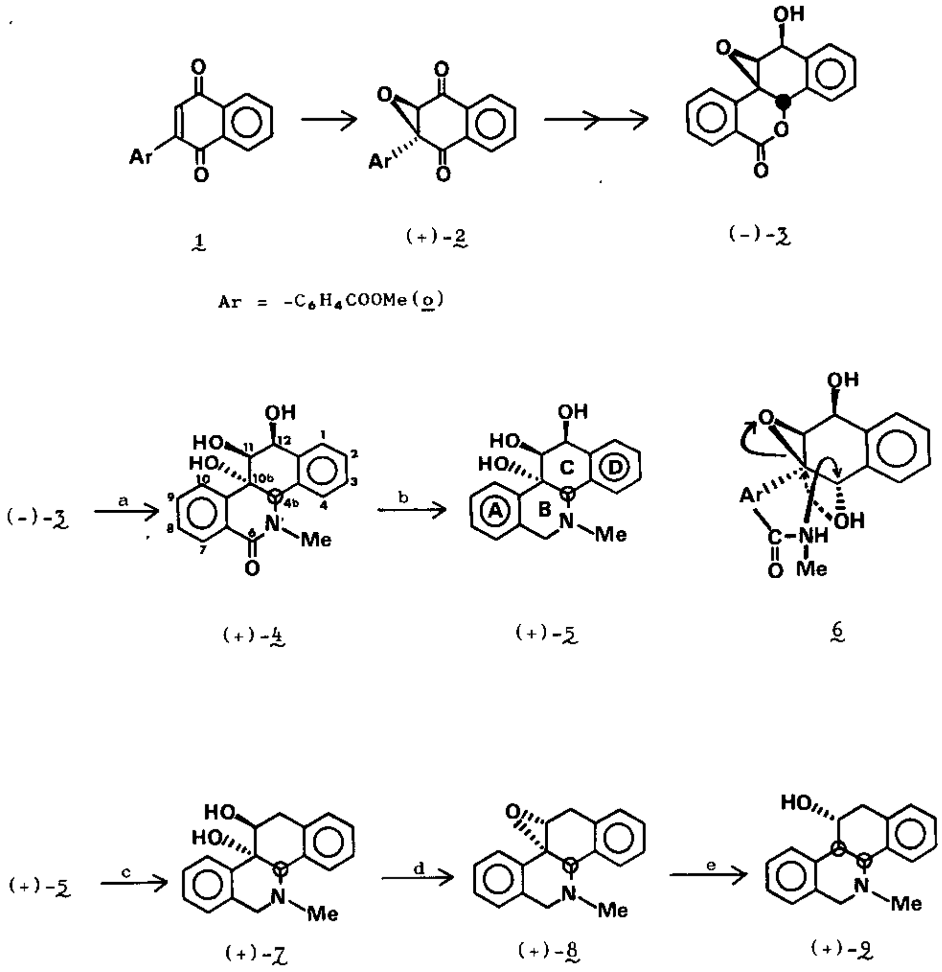
Abstract — Reaction of the (-)-epoxyhydroxy lactone (3) with methylamine stereospecifically gives the (+)-trihydroxy lactam (4) which is converted into the (+)-10b-hydroxychelidonine (7) and (+)-11-epichelidonine analogs (9) *via* several steps. The absolute configurations of these compounds are decided on the basis of that of (-)-3 and the spectral data observed.

We previously reported that the phase-transfer chiral epoxidation of the naphthoquinone (1) gave the (+)-naphthoquinone epoxide (2) (95%, 78% ee) which was recrystallized from ethanol to yield (+)-2 (63%, 100% ee) and that reduction of (+)-2 (100% ee) with sodium borohydride afforded the (-)-epoxyhydroxy lactone (3) (44%, 100% ee) having the 4b*S*,10b*R*,11*S*,12*S* configuration.[2] We now report the stereospecific syntheses of chiral analogs of chelidonine from (-)-3.

Treatment of (-)-3 (84% ee)[3] with aqueous methylamine gave the (+)-trihydroxy lactam (4) (99%), $(\alpha)_D^{18.5}$+83.3° (c=0.108, dioxane), which was reduced with lithium aluminum hydride to yield the (+)-trihydroxy amine (5) (99%), $(\alpha)_D^{20.5}$ +102.9° (c=0.105, dioxane). The ir and ^{1}H nmr spectra of (+)-5 showed Bohlmann bands (2775 and 2700 cm^{-1}), and a W-path coupling (2 Hz) between the 4b- and 11-protons and a coupling (3 Hz) between the 11- and 12-protons, respectively. Thus, the *cis* steroidal conformation having the $10b_{ax}$-, 11_{ax}- and 12_{eq}-hydroxyl groups in the C ring can be assigned to the B/C ring fusion in (+)-5. Treatment of (±)-3 with anhydrous ethanolic methylamine afforded (±)-4 as a sole product. This result proves that water does not take part in the opening of the oxirane ring. Since the structure of (+)-4 should be similar to that of (+)-5, the formation of (+)-4 from (-)-3 is thought as follows. The dihydroxyepoxy amide (6), presumably resulted from reaction of (-)-3 with methylamine, would recyclize to form (+)-4 by an S_N reaction of the amide group at the 1-position, accompanied by a concerted migration of the 1-hydroxyl group to the 2-position from the back



a) $MeNH_2$ b) $LiAlH_4$ c) H_2/Pd-C d) $MeSO_2Cl$ e) $LiAlH_4$/$AlCl_3$

Chart 1

side with respect to the oxirane ring in a *trans* ring opening mode. This is in accord with the finding that aminolysis of the (±)-4b-isomer[1] of (−)-3 with aqueous methylamine resulted in the formation of the (±)-1-isomer of 6. Thus, on the basis of the absolute configuration of (−)-3, the 4b*R*,10b*S*,11*S*,12*S* configurations are assigned to (+)-4 and (+)-5.

Hydrogenolysis of (+)-5 over palladium-carbon gave the (+)-10b-hydroxychelidonine analog (7) (78%): 4b*R*,10b*S*,11*S*; $(\alpha)_D^{19}$+125.2° (c=0.115, chloroform); ir, Bohlmann bands (2775 and 2700 cm^{-1}); ^{1}H nmr, $J_{4b,11}$ 2 Hz. Reaction of (±)-2-phenylbutanoic anhydride with (+)-7 and subsequent isolation of the partially resolved (−)-acid lead to the assignment of the *S* configuration to the 11-position in (+)-7.[2,4]

Treatment of (+)-7 with mesyl chloride afforded the (+)-epoxy amine (8) (93%, 80% ee)[3]: $(\alpha)_D^{24.5}$+193.0° (c=0.147, chloroform); ir, Bohlmann bands (2775 and 2680 cm^{-1}); ^{1}H nmr, $J_{4b,11}$ 2 Hz. The spectral properties indicate (+)-8 to have the 4b*R*,10b*S*,11*R* configuration with the B/C *cis* steroidal conformation.

Reduction of (+)-8 (80% ee) with lithium aluminum hydride/aluminum chloride gave the (+)-11-epichelidonine analog (9) (27%): $(\alpha)_D^{26.5}$+48.0° (c=0.050, chloroform); ir, Bohlmann bands (2770 and 2675 cm^{-1}); ^{1}H nmr, $J_{4b,10b}$ 3 and $J_{10b,11}$ 9 Hz.[5] On the basis of the spectral data, the 4b*S*,10b*R*,11*R* configuration can be assigned to (+)-9. The formation of (+)-9 is thought to arise *via* an initially formed oxirane-alane complex, followed by reduction at the 10b-position in a *cis* ring opening mode.[6]

REFERENCES AND NOTES

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3. The enantiomeric excess (ee) was determined from the ^{1}H nmr spectrum using Eu(hfc)$_3$, and a distinct difference in the 11-proton signal was observed.
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