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A REMARKABLE INFLUENCE OF THE ELECTROLYTE IN ANODIC CYCLIZATION OF 1-BENZYLTETRAHYDROISOQUINOLINES TO NEOSPIRODIENONES OR MORPHINANDIENONES[1]

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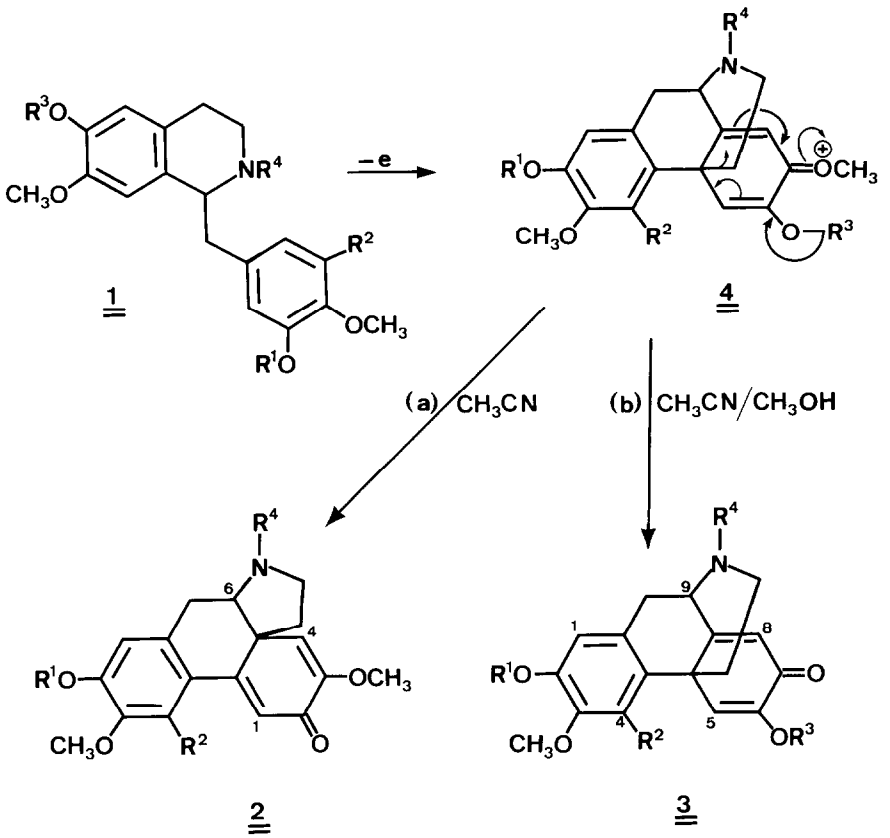
SUMMARY. *N*-Trifluoracetyl-1-benzyltetrahydroisoquinolines 1 cyclize on anodic oxidation in acetonitrile to neospirodienones, whilst in methanol/acetonitrile as electrolyte morphinandienones are formed.

Morphinandienones of the flavinantine-type can be obtained in good yield (24 - 98 %) by anodic *para-para* coupling of 1-benzyltetrahydroisoquinolines[2]. Unfortunately steric and electronic reasons disfavour the more desired *para-ortho* coupling to salutaridine derivatives, that may be converted to morphine. Attempts, to enforce the *para-ortho* coupling by using halo-[3], nitro-[4] or *N*-acetylamino-substituents[4] in the benzylring as blocking groups, thus far have failed. In the phenol coupling of reticuline Schwartz[5] was able to improve the yield of salutaridine from 0.03 %[6] to 11 % and 23 % by oxidizing *N*-trifluoracetyl- and *N*-ethoxycarbonylnorreticuline with $Tl(O_2CCF_3)_3$.

To find out, wether the *N*-CF_3CO- or the *N*-EtO_2C-group influences the regioselectivity of the anodic phenolether coupling, we electrolyzed the 1-benzyltetrahydroisoquinolines 1. Whilst 1e yielded only cleavage products, the electrolysis of 1a - d in acetonitrile (0.1 m $LiClO_4$) did not afford morphinandienones but the neospirodienones 2 in good yield (table). These could be



	a	b	c	d	e
R^1	Bz	Bz	CH_3	CH_3	Bz
R^2	H	OBz	H	H	H
R^3	CH_3	CH_3	Bz	CH_3	CH_3
R^4	CF_3CO	CF_3CO	CF_3CO	CF_3CO	EtO_2C

Table: Cyclization of 1-benzyltetrahydroisoquinolines 1 to neospirodienones 2 or morphinandienones 3

1-Benzyltetrahydroisoquinoline[a]	Neospirodienone[b] yield (%)[c]		Morphinandienone[d] yield (%)[c]	
1a	2a	56 %		
1b	2b	38 %		
1c	2c	82 %	3c	58 %
1d	2c[e]	59 %	3d[f]	66 %

a) Prepared by the Bischler-Napieralski route from *N*-phenethylarylacetamides, $NaBH_4$-reduction and trifluoracetylation. - b) Conditions: divided cell, Pt-anode (5 cm^2), 1 mmol 1 in 150 ml anolyte: 0.1 m $LiClO_4/CH_3CN$, Na_2CO_3, 0° to -15° C at 0.9 to 1.0 V versus Ag/Ag^+. - c) Isolated yield; products characterized by elemental analysis and spectra. - c) Conditions as b) but in 0.1 m $LiClO_4$-CH_3CN/CH_3OH (2 to 1 : 1, v/v). - e) 2c: ^{1}H-NMR ($CDCl_3$) : δ = 6.79, 6.66 (ss, 1H, 1-H), 5.84, 5.67 (ss, 1H, 4-H), 4.66, 4.52 (m, m, 1H, 6-H); IR (KBr) 1645, 1627 cm^{-1} (cyclohexadienone); UV (EtOH), λ_{max} (log ε): 242, 268 (4.06), 292 (3.93), 361 (4.03); MS: m/e = 423 (100 %, M^+); spectroscopic data of the corresponding *N*-formyl derivative: S.M. Kupchan, A.J. Liepa, V. Kameswaran, R.F. Bryan, J. Amer. Chem. Soc. 95, 6861 (1973). - f) 3d: ^{1}H-NMR ($CDCl_3$) : δ = 6.86, 6.63, 6.41, 6.37 (4s, 4H, 1-H, 4-H, 5-H, 8-H), 5.61 (m, 1H, 9-H); IR (KBr): 1665, 1645 cm^{-1} (cyclohexadienone); UV ($CHCl_3$), λ_{max} (log ε): 242 (4.24), 288 (3.89); MS: m/e = 423 (90 %, M^+), 297 (100 %).

formed by rearrangement of an intermediate morphinandienone-type cation 4, as indicated (path a). Such an isomerization has been discussed by Kupchan[7] in the VOF_3-oxidation of *N*-formylnorlaudanosine. The corresponding *N*-methyl derivatives of 1 lead without rearrangement to morphinandienones[2], here a stabilization of the corresponding cations 4 by homoconjugation is assumed. The migration in the case of 1 thus could be due to a decreased homoconjugation of 4 caused by the reduced basicity of the nitrogen.

By adding a nucleophile to the electrolyte it should be possible to intercept 4 before its rearrangement (path b). Indeed in acetonitrile/methanol (0.1 m $LiClO_4$) not 2, but 3 is yielded (table). There is however no influence of the trifluoracetyl group on the regioselectivity of the coupling, as

exclusively the *para-para* coupled product is formed.

This is another example[9], how the product distribution in electrolysis can be drastically altered by minor changes in the electrolyte.

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