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A CONVENIENT TRANSFORMATION OF SPIROBENZYLISOQUINOLINES TO DEHYDROPHTHALIDEISOQUINOLINES

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Treatment of spirobenzylisoquinoline N-oxides (**4**), derived from protoberberines (**2**), with trifluoroacetic anhydride easily afforded dehydrophthalideisoquinolines (**1**).

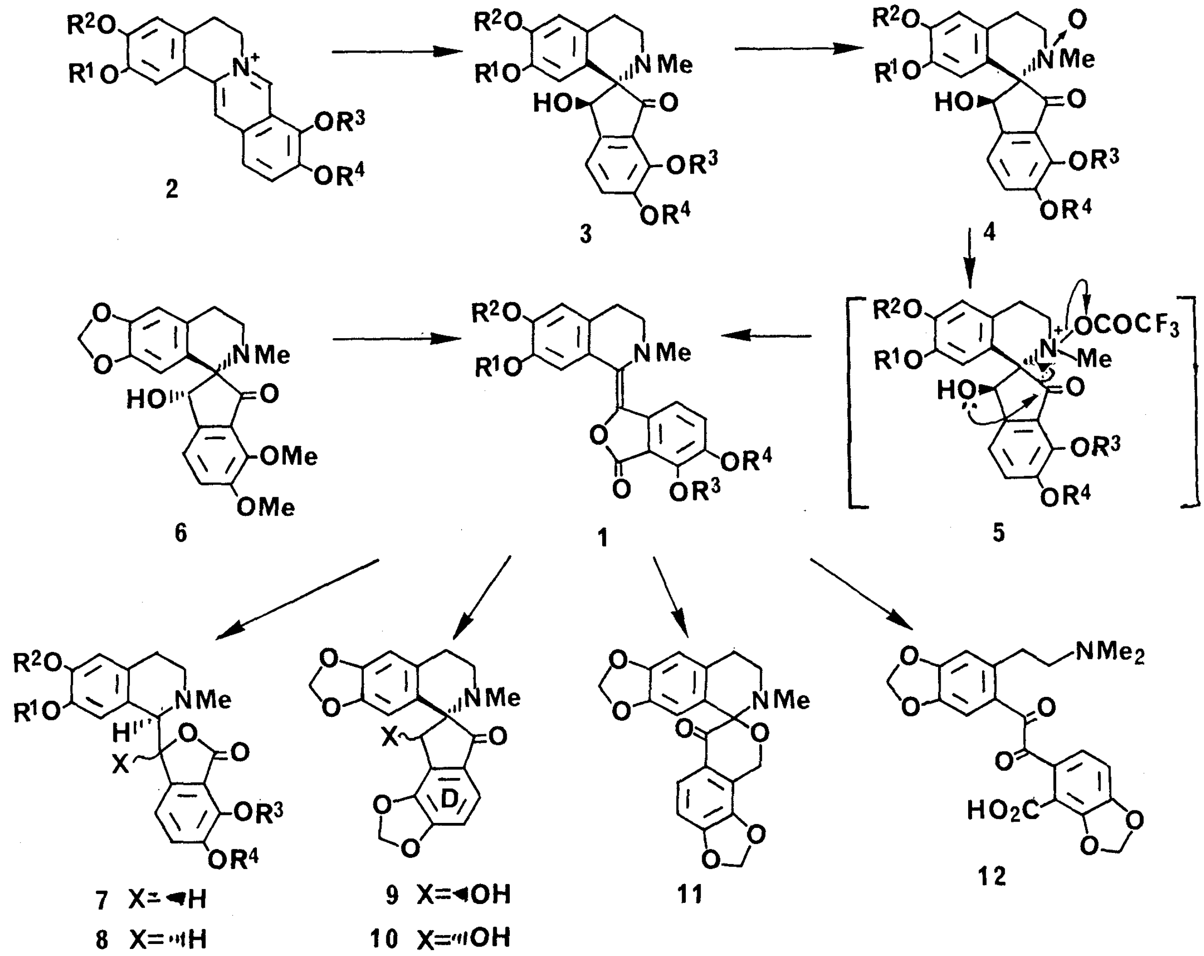
KEYWORDS — dehydrophthalideisoquinoline; phthalideisoquinoline alkaloid; spirobenzylisoquinoline alkaloid; protoberberine alkaloid; Polonovski reaction; trifluoroacetic anhydride

Dehydrophthalideisoquinolines (**1**), synthetic precursors of various phthalideisoquinoline alkaloids,[1)] have been synthesized by several methods[2-5)] including the original Haworth synthesis.[2)] And these compounds are versatile starting materials for spirobenzylisoquinoline,[5,6)] secoberbine,[7)] and secophthalideisoquinoline[7)] alkaloids.

Recently we have developed[8)] a novel and efficient synthesis of spirobenzylisoquinoline alkaloids from protoberberine alkaloids. And we describe here a new and convenient conversion of the readily available spirobenzylisoquinolines to dehydrophthalideisoquinolines.[9)]

Oxidation of the spirobenzylisoquinoline (**3a**)[10)] derived from berberine (**2a**) with m-chloroperbenzoic acid (m-CPBA) in dichloromethane at 0°C afforded the rather unstable N-oxide (**4a**). On treatment with trifluoroacetic anhydride (TFAA) in dichloromethane at 0°C, the N-oxide (**4a**) gave dehydrohydrastine (**1a**) [49% from **3a**; mp 201-203°C (lit. mp 204-205°C,[2)] mp 203°C (dec.)[5)]); m/z 381 (M^+); ν 1750; δ 7.92 (1H, s), 7.89, 7.30 (2H, AB-q, J=8.5), 6.63 (1H, s), 5.96 (2H, s), 4.12, 3.95, 2.73 (each 3H, s)]. The formation of **1a** can be rationalized in terms of the intermediacy of the trifluoroacetate (**5**) and subsequent fragmentation as depicted. In order to examine the stereochemical effect of the hydroxyl group in this Polonovski reaction,[11)] the diastereoisomer (**6**)[12)] was treated under the same reaction conditions resulting in dehydrohydrastine (**1a**) in 40% overall yield. So this reaction was found to be independent of the configuration of the hydroxyl group. Hydrogenation of the product (**1a**) in acetic acid over platinum oxide[2)] yielded (±)-α- and (±)-β-hydrastine (**7a** and **8a**), which were proved to be identical with the corresponding authentic samples.[13)]

Similarly, treatment of the spirobenzylisoquinolines (**3b**[14)] and **3c**[16)]) with m-CPBA, followed by TFAA, gave dehydrocordrastine (**1b**) [25%; mp 139-141°C (lit. mp



a: $R^1+R^2=CH_2$, $R^3=R^4=CH_3$; b: $R^1=R^2=R^3=R^4=CH_3$; c: $R^1+R^2=R^3+R^4=CH_2$

136-136.5°C,[2] mp 139-141°C,[4] mp 140-142°C[5])] and dehydrobicuculline (**1c**) [54%; mp 259-260°C (lit.[5] mp 259°C)], respectively. The spectral data[17] of these products were in good agreement with those reported.[4,5] Dehydrocordrastine (**1b**) has already been reduced to (±)-cordrastine I (**7b**) and (±)-cordrastine II (**8b**),[2,4] and dehydrobicuculline (**1c**) to (±)-adlumidine (**7c**) and (±)-bicuculline (**8c**).[5] And an interesting reductive conversion of **1c** to spirobenzylisoquinoline alkaloids, (±)-sibiricine (**9**)[5,6] and (±)-corydaine (**10**)[5,6] has been reported. This conversion is exactly the reverse of the present oxidative conversion, though the position of the methylenedioxy group in the D ring is transposed. In addition, **1c** has been converted to the secoberbine alkaloid hypecorinine (**11**)[7] and the secophthalideisoquinoline alkaloid bicucullinine (**12**).[7]

Thus, the present transformation provides a simple synthesis of versatile dehydrophthalideisoquinolines and a formal synthesis of phthalideisoquinoline, secoberbine, secophthalideisoquinoline and spirobenzylisoquinoline alkaloids.

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12) Synthesis of the compound (**6**) will be reported later.

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14) This compound (**3b**) was prepared by *N*-methylation of its *N*-demethyl derivative[15] derived from palmatine (**2b**).

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16) This compound (**3c**) was synthesized from coptisine (**2c**) according to the synthetic procedure for **3a**.[10]

17) Mass, IR, and ^{1}H-NMR spectral data; **1b:** m/z 397 (M^+), ν 1750, δ 8.03 (1H, s), 7.92, 7.30 (2H, AB-q, J=8.5), 6.65 (1H, s), 4.13, 3.98, 3.95, 3.91, 2.75 (each 3H, s). **1c:** m/z 365 (M^+), ν 1755, δ 7.90 (1H, s), 7.72, 7.25 (2H, AB-q, J=8), 6.64 (1H, s), 6.21, 5.96 (each 2H, s), 2.73 (3H, s).

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