

NITROGEN ASSISTED ENOL ETHER FORMATION

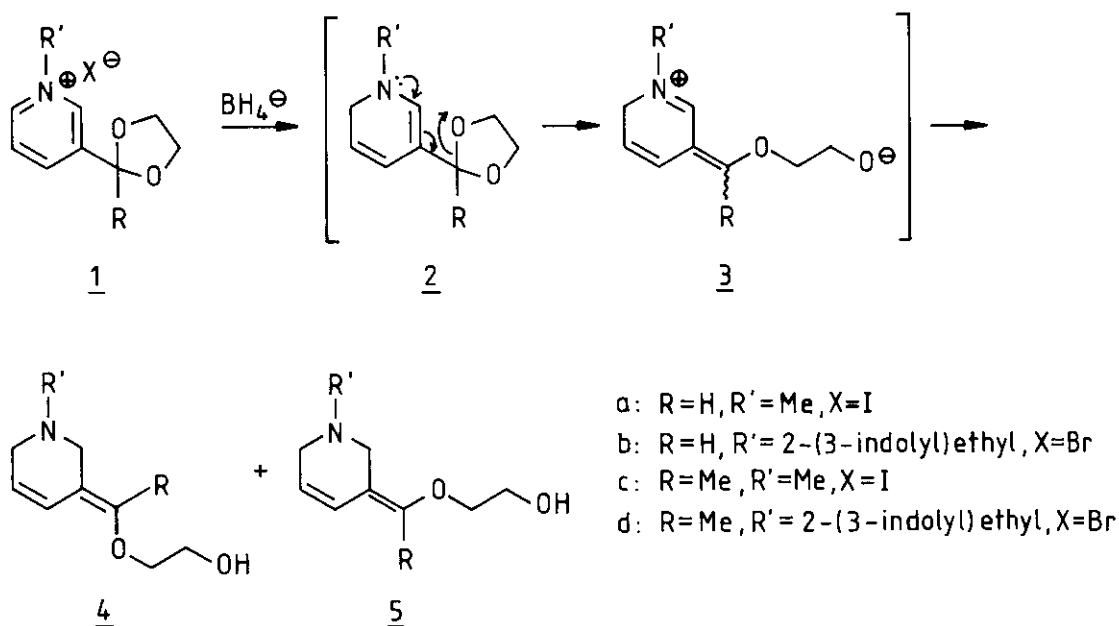
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Abstract - A nitrogen assisted enol ether formation via cyclic acetal ring opening is described.

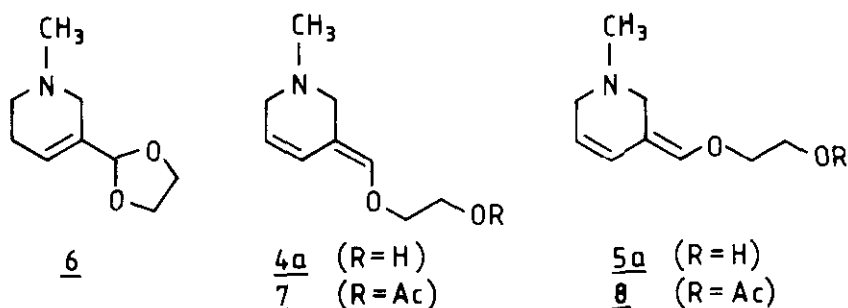
There are only a very few special cases known, where enol ethers are formed via cyclic acetal ring opening.¹ We have found that treatment of N-alkyl salts of 3-formyl- and 3-acetylpyridine acetals 1a-1d with NaBH₄ yields enol ethers 4a-d and 5a-d, respectively.

The mechanism of the transformation can be explained by the formation of 1,6-dihydrointermediate 2 in which the nitrogen assisted acetal ring opening takes place (Scheme 1). The reaction is completed by the reduction and protonation of the formed iminium species 3.



Scheme 1

3-Formylpyridine acetal methiodide 1a² was reduced with NaBH₄ in the usual manner (ethanol, 0°C). In addition to the normal reduction product 6³, two stereoisomers, 4a⁴ (trans) and 5a⁵ (cis), with an exocyclic double bond were formed via acetal ring opening.



The ratio of the trans- and cis-isomers 4a and 5a was ca. 5:1, determined from NMR spectra. The stereochemistry of the major isomer was assigned trans on the basis of ¹³C NMR chemical shifts (Fig. 1): the carbon atoms in the exocyclic double bond of the cis-isomer were expected to possess lower field signals.

Isomers 4a and 5a were both quite unstable and so they were converted to their more stable acetates 7⁶ and 8⁷ (for their ¹³C NMR data, see Fig. 1).

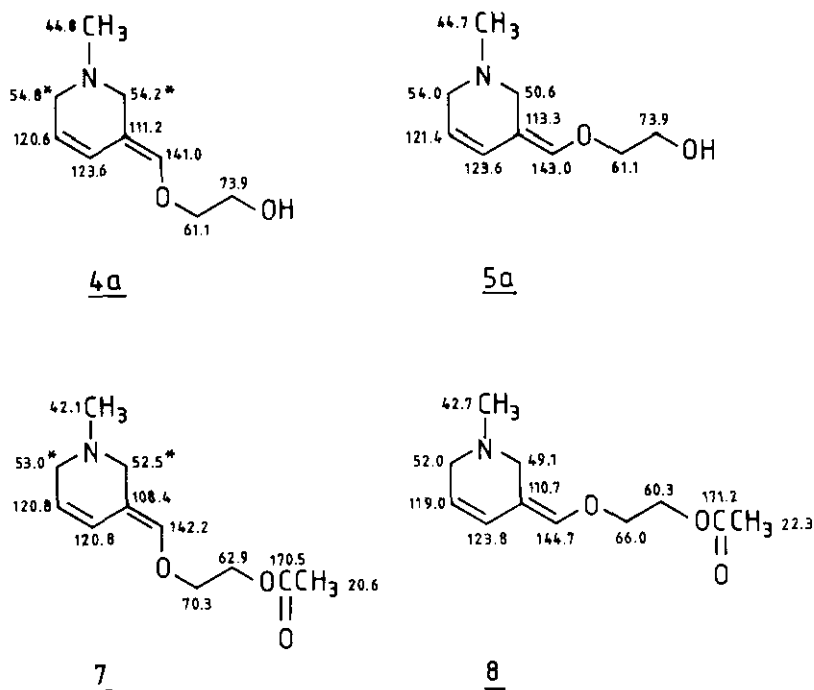
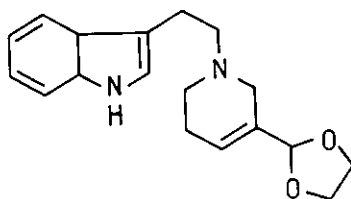


Fig. 1.

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The reduction of the tryptophyl salt 1b gave, besides tetrahydropyridine 9⁸, the expected enol ether 4b⁹ (trans; traces of the cis-isomer 5b were detected).

This compound was also more conveniently handled as its acetate 10.¹⁰ The ¹³C NMR chemical shifts of the trans-isomer 4b and the acetate 10 are given in Fig. 2.

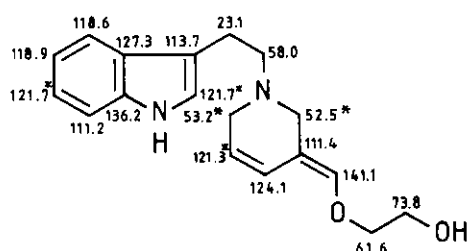
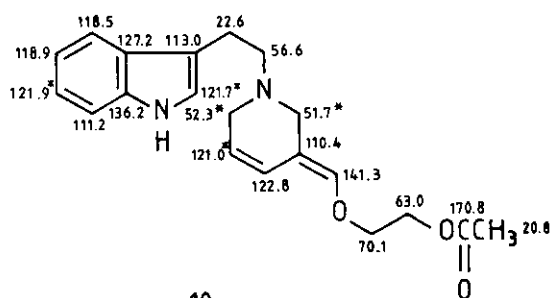
4b10

Fig. 2.

The acetal ring opening was found to take place in a similar manner in the carbonyl protected keto series, i.e. starting from 3-acetylpyridine. Its ketal methyl salt 1c yielded the isomeric mixture 4c and 5c (total yield 35%, ratio ca. 4:3). Similarly, its ketal tryptophyl salt 1d afforded the isomeric mixture 4d and 5d (total yield 40%, ratio ca. 4:3).

REFERENCES AND NOTES

1. E.g. for the reaction of 2-substituted 1,3-dioxolanes with Grignard reagents leading to 2-hydroxyalkyl enol ethers, see G. Westera, C. Blomberg and F. Bickelhaupt, *J. Organomet. Chem.*, 1978, 144, 291.
2. M. Lounasmaa, T. Tamminen and R. Jokela, *Heterocycles*, 1985, 23, 1735.
3. Compound 6: Yellow oil, yield ~ 40 %. IR (ν cm⁻¹, CHCl₃): 2900 (st), 2810 (st), 2400 (w), 1720 (m), 1680 (w), 1660 (w). ¹H NMR (δ , CDCl₃): 5.94 (1H, br s), 5.17 (1H, s), 3.92 (4H, br s), 2.94 (4H, m), 2.50 (2H, m), 2.36 (3H, s). ¹³C NMR (δ , CDCl₃): 133.4 (s), 125.0 (d), 104.5 (d), 64.8 (t) (2C), 51.4 (t) (2C), 45.5 (q), 25.3 (t). MS (EI 70 eV, m/z): 169 (M⁺, 50), 124 (73), 96 (100).

4. Compound 4a: Colourless oil, yield ~ 20 %. IR (ν cm^{-1} , CHCl_3): 3300 (st), 2950 (st), 2800 (st), 1660 (st), 1610 (m). ^1H NMR (δ , CDCl_3): 6.56 (1H, d, $J_{\text{AB}} = 10.5$ Hz), 5.94 (1H, br s), 5.62 (1H, d, $J_{\text{AB}} = 10.5$ Hz), 3.77 (4H, m), 2.98 (4H, m), 2.34 (3H, s). ^{13}C NMR (δ , CDCl_3): see Fig. 1. MS (EI, 70 eV, m/z): 169 (M^+ , 50), 124 (100), 122 (25), 108 (15), 94 (95).
5. Compound 5a: Colourless oil, yield ~ 4 %. IR (ν cm^{-1} , CHCl_3): 3300 (st), 2800 (st), 1660 (st). ^1H NMR (δ , CDCl_3): 6.56 (1H, d, $J_{\text{AB}} \sim 10$ Hz), 6.10 (1H, br s), 5.61 (1H, d, $J_{\text{AB}} \sim 10$ Hz), 3.76 (4H, m), 2.98 (4H, m), 2.34 (3H, s). ^{13}C NMR (δ , CDCl_3): see Fig. 1. MS (EI, 70 eV, m/z): 169 (M^+ , 50), 124 (100).
6. Compound 7: Yellow oil, yield 90 %. IR (ν cm^{-1} , CHCl_3): 3050 (st), 1740 (m), 1680 (m). ^1H NMR (δ , CDCl_3): 6.58 (1H, d, $J_{\text{AB}} = 10.2$ Hz), 5.96 (1H, br s), 5.60 (1H, d, $J_{\text{AB}} = 10.2$ Hz), 4.11 (4H, m), 3.20 (4H, m), 2.44 (3H, s), 2.07 (3H, s). ^{13}C NMR (δ , CDCl_3): see Fig. 1. MS (EI, 70 eV, m/z): 211 (M^+ , 26), 124 (100), 96 (24), 87 (35).
7. Compound 8: Yellow oil, yield 90 %. IR (ν cm^{-1} , CHCl_3): 3100 (st), 1740 (m), 1680 (m). ^1H NMR (δ , CDCl_3): 6.60 (1H, d, $J_{\text{AB}} \sim 10$ Hz), 6.16 (1H, br s), 5.60 (1H, d, $J_{\text{AB}} \sim 10$ Hz), 4.10 (4H, m), 3.20 (4H, m), 2.44 (3H, s), 2.05 (3H, s). ^{13}C NMR (δ , CDCl_3): see Fig. 1. MS (EI, 70 eV, m/z): 211 (M^+ , 30), 124 (100).
8. Compound 9: Yellow foam, yield ~ 50 %. IR (ν cm^{-1} , CHCl_3): 3350 (m), 3030 (st), 1710 (w), 1660 (st), 1610 (m). ^1H NMR (δ , CDCl_3): 8.81 (1H, br s), 7.60–7.00 (4H, m), 6.87 (1H, d, $J = 2$ Hz), 5.95 (1H, br s), 5.18 (1H, s), 3.87 (4H, s), 3.15–2.65 (8H, m), 2.22 (2H, m). ^{13}C NMR (δ , CDCl_3): 136.0 (s), 133.3 (s), 127.1 (s), 125.8 (d), 121.7 (d), 121.3 (d), 18.6 (d), 118.4 (d), 113.4 (s), 110.9 (d), 104.6 (d), 64.9 (t) (2C), 58.8 (t), 49.6 (t) (2C), 25.3 (t), 22.8 (t). MS (EI 70 eV, m/z): 298 (M^+ , 35), 170 (40), 168 (100), 144 (23), 130 (19), 108 (51).
9. Compound 4b: Yellow foam, yield ~ 25 %. IR (ν cm^{-1} , CHCl_3): 3300 (st), 2950 (st), 1665 (st), 1620 (m). ^1H NMR (δ , CDCl_3): 8.42 (1H, br s), 7.60–7.10 (4H, m), 6.97 (1H, d, $J = 2$ Hz), 6.60 (1H, d, $J_{\text{AB}} = 10.7$ Hz), 5.91 (1H, br s), 5.67 (1H, d, $J_{\text{AB}} = 10.7$ Hz), 3.80 (4H, br s), 3.30–2.80 (8H, m). ^{13}C NMR (δ , CDCl_3): see Fig. 2. MS (EI, 70 eV, m/z): 298 (M^+ , 10), 168 (35), 144 (22), 130 (48), 108 (95), 84 (100).
10. Compound 10: Yellow oil, yield 90 %. IR (ν cm^{-1} , CHCl_3): 3300 (m), 3010 (st), 1720 (st), 1660 (m). ^1H NMR (δ , CDCl_3): 8.74 (1H, br s), 7.65–7.10 (4H, m), 6.97 (1H, d, $J = 2$ Hz), 6.59 (1H, d, $J_{\text{AB}} = 9.7$ Hz), 5.83 (1H, br s), 5.63 (1H, d, $J_{\text{AB}} = 9.7$ Hz), 4.05 (4H, m), 3.30–2.90 (6H, m), 2.20 (2H, m), 2.04 (3H, s). ^{13}C NMR (δ , CDCl_3): see Fig. 2. MS (EI, 70 eV, m/z): 340 (M^+ , 80), 300 (20), 253 (18), 226 (22), 211 (32), 210 (50), 168 (95), 142 (20), 130 (100).

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