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LETTERS

Regioselective Reduction of the α, β - Double Bond of Some Naturally Occurring Dienamides Using $NaBH_4/I_2$ System[1]

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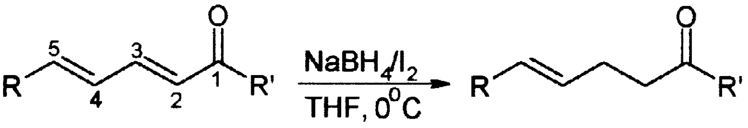
Abstract: The regioselective reduction of the α, β - double bond of the naturally occurring dienamides, piperine, piperlonguminine and N - isobutyl - 2E, 4E - decadienamide was achieved by using $NaBH_4/I_2$ system.

The amides of *Piper* species have been found to exhibit promising pesticidal and antitumour properties[2-4]. Several transformations of naturally occurring amides have been carried out [2,5,6] in recent years to prepare their analogues which may possess better activity. In continuation of our current investigation [6,7] on the amides of *Piper longum* Linn (Piperaceae) we have developed a novel and efficient method for the regioselective reduction of the α, β - double bond of the dienamide constituents of the plant, piperine (**1**), piperlonguminine (**2**) and N- isobutyl - 2E, 4E - decadienamide (**3**) by using $NaBH_4/I_2$ system to prepare the analogues of the compounds (**1–3**) for bioevaluation.



1 – 3 **4 – 6**

1 and **4** : R = 3, 4-Methylenedioxyphenyl, R' = Piperidyl
2 and **5** : R = 3, 4-Methylenedioxyphenyl, R' = i-BuNH-
3 and **6** : R = C_5H_{11}- , R' = i-BuNH-

The dienamides **1–3** remained unchanged by treatment with $NaBH_4$. However, the combination of $NaBH_4$ (0.0025 mole) and I_2 (0.001 mole) in THF was found to reduced[8] smoothly the α, β - double bond of the compounds (**1–3**) (0.002 mole) to afford the products **4-6** respectively under mild reaction conditions in high yields (72-75%). The regioselectivity of the reaction was found to decrease when $NaBH_4$ and I_2 were taken in excess. Thus, piperine (0.002 mole) on treatment with $NaBH_4$ (0.008 mole) and I_2 (0.003 mole) in THF produced[8] the tetrahydropiperine (7) as the major product (58%) along with the minor compound **4** (14%). The structures of all the reaction products were settled from their spectral properties[9].

It has been established that the combination of $NaBH_4/I_2$ in THF is a source of diborane[10, 11]. The regioselective reduction of the α, β - double bond of the dienamides can be rationalized by assuming a six-

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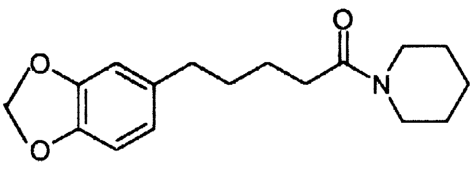
membered cyclic model **8** formed by the reacting dienamide with the generated diborane. The cleavage of THF and piperidyl moiety was not observed under the reaction conditions.



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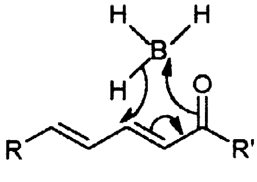

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In conclusion, the readily accessible $NaBH_4/I_2$ system has been utilized conveniently under mild reaction conditions for the regioselective reduction of the α, β - double bond of the natural dienamides **1–3**. Such conversion of a naturally occurring dienamide was not previously reported by any other method.

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References and Notes:

1 Part IV in the series "Synthetic Studies on Natural Products"; for Part III, see Das, B.; Madhusudhan, P. and Kashinatham, A. *J. Chem. Research* (S), **1997** (submitted). IICT Communication No. 3912.

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8 A typical experimental procedure is as follows. A slurry of $NaBH_4$ (0.09g, 0.0025 mole) and piperine (0.57g, 0.002 mole) in THF (10ml) was stirred at 0^0C. To this mixture, I_2 (0.25g, 0.001 mole) in THF (10ml) was added dropwise over a period of 10 min. under N_2 atmosphere. After 20 min. the reaction mixture was quenched with MeOH till the effervescence was ceased. Evaporation of the solvent followed by purification of the crude product by column chromatography over silica gel afforded dihydropiperine **4** (0.42g, 74%).

When piperine (0.57g, 0.002 mole) was treated with $NaBH_4$ (0.30g 0.008 mole) and I_2 (0.76g, 0.003 mole) under above conditions two reaction products, tetrahydropiperine **7** (0.33g, 58%) and dihydropiperine **4** (0.08g, 14%) were obtained.

9 The spectral data of two representative molecules **4** and **7** are as follows: For **4**: ^1H NMR (200MHz, $CDCl_3$): δ 6.81 (1H, brs, Ar-H), 6.64 (2H, brs, Ar-H), 6.28 (1H, d, J=15.0Hz, H-5), 5.98 (1H, m, H-4), 5.85 (2H, s, $-OCH_2O-$), 3.49 (2H, t, J=5.5 Hz, $>NCH_2-$), 3.32 (2H, t, J=5.5 Hz, $>N-CH_2-$), 2.48-2.34 (4H, m, H_2-2 and H_2-3), 1.62-1.39 (6H, m, $-(CH_2)_3-$ from piperidyl moiety); MS m/z (%): 287 (M^{+},5), 149 (12), 135 (18), 98 (100).

For 7 : 1H NMR (200 MHz, $CDCl_3$) : δ 6.86-6.53 (3H, m, Ar-H), 5.88 (2H, s, $-OCH_2O-$), 3.52 (2H, t, J=5.5Hz, $>NCH_2-$), 3.36 (2H, t, J=5.5 Hz, $>NCH_2-$), 2.57 (2H, t, J=7.5 Hz, H-5), 2.30 (2H, t, J=7.5 Hz, H-2), 1.71-142 (10H, m, H_2-3, H_2-4 and $-(CH_2)_3$-from piperidyl moiety) MS m/z (%) : 289 (M^{+}, 45), 204 (18), 135 (48), 127 (100).

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