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Practical One-Pot Procedure for the Synthesis of 1,2,3,4-Tetrahydroquinolines by the Imino-Diels-Alder Reaction

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Practical One-Pot Procedure for the Synthesis of 1,2,3,4-Tetrahydroquinolines by the Imino-Diels-Alder Reaction

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Abstract: A novel-one-pot procedure for the synthesis of tetrahydroquinolines via the imino-Diels-Alder reaction is described. This procedure gives better yields and exhibits better versatility for alkene substrates than the existing hemi-aminal based methodologies.

Keywords: Imino-Diels-Alder reaction, one-pot procedure, tetrahydroquino lines

Many tetrahydroquinolines with biologically interesting properties have been discovered in the past few years, and they have been investigated as drug candidates against type II diabetes,[1] cancer,[2] obesity,[3] depression,[4] inflammation,[5] and heart failures.[6] Therefore, research directed toward the discovery of better methodologies to prepare tetrahydroquinolines is an ongoing effort. One of the most powerful tools for the synthesis of tetrahydroquinolines is the imino-Diels-Alder reaction, where the tetrahydroquinoline (**4**) is formed by the condensation of **3** with an alkene (Scheme 1). In the past, the azadiene (**3**) was generated in situ (pathway A) or from a hemi-aminal **2a–c** (pathway B, Scheme 1).

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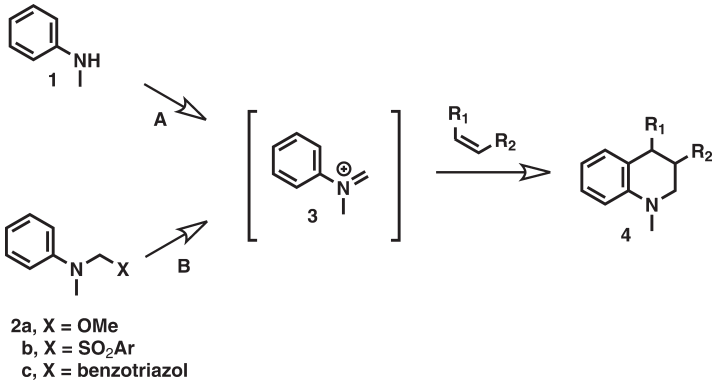

Scheme 1. Synthesis of 1,2,3,4-tetrahydroquinoline 4 by imino-Diels-Alder reaction.

However, there are reports that early imino-Diels-Alder reactions were carried out using pathway A and gave tetrahydroquinolines in good yields but worked only with specific alkene substrates.[7] For example, Hesse[7] obtained tetrahydroquinolines by condensation of N-methylaniline and β-methylstyrene in the presence of aqueous formaldehyde and sulfuric acid. However, this procedure works only with styrenes. Another one-pot procedure was developed by Posson et al.[8] in which they reacted a mixture of aqueous formaldehyde and hydrochloride salts of N-alkylanilines to generate tetrahydroquinolines. Still, this method works only with cyclopentadiene.

A different one-pot procedure that works well with electron-rich alkenes was introduced by Chen and Qian.[9] According to this methodology, N-methylaniline and enol ethers were condensed in the presence of $Dy(OTf)_3$ catalyst. Even though this method works well with electron-rich olefins, it gives only moderate yields with isolated olefins such as 1-hexene and styrene. In addition to the previously mentioned methods, newer procedures[10–12] were introduced to synthesize tetrahydroquinolines **4** from hemi-aminals **2a–c**. In these procedures, the iminium intermediate (**3**) is generated via pathway B and reacted with a variety of alkenes. These procedures work well with alkenes of varying reactivities, although this better flexibility for alkene substrates comes at the expense of an additional chemical step, namely the formation of the hemi-aminals, **2a–c**.

For example, Shonos et al.[10] formed the iminium intermediate (**3**) by treating an electrochemically generated methoxy-N-methylaniline (**2a**) with titanium tetrachloride. The iminium ion (**3**) thus generated reacted with various alkenes to form tetrahydroquinolines **4** in moderate to good yields.

Beifuss et al.[11] generated iminium **3** from α-arylaminosulfones **2b**, followed by cycloaddition with styrenes in good yields. On a preparative scale, the most useful method to synthesize tetrahydroquinolines was introduced by Katrizky et al.[12] They generated **3** from α-aminoalkyl benzotriazol **2c** upon Lewis acid treatment, followed by reaction with a

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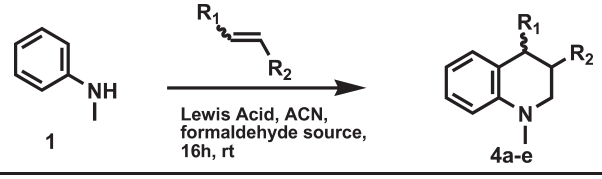
variety of activated and unactivated alkenes, to obtain tetrahydroquinolines **4** in good yields with good regioselectivity. This method works well with unactivated mono- and disubstituted alkenes, cyclic alkenes, and styrenes. However, the overall synthesis of **4** with all the previously mentioned methods, calls for two synthetic steps, namely (a) formation of the hemi-aminals (**2a**–**c**) and (b) subsequent condensation reaction.

In the present work, 1,2,3,4-tetrahydroquinolines **4** were synthesized in a one-pot procedure starting from N-methylaniline and formaldehyde in the presence of a Lewis acid. Different alkenes, solvents, and a variety of Lewis acids were investigated for this mentioned transformation. Among the various solvents tried, acetonitrile turned out to be preferred. In a typical experiment, a mixture of substituted alkenes, a formaldehyde source, N-methylaniline, and a variety of Lewis acids (2.5 eq) were suspended in acetonitrile at 0°C and stirred for 16 h at room temperature. After workup, the products were purified and the yields determined as listed in Table 1.

Initially, we studied the effect of different formaldehyde sources for this reaction, using BF_3 as Lewis acid and cyclopentene as alkene. As can be seen from entries 1–4, the highest yields were achieved in this order: paraformaldehyde > 1,3,5 trioxan > aqueous formaldehyde solution, whereas the use of 1,1-dimethoxymethane led only to the formation of side

Table 1. New one-pot procedure for the synthesis of tetrahydroquinolines **4**



Entry	Product	R_1	R_2	Lewis acid	Formaldehyde source	Yield (%)
1	**4a**	$(CH_2)_3$		$BF_3 \cdot OEt_2$	Paraformaldehyde	87
2		$(CH_2)_3$		$BF_3 \cdot OEt_2$	1,3,5-Trioxan	76
3		$(CH_2)_3$		$BF_3 \cdot OEt_2$	37% aq HCHO-sol.	21
4		$(CH_2)_3$		$BF_3 \cdot OEt_2$	Dimethoxymethane	—
5		$(CH_2)_3$		$SnCl_4$	Paraformaldehyde	94
6		$(CH_2)_3$		$ZrCl_4$	Paraformaldehyde	59
7		$(CH_2)_3$		$TiCl_4$	Paraformaldehyde	—
8	**4b**	n-Bu	H	$BF_3 \cdot OEt_2$	Paraformaldehyde	67
9		n-Bu	H	$SnCl_4$	Paraformaldeyde	77
10	**4c**	n-Hex	H	$BF_3 \cdot OEt_2$	Paraformaldehyde	59
11		n-Hex	H	$SnCl_4$	Paraformaldehyde	68
12	**4d**	Ph	H	$BF_3 \cdot OEt_2$	Paraformaldehyde	78
13		Ph	H	$SnCl_4$	Paraformaldehyde	—
14	**4e** (trans)	Ph	Me	$BF_3 \cdot OEt_2$	Paraformaldehyde	84
15	**4f** (cis)	Ph	Me	$BF_3 \cdot OEt_2$	Paraformaldehyde	67

products. Next, the effect of several Lewis acids was investigated using paraformaldehyde, N-methylaniline, and cyclopentene (Table 1, entries 5–7).

Interestingly, $SnCl_4$ (entry 5) works as well as $BF_3 \cdot ZrCl_4$ (entry 6), and $TiCl_4$ (entry 7) gave lower yields of final product **4a**. Finally, the versatility of this methodology was demonstrated by reacting N-methylaniline with 1-octene or 1-hexene in the presence of either BF_3 or $SnCl_4$, using paraformaldehyde as the aldehyde source (entries 8–11). The actual yields for **4b** and for **4c** with the present one-pot procedure are higher than literature yields using hemi-aminal methodologies.[11–13] Our methodology also works well with styrenes (entries 12–15) using BF_3 as the Lewis acid. However, when $SnCl_4$ was used as the Lewis acid (entry 13), no product was isolated, and this may be due to competing styrene polymerization.

To gain insight into the reaction mechanism, Z- and E-β-methylstyrene were used as dienophiles (entries 14 and 15). Using E-β-methylstyrene tetrahydroquinoline **4e** (trans) was formed exclusively in 84% yield, but when Z-β-methylstyrene was used, the tetrahydroquinoline **4f** (cis) and **4e** (trans) were formed as a mixture of stereoisomers in a 3:1 ratio. The formation of **4e** (trans) under these reaction conditions (entry 15) can be explained either by isomerization of the Z-β-methylstyrene or the product **4f** (cis), or alternatively by a partly stepwise mechanism for the ring formation. We could show experimentally that isomerization of the product or the starting material did not play a role in the formation of **4e** (trans) by subjecting both compounds to the reaction conditions for 2 days. Therefore, the generation of **4e** (trans) must have occurred during the cyclization step and should be rationalized by the reaction mechanism. The formation of both syn- and anti-tetrahydroquinolines **4f** (cis) **4e** (trans) suggests the pericyclic [4 + 2] cycloaddition may be in competition with a stepwise mechanism involving a cationic species. Both mechanisms have been reported earlier for this reaction.[10,12]

CONCLUSION

In summary, a novel one-pot procedure for the synthesis of tetrahydroquinolines was introduced. The method is facile for both cyclic and acyclic alkenes and works well with activated and unactivated 1-alkenes and 1,2-alkenes. The current method offers an advantage over existing methods because it avoids the use of hemi-aminals.

Avoiding a chemical step, namely the formation of hemi-aminal, is especially important in scaling the reaction, because an additional chemical step means additional costs. Our method is also environmentally friendlier then older methods because of its better atom economy.

Overall, the present procedure is a useful variation of existing methods that will be valuable for the preparation of biologically important 1,2,3,4-tetrahydroquinoline derivatives.

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EXPERIMENTAL

General Experimental Procedure for the Synthesis of Tetrahydroquinolines 4

To a stirred solution/suspension of N-methylaniline (15 mmol), alkene (4 eq), and formaldehyde source (1.4 eq) in anhydrous acetonitrile (17 mL) at 0°C, Lewis acid (2.5 eq) was added over a period of 5 min. The reaction mixture was stirred for 16 h. After 16 h, another 0.3 eq of formaldehyde source was added, and the reaction mixture was stirred for another 12 h. After evaporation of solvents, aqueous NaOH (2.5 N) (25 mL) was added, and the aqueous layer was extracted with ether (3 × 50 mL). The combined organic layer was dried over $MgSO_4$, and the tetrahydroquinoline was isolated by flash chromatography using hexane/ethyl acetate (40:1). For yields, see Table 1.

5-Methyl-2,3,3a,4,5,9b-hexahydro-1H-cyclopenta[c]quinoline (4a)

^{1}H NMR (300 MHz, DMSO-d6): $\delta = 7.04–6.96$ (m, 2H), 6.63–6.58 (m, 2H), 2.98–2.78 (m, 2H), 2.63 (t, $J = 9.93$ Hz, 1H), 2.33 (m, 1H), 2.13 (m, 1H), 1.93 (m, 1H), 1.60–1.34 (m, 4H) ppm. ^{13}C NMR (100 MHz, DMSO-d6): $\delta = 146.6$, 129.0, 127.1, 126.2, 116.7, 111.0, 53.4, 40.5, 39.1, 35.5, 35.5, 29.3, 23.0 ppm. IR (neat, cm^{-1}): 2945, 2862, 2806, 1601, 1574, 1498, 1446, 1281, 1206, 1087, 1048, 742. HRMS (FT) [M + H] calcd. for $C_{13}H_{17}N$ 188.14338; found 188.14303.

4-Butyl-1-methyl-1,2,3,4-tetrahydroquinoline (4b)

^{1}H NMR (300 MHz, DMSO-d6): $\delta = 7.16–6.90$ (m, 2H), 6.57–6.49 (m, 2H), 3.32–3.19 (m, 1H), 3.17–3.09 (m, 1H), 2.81 (s, 3H), 2.64–2.62 (m, 1H), 1.85–1.82 (m, 1H), 1.77–1.75 (m, 1H), 1.34–1.25 (m, 8H), 0.88 (t, $J = 6.8$ Hz, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d6): $\delta = 145.7$, 128.0, 126.7, 126.3, 115.4, 110.6, 46.8, 38.5, 35.9, 35.4, 29.4, 25.8, 22.2, 13.9 ppm. IR (neat, cm^{-1}): 2925, 2857, 1601, 1501, 1466, 1429, 1322, 1208, 1010, 738. HRMS (FT) [M + H] calcd. for $C_{14}H_{21}N$ 204.17468; found 204.17431.

4-Hexyl-1-methyl-1,2,3,4-tetrahydroquinoline (4c)

^{1}H NMR (300 MHz, DMSO-d6): $\delta = 7.16–6.90$ (m, 2H), 6.56–6.35 (m, 2H), 3.25–3.15 (m, 1H), 3.14–3.07 (m, 1H), 2.81 (s, 3H), 2.63 (m, 1H), 1.90–1.75 (m, 1H), 1.68–1.58 (m, 1H) 1.68–1.58 (m, 1H), 1.56–1.18 (m, 10H) ppm. ^{13}C NMR (100 MHz, DMSO-d6): $\delta = 144.6$, 127.0, 125.6, 125.3, 114.3, 109.5, 45.7, 37.4, 35.1, 34.3, 30.2, 27.2, 25.2, 24.7, 21.0, 12.9 ppm. IR (neat, cm^{-1}): 2924, 2855, 1602, 1502, 1466, 1322, 1209, 907, 729. HRMS (FT) [M + H] calcd. for $C_{16}H_{25}N$ 232.20598; found 232.20512.

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1-Methyl-4-phenyl-1,2,3,4-tetrahydroquinoline (4d)

^{1}H NMR (300 MHz, DMSO-d6): $\delta = 7.35-7.27$ (m, 2H, 7.21 (tt, $J = 7.1$, 1.2 Hz, 1H), 7.08–7.03 (m, 3H), 6.66 (d, $J = 8.0$ Hz, 1H), 6.58 (d, $J = 7.1$ Hz, 1H), 6.47 (tt, $J = 7.3$, 1.2 Hz, 1H), 4.1 (t, $J = 6.1$ Hz, 1H), 3.18 (m, 1H), 2.87 (s, 3H), 2.14 (m, 1H), 2.01–1.07 (m, 1H) ppm. ^{13}C NMR (100 MHz, DMSO-d6): $\delta = 146.9$, 146.8, 129.6, 128.7, 128.6, 127.7, 126.3, 124.7, 116.0, 111.3, 48.0, 42.8, 39.1, 30.7 ppm. IR (neat, cm^{-1}): 2943, 1601, 1503, 1451, 1325, 1208, 1033, 905, 727, 699. HRMS (FT) [M + H] calcd. for $C_{16}H_{17}N$ 224.14338; found 224.14342.

trans-1,3-Dimethyl-4-phenyl-1,2,3,4-tetrahydroquinoline (4e)

^{1}H NMR (300 MHz, DMSO-d6): $\delta = 7.30-7.27$ (m, 2H), 7.21 (m, 1H), 7.09–7.06 (m, 2H), 7.00 (m, 1H), 6.64 (d, $J = 8.3$ Hz, 1H), 6.44 (m, 2H), 3.64 (d, $J = 8.6$ Hz, 1H), 3.17 (dd, $J = 11.3$, 3.8 Hz, 1H), 2.94 (m, 1H), 2.88 (s, 3H), 2.12 (m, 1H), 0.84 (d, $J = 7.0$ Hz, 1H) ppm. ^{13}C NMR (100 MHz, DMSO-d6): $\delta = 146.7$, 146.0, 130.0, 129.2, 128.6, 127.4, 126.5, 125.2, 116.3, 111.1, 55.9, 51.1, 39.3, 34.5, 18.2 ppm. IR (neat, cm^{-1}): 3022, 2965, 2880, 1596, 1571, 1497, 1449, 1429, 1332, 1213, 1201, 769, 756, 703. MS: (m/z) 238.2 (M + H). Anal. calcd. for $C_{17}H_{19}N$: C, 86.03; H, 8.07; N, 5.29. Found: C, 86.03; H, 8.19; N, 5.75.

cis-1,3-Dimethyl-4-phenyl-1,2,3,4-tetrahydroquinoline (4f)

^{1}H NMR (300 MHz, DMSO-d6): $\delta = 7.25-7.16$ (m, 3H), 7.07–6.94 (m, 3H), 6.75 (d, $J = 8.0$ Hz, 1H), 6.44 (m, 2H), 6.69 (d, $J = 12.1$ Hz, 1H), 6.46 (m, 1H), 3.97 (d, $J = 6.6$ Hz, 1H), 3.00 (dd, $J = 12.1$, 4.6 Hz, 1H), 2.92 (s, 3H), 2.92–2.85 (m, 1H), 2.25 (m, 1H), 0.68 (d, $J = 6.8$ Hz, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d6): $\delta = 146.0$, 143.2, 130.0, 130.0, 127.9, 127.8, 126.3, 125.0, 115.9, 110.9, 53.0, 48.3, 38.8, 30.9, 16.6 ppm. IR (neat, cm^{-1}): 2952, 2898, 1601, 1504, 1280, 1208, 1044, 998, 748, 699. MS: (m/z) 238.2 (M + H). Anal. calcd. for $C_{17}H_{19}N$: C, 86.03; H, 8.07; N, 5.29. Found: C, 86.16; H, 7.78; N, 5.67.

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REFERENCES

1. Borella, C.; Foley, K.; Sun, L.; Chim-Manamada, D. U.; Li, H.; Xia, Z.; Vo, N.; Bohnert, G.; Chen, S.; Wu, Y. Tetrahydroquinolines for Prevention and Treatment of Metabolic Disorders. PCT. Int. Appl. WO 2006065842, 2006.
2. (a) Schiemann, K.; Bruge, D.; Buchstaller, H.-P.; Finsinger, D.; Staehle, W.; Amendt, C.; Emde, U.; Zenke, F. Preparation of Fused Tetrahydroquinolines as Anticancer Drugs. Pct. Int. Appl., WO2006002726, 2006; (b) Perry, N. B.; Blunt, J. W.; McCombs, J. D.; Munro, M. H. G. Dicorhabdin C, a cytotoxic pigment from a sponge of the genus latrunculia. *J. Org. Chem.* **1986**, *51*, 5476.
3. Ramammorthy, S. P. Preparation of [1,4]Diazepino[6,7,1-ij]quinoline Derivatives as Antipsychotic and Antiobesity Agents. Pct. Int. Appl., WO2003091250, 2003.
4. Carruthers, N. I.; Gomez, L. A.; Jablonski, J. A.; Keith, J. M.; Letavic, M. A.; Ly, K. S.; Miller, J. M.; Stocking, E. M.; Wolin, R. L. Preparation of Tetrahydroisoquinolines as Histamine H3 Receptor and Serotonin Transporter Modulators for Treatment of Central Nervous System Disorders. Pct. Int. Appl., WO2006066197, 2006.
5. (a) Barbarchyn, M. R.; Dobrolski, P. J.; Hurd, A. R.; McNamara, D. J.; Palmer, J. R.; Romero, A. G.; Ruble, J. C.; Sherry, D. A.; Thomasco, L. M.; Toogood, P. L. Tricyclic Tetrahydroquinoline Antibacterial Agents. Pct. Int. Appl., WO2004031195, 2004; (b) Williamson, N. M.; March, D. R.; Ward, A. D. An improved synthesis of 2,2-disubstituted-1,2-dihydroquinolines and their conversion to 3-chloro-2,2-disubstituted-tetrahydroquinolines. *Tetrahedron Lett.* **1995**, *36*, 7721; (c) Francis, C. L.; Ward, A. D. Attempted heterocyclic synthesis through electrophilic ring closure reactions of 2-allylaniline systems containing larger side chains. *Aust. J. Chem.* **1994**, *47*, 2109.
6. Kimura, T.; Imanishi, S.; Arita, M. Electrophysiologic effects of nicainoprol, a putative class I antiarrhythmic agent, on the guinea pig ventricular papillary muscle. *J. Cardiovasc. Pharmacol.* **1989**, *49*, 245.
7. Hesse, K. D. Synthese von 1,2,3,4-Tetrahydro-chinolinen. *Justus Liebigs Ann. Chem.* **1970**, *741*, 117.
8. Posson, H.; Hurvois, J. P.; Moinet, C. Imino diels-alder reaction: Application to the synthesis of diverse cyclopenta[c]quinoline derivatives. *Synlett* **2000**, *2*, 209.
9. Chen, R.; Qian, C. One-Pot synthesis of tetrahydroquinolines catalyzed by $Dy(OTf)_3$ in aqueous solution. *Synth. Commun.* **2002**, *16*, 2543.
10. Shono, T.; Matsumura, Y.; Inoue, K.; Ohmizu, H.; Kashimura, S. Electro organic chemistry. 62. reaction of iminium ion with nucleophile: A versatile synthesis of tetrahydroquinolines and julodines. *J. Am. Chem. Soc.* **1982**, *104*, 5753.
11. Beifuss, U.; Kunz, O.; Ledderhose, S.; Tarashewski, M.; Tonko, C. Cationic 2-azabutadienes from α-arylaminosulfones and α-arylaminonitriles: Intermolecular $[4\pi + 2\pi]$ cycloadditions for the regio- and diastereoselective synthesis of 1,2,3,4-tetrahydroquinolines. *Synlett* **1996**, 34.
12. Katrizky, A. R.; Nichols, D. A.; Qi, M.; Yang, B. Lewis acid assisted reactions of N-(α-aminoalkyl)benzotriazoles and unactivated alkenes for the facile synthesis of 4-, 2,4- and 3,4-substituted 1,2,3,4-tetrahydroquinolines. *J. Heterocycl. Chem.* **1997**, *34*, 1259.
13. Katrizky, A. G.; Rachwal, B.; Rachwal, S. The synthesis of benzotriazolomethylanilines **2c** works in 78% yield. *J. Org. Chem.* 1995, 60, 2588 and that Ref. [12] reports mainly GC-yields.