

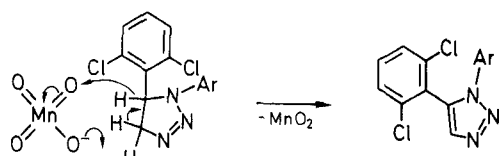
Triazolines XVIII.¹ Nickel Peroxide Oxidation of 4,5-Dihydro-1*H*-1,2,3-triazoles Bearing Sterically Crowded *ortho*-Substituted 5-Phenyl Groups

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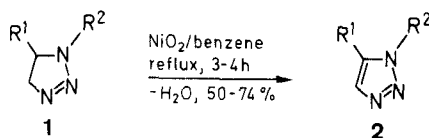
Nickel peroxide functions as an efficient oxidizing agent, superior to permanganate (phase-transfer catalytic system), in the oxidative dehydrogenation of 4,5-dihydro-1*H*-1,2,3-triazoles **1a–l**, bearing sterically crowded *ortho*-substituted 5-phenyl groups, to 1*H*-1,2,3-triazoles **2a–l**.

We have reported earlier that the oxidative dehydrogenation of 1,5-substituted 4,5-dihydro-1*H*-1,2,3-triazoles bearing a 5-pyridyl group, using potassium permanganate in a refluxing two-phase system (e.g. benzene/water) in the presence of a phase-transfer catalyst, provides a convenient route for the synthesis of 1-aryl-5-pyridyl-1*H*-1,2,3-triazoles.^{3,4} However, an extension of the reaction to 1,5-diaryl-4,5-dihydro-1*H*-1,2,3-triazoles indicated that the scope of this oxidation procedure was limited by its failure to afford satisfactory results in the case of those dihydrotriazoles where a sterically crowded *ortho*-substituted phenyl group was present in the 5-position.⁴ Such steric crowding apparently prevents the bulky permanganate ion from approaching the dihydrotriazole molecule, which is an essential requisite for effecting the oxidative dehydrogenation, as shown in Scheme A.⁵



Scheme A

In the course of our continued interest in the oxidation of dihydrotriazoles as a synthetic route for 1*H*-1,2,3-triazoles, we now report for the first time that nickel peroxide functions as an efficient oxidizing agent for the



1, 2	R ¹	R ²
a	2-ClC ₆ H ₄	4-MeOC ₆ H ₄
b	2-ClC ₆ H ₄	3,4-Cl ₂ C ₆ H ₃
c	2,4-Cl ₂ C ₆ H ₃	Ph
d	2,4-Cl ₂ C ₆ H ₃	4-ClC ₆ H ₄
e	2,4-Cl ₂ C ₆ H ₃	3-ClC ₆ H ₄
f	2,4-Cl ₂ C ₆ H ₃	4-FC ₆ H ₄
g	2,4-Cl ₂ C ₆ H ₃	4-CF ₃ C ₆ H ₄
h	2,4-Cl ₂ C ₆ H ₃	3-CF ₃ C ₆ H ₄
i	2,6-Cl ₂ C ₆ H ₃	Ph
j	2,6-Cl ₂ C ₆ H ₃	4-ClC ₆ H ₄
k	2,6-Cl ₂ C ₆ H ₃	3-ClC ₆ H ₄
l	2,6-Cl ₂ C ₆ H ₃	4-BrC ₆ H ₄

Scheme B

dihydrotriazole ring system,⁶ particularly for the oxidative dehydrogenation of sterically crowded dihydrotriazoles bearing *ortho*-substituted 5-phenyl groups (Scheme B). Unlike the potassium permanganate oxidation, where the permanganate ion has to closely approach the reaction site (Scheme A),⁵ nickel peroxide oxidation presumably occurs via reactions involving hydroxyl radicals.^{7,8} The effectiveness of nickel peroxide in the oxidation of a variety of sterically crowded dihydrotriazoles is apparent from the results presented in the Table, which are in agreement with that expected from the oxidation mechanisms of the two oxidants.

Table. Compounds **2** Prepared by NiO₂ Oxidation of **1**

Prod- uct	Reac- tion Time (h)	Yield ^a (%)	mp (°C)	Molecular Formula ^b or Lit. mp (°C)	¹ H-NMR (CDCl ₃ /TMS) δ, triazole ring CH (s)
2a	4	63	95–97	C ₁₅ H ₁₂ ClN ₃ O (285.8)	7.87
2b	3	63	97–99	99–100 ⁴	7.94
2c	4	65	90–92	C ₁₄ H ₉ Cl ₂ N ₃ (290.2)	7.88
2d	3	56	143–145	C ₁₄ H ₈ Cl ₃ N ₃ (324.6)	8.00
2e	4	56	97–99	C ₁₄ H ₈ Cl ₃ N ₃ (324.6)	7.88
2f	4	52	147–149	C ₁₄ H ₈ Cl ₂ FN ₃ (308.2)	7.87
2g	4	70	114–116	C ₁₅ H ₈ Cl ₂ F ₃ N ₃ (358.2)	7.89
2h	4	60	78.5–80.5	C ₁₅ H ₈ Cl ₂ F ₃ N ₃ (358.2)	7.90
2i	4	50	134–136	C ₁₄ H ₉ Cl ₂ N ₃ (290.2)	7.85
2j	4	63	137–139	C ₁₄ H ₈ Cl ₃ N ₃ (324.6)	7.85
2k	3	52	103–106	91–98 ⁴	7.98
2l	3	74	152–155	155–158 ⁴	7.95

^a Yield of pure isolated products. Compounds **1b**, **k**, **l** were oxidized with KMnO₄ under phase-transfer conditions to give **2b**, **k**, **l** in 17% (18 h), 34% (4 h) and <1% (18 h) yields, respectively.

^b Satisfactory microanalyses obtained: C ± 0.22, H ± 0.03, N ± 0.10.

The superior efficacy of nickel peroxide over the permanganate oxidizing agent is exemplified by the yield obtained for compounds **2b**, **k**, **l** as shown in the Table. The permanganate oxidation yields only less than 1% of pure triazole **2l** after 18 hours of reaction,⁴ while an outstanding yield of 74% is obtained in the nickel peroxide oxidation in 3 hours. Likewise, nickel peroxide oxidation leads to yields of 63% and 52%, respectively, for triazoles **2b** and **2k**. The permanganate oxidation of

1k fails to yield a pure compound **2k** when the oxidation is run for the same period of time (4 hours) as that for the nickel peroxide reaction.

In summary, nickel peroxide oxidation of sterically crowded dihydrotriazoles **1** provides a simple, versatile route for the synthesis of a number of hitherto unknown sterically crowded 1*H*-1,2,3-triazoles **2**. The synthetic utility of azide addition to acetylenes to prepare **2** is limited by the nonregiospecific nature of the addition and the general lack of reactivity of acetylenes in cycloaddition reactions.⁹

Melting points were determined in a Thomas-Hoover capillary melting point apparatus. ¹H-NMR spectra were recorded on a Varian XL-300 (300 MHz) spectrometer.

1*H*-1,2,3-Triazoles **2; General Procedure:**

To a solution of the dihydrotriazole **1**¹⁰⁻¹² (0.005 mol) in benzene (100 mL), is added dried, finely powdered NiO₂¹³ (0.060 mol) and the mixture is refluxed with vigorous magnetic stirring for 3–4 h. The mixture is then filtered and the benzene solution combined with further benzene or CHCl₃ extracts of the residual NiO₂. Removal of the solvent in a rotary evaporator gives an oily residue, which upon cooling and trituration with Et₂O/petroleum ether (bp 32–36°C), readily yields the triazole as a white crystalline solid. Recrystallization from acetone/petroleum ether (bp 36–60°C) gives analytically pure samples (Table).

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(1) This paper was presented in part at the 10th International Congress of Heterocyclic Chemistry, Waterloo, Canada, 1985.

- (2) This paper is based on the undergraduate honors paper of S.B.E. submitted to the Independent Problems Course in Chemistry. It won first prize in the 1984–85 Oswald Research and Creativity Competition for undergraduate students at the University of Kentucky.
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