



A Novel Variation in Fischer Indole Reaction for Viable and Rapid Synthesis of 1,2,3,4-Tetrahydro-6,8-Dinitro-9H-Carbazole

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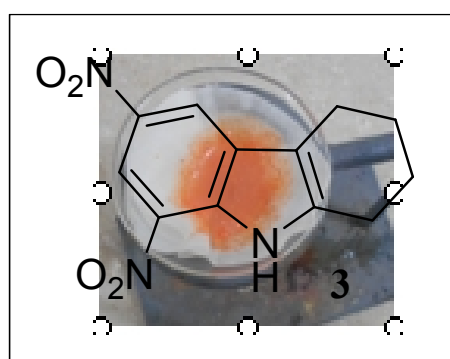
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ABSTRACT

A very stimulating variation in Fischer indole reaction by adopting solvent and catalyst free conditions is reported in this work. A concise synthesis of dinitro tetrahydrocarbazole derivative **3** was introduced without using any accelerating agent at ambient temperature with fairly good yield. This procedure has been actually reported for the first time within this work. Additionally, the validity of product was fully corroborated by the obtained characterizing results from the employed spectroscopic techniques such as ultra violet (UV), Fourier transform infrared (FT-IR) and proton and carbon nuclear magnetic resonance (¹H and ¹³C NMR), Mass spectrometer (MS) and carbon, hydrogen and nitrogen (CHN) analyzer. And finally, it could be mentioned that the investigated reaction could be equally run without use of any catalyst as a favorable approach to adopt Green Chemistry.



Keywords:

Tetrahydrocarbazole;
Solvent free synthesis;
Fischer indole reaction.

Introduction

A series of tetrahydrocarbazole derivatives with various functionalities have been synthesized using Fischer indole reaction since its discovery in 1883 [1]. There is no doubt that the mentioned reaction is considered as the basis of aromatic heterocycle indole generation from phenylhydrazine and aldehyde/ketone scaffold under acidic catalysts [2-4]. Many review works have been published to this time to admire this blessed organic reaction focusing on details of mechanism, nature of substrate, acid choice and

reaction conditions [5]. Recently, as synthetic trend moves to environment beginning approach, many reports are available on this intramolecular cyclization in the microwave reactor [6, 7]. In this case, glacial acidic acid was found to be the best acid choice for obtaining good yield of reaction [8]. The proposed synthetic route of this work is based on Fischer indole reaction but without using any catalyst. Our accidental happening achievement is supported by the fact that hydrazones are stable at neutral pH and they could be preceded via bell shaped curve in aqueous medium as reported in

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literature [9]. Behind this fortuitous happening, laboratory temperature was the major controlling factor of reaction. There is no need to acidic media in the convenient high temperature condition to accelerate cyclohexanone molecule. Thereby, successful execution of reaction takes place in neutral medium. In the case of low temperature condition, cyclohexanone requires microwave irradiation just for 5 seconds to excite the molecule. Hence, this sudden phenomenon is a contribution to modern research that rule out the use of acid in Fischer indole synthesis. Schematic information is represented in Fig. 1 and are described in the following text.

Materials and Methods

Synthesis of 1,2,3,4-Tetrahydro-6,8-Dinitro-9H-Carbazole

Conventional Method: To a rapidly stirring solution of cyclohexanone (1 mol, 98 g) 1 in glacial acetic acid (3 mol, 180 g), small portions of 2,4-dinitrophenylhydrazine (1 mol, 198g) 2 were added at reflux point for 1 h. Initial bright orange colour turned from dark to dullness with time. After an additional 1 h reflux, the contents of flask were poured into a beaker. To ensure complete precipitation, it was placed in the ice bath with continuous shaking. Solidified product 3 was filtered, washed and recrystallized with DCM.

State: Orange red crystals; Mol. Formula $C_{12}H_{11}N_3O_4$; Mol. wt. 261.23 g/mol; m.p. 132°C ; Yield 65%; UV λ_{max} (MeOH): 227, 275, 287, 315 nm; (KBr, umax. cm^{-1}): 1415 (NO_2), 848 (C-N), 1695 (C=O), 2992 (CH-aliphatic), 3144 (aromatic ring), 3447 (NH); $^1\text{H-NMR}$ (δ , ppm): 2.34 (t, 2H), 1.7-1.9 (m, 2H, 2CH₂ cyclo), 2.45 (t, 2H), 7.39 (s, 1H, Ar-H), 8.05 (s, 1H, Ar-H), 10.14 (s, 1H, NH); $^{13}\text{C-NMR}$ (δ , ppm): 23.9, 24.2, 26, 26.3, 108.3, 109.7, 122, 125.4, 130, 131.2, 136, 137.9; MS (ES^+): 261 (MH^+); Anal. Calcd (Found): C 55.27 (55.20), H 4.30 (4.25), N15.99 (16.09), O 24.46 (24.57).

Microwave Mediated Synthesis: Cyclohexanone (0.001 mol, 0.098 g), 2, 4-dinitrophenylhydrazine (0.001 mol, 0.198 g) were activated under microwaves for 1 s only. Acetic acid (0.003 mol, 0.180 g) was injected in reaction mixture and again irradiated by microwaves with the interval of 1 s. TLC indicated 5 s were enough to complete the reaction. After this, product 3 was filtered and dried to get the pure precipitates.

Solvent Free/Neutral Medium Approach: 0.001 mole of cyclohexanone (0.098 g) was introduced in the reaction pot at lab temperature and it was well covered with parafilm. After a while, 0.001 mole of 2, 4-dinitrophenylhydrazine (0.198 g) was added with vigorous manual shaking. At no instance, product 3 was solidified and recrystallized from DCM.

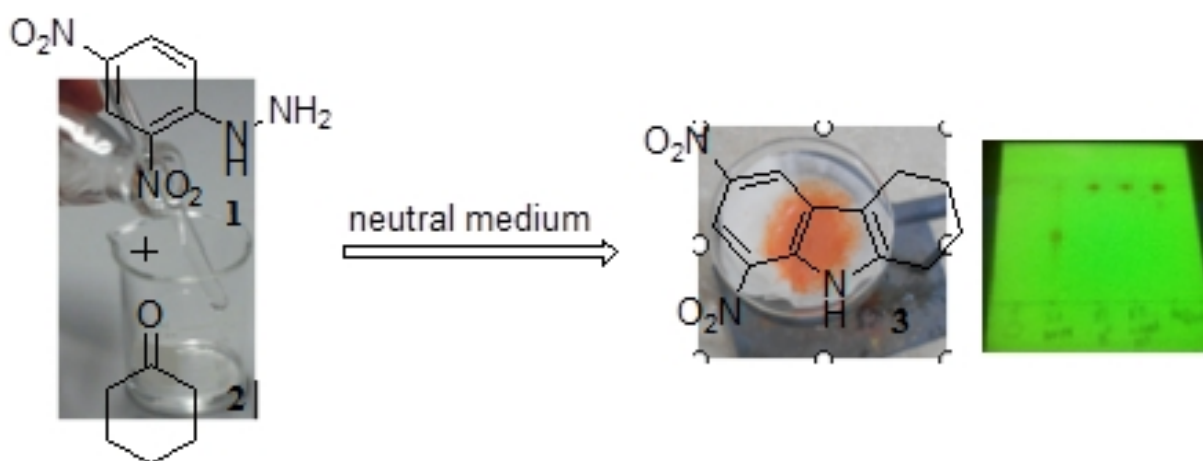


Fig. 1. Catalyst free synthesis of 1,2,3,4-tetrahydro-6,8-dinitro-9H-carbazole.

Results and Discussion

The results of this work indicated that the investigated Fischer indole reaction could be equally run without use of any catalyst. To the best of our knowledge, this research article is the first report furnishing substituted tetrahydrocarbazole in neutral medium. Treatment of compound 1 with 2, successfully executed product 3 in fairly good yield (87%). Conventional conditions, as compared to microwave technology, ultimately offer a favorable approach to adopt green chemistry. However, TLC indicated the same

position of product, no matter what method is adopted for its synthesis.

Conclusion

In the present study, we explored the behavior of Fischer indole reaction for the synthesis of 1,2,3,4-tetrahydro-6,8-dinitro-9H-carbazole. This work has been actually done for the first time. As a concluding remark of this work, it could be mentioned that the investigated reaction could be equally run without use of any catalyst as a favorable approach to adopt Green Chemistry.

References

1. Dufour F, Kirsch G. Carbazolo[2,1-a]carbazole derivatives via Fischer indole synthesis. *J. Heterocycl. Chem.* 2008;45:161-163.
2. Fischer E, Jourdan F. Ueber die hydrazine der brenztraubensäure, *Berich. Deutsch. Chem. Gesellsch.* 1883;16:2241-2245.
3. Fischer E, Hess O. Synthese von indolderivaten, *Berich. Deutsch. Chemisch. Gesellsch.* 1884;17:559-568.
4. Kohling P, Schmidt AM, Eilbracht P. Tandem hydroformylation/Fischer indole synthesis: A novel and convenient approach to indoles from olefins. *Org. Lett.* 2003;5:3213-3216.
5. Hughes DL. Progress in the Fischer indole reaction: a review. *Org. Prep. Proced. Int.* 1993;25:607-632.
6. Chitra S, Paul N, Muthusubramanian S, Manisankar P. A facile, water mediated microwave-assisted synthesis of 4,6-diaryl-2,3,3a,4-tetrahydro-1H-pyrido[3,2,1-jk]carbazoles by a domino Fischer indole reaction-intramolecular cyclization sequence. *Green Chem.* 2011;13:2777-2785.
7. Barbieri V, Ferlin MG. Microwave-assisted one-pot synthesis of substituted tetrahydrocarbazole and 8,9,10,11-tetrahydro-7H-pyrido[a]carbazoles. *Tetrahed. Lett.* 2006;47:8289-8292.
8. Balamurali R, Prasad KJR. Synthesis, characterization and pharmacological activities of 5,6,11,12-tetrahydroindolo[2,3-a]carbazole derivatives, *Short Commun.* 2001;56:229-232.
9. Gutte B. Peptides: synthesis, structures and applications, Academic press, Inc.: 1995; p 4286.

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