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Quantum-chemical studies on thermodynamic feasibility of 1-methyl-2,4,5-trinitroimidazole processes

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Abstract 1-Methyl-2,4,5-trinitro imidazole (MTNI) is a well-known melt cast explosive possessing good thermal stability and impact insensitivity. MTNI has been synthesized from multi-step nitration followed by methylation of imidazole exhibiting low yield. It is desirable to screen the process thermodynamically for evaluating feasibility of the process. In the present investigations, B3LYP method in combination with 3-21G** basis set has been chosen to evaluate the enthalpy of formation for reaction species by designing reasonable isodesmic reactions. Thermodynamic feasibility of the processes has been worked out assuming free energies of reactions as derived from standard enthalpy and entropy of the reaction species. All possible synthesis routes for the target molecule, MTNI has been conceptualized from different precursors/intermediates viz. imidazole, 2-nitroimidazole, 4-nitroimidazole, 1-methyl imidazole and 2,4,5-triiodoimidazole. Various nitrating agents have been employed and their effect studied for deciding the feasibility of the reaction. It has been found that reaction entropy and enthalpy are favorable on usage of NO_2BF_4 as nitrating agent. The charge on nitro group ($-Q_{NO2}$) has been used for better understanding of the reactivity of substrates/intermediates. Overall, the study helped in screening several possible routes for MTNI synthesis and identified the thermodynamically feasible process by using NO_2BF_4 as nitrating agent.

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Introduction

Polynitroimidazoles are promising candidates for high energy materials due to their favorable insensitivity and performance [1–6]. Imidazole derivatives with two or more nitro groups are expected to be potential ingredients for insensitive high energy formulations. 2,4-Dinitroimidazole, 4,5-dinitroimidazole, 2,4,5-trinitroimidazole, and MTNI (shown in Fig. 1) have been synthesized and tested as high energy materials and show good thermal stability and impact insensitivity [3, 4, 7]. Among these nitroimidazoles, MTNI is an excellent candidate for inclusion in melt-castable explosives due to its low melting point (82 °C), better density (1.78 g/cm³) and high detonation performance (D=8.80 km s⁻¹, P=34.66 GPa). Detonation velocity (D) and detonation pressure (P) are two important performance parameters for an energetic material and detonation performance of MTNI found comparable to 1,3,5-trinitro-1,3,5-triazacyclohexane (RDX, D=8.60 km s⁻¹, P=33.92 GPa) [8, 9]. In addition, sensitivity tests reveal that MTNI is a promising candidate as an insensitive high explosive. TNT is widely used in current melt cast formulations and well-known TNT based formulations are Torpex (42 % RDX, 40 % TNT, 18 % Al), Pentolite (50 % PETN, 50%TNT), Ammonite (80 % NH_4NO_3, 20 % TNT) Octol (70–75 % HMX, 25–30 % TNT) and TNTO (50 % TNT, 50 % NTO) [10, 11]. These compositions are found brittle and prone to cracking and thermal instability; hence, search for an alternative mixture with improved performance, high thermal stability and insensitivity gained more attention. MTNI possess higher performance than TNT and hence it may be a potential
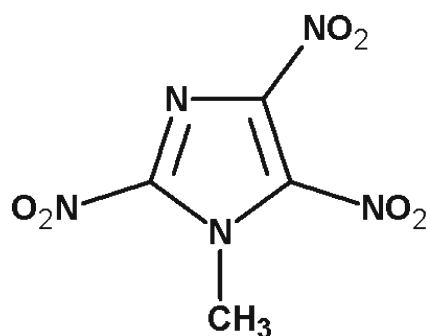
Fig. 1 Chemical structure of 1-methyl-2,4,5-trinitroimidazole (MTNI)

replacement for TNT in melt-cast formulations. However, it is technically unsuitable due to low yield and high production cost of MTNI.

The transformation of raw materials into the desirable products of greater value by chemical reaction is the major goal of chemical synthesis. The feasibility of chemical synthesis needs to be experienced with thermodynamic properties of reaction species. Heat of reaction (ΔH_r) and free energy of reaction (ΔG_r) are the important entities to evaluate the feasibility of the process. These entities are being derived from thermo-chemical information on heats of formation (ΔH^0_f) and entropies of reaction species. The standard enthalpies of formation and entropies are to some extent dependent on temperature. If the reaction temperature is not far away from room temperature (298.15 K), the standard state enthalpy and entropy (ΔH° and ΔS°) are assumed to be temperature independent [12]. Hence, free energy (ΔG_r) can be derived at different temperatures from ΔH° and ΔS°.

The present study is aimed to assess thermodynamic feasibility of these reported routes and derive alternative thermodynamically practicable routes for preparation of MTNI. Various routes for MTNI synthesis have been thermodynamically evaluated from the computed information on ΔH°, ΔS°, ΔG°, ΔH_r, ΔS_r, and ΔG_r.

Computational methodology

Thermo-chemical properties are widely being predicted by empirical approach, quantum mechanics or a combination of both. Computational chemistry simulates chemical structure and reactions numerically, based in full or in part on the

fundamental laws of physics and a vital adjunct to experimental studies. All calculations were carried out using the Gaussian 03 program package [13]. Density functional methods (DFT) [14] are attractive because they include the effects of electron correlation and least expensive compared to the ab initio methods. The DFT methods with B3LYP [15, 16] hybrid model can produce reliable geometries and energies, which require less time and computer resources. The B3LYP method in combination with 3-21G** [17, 18] basis set has chosen to evaluate the enthalpy of formations for reaction species by designing reasonable isodesmic reactions [19, 20]. The isodesmic reaction, in which numbers of electron pairs and chemical bond types are conserved in the reaction, allows canceling of errors inherent in the approximate treatment of electron correlation in the solutions to quantum mechanic equations. Previous studies [21] show that isodesmic reaction approach predicts reasonably accurate heat of formation, even at relatively low levels of theory. Figure 2 shows the scheme of isodesmic reaction used for computation of ΔH^0_f of MTNI. Molecular geometries have been optimized and characterized to the relative energy minimum of the potential surface by frequency calculation. Thermal corrections to the enthalpy have also been obtained from frequency calculation at 298.15 K. The computed thermo-chemical information of reaction species is listed in Table 1. Recently, Zhang [22] evaluated the product occurrence ratio of some nitrating reactions assuming charge on nitro groups. In addition, Q_{NO2} is more sensitive to structural changes and investigated more effectively for the prediction of the nitrating reaction of imidazole. More negative charge on the nitro group corresponds to easier and faster reactions. Charge on nitro groups have been calculated by using NBO analysis at B3LYP/3-21G** method [23]. Charge on a nitro group is the algebraic sum of charges of all atoms on a nitro group.

Results and discussion

Several possible routes of MTNI synthesis derived from imidazole (I), methyl imidazole (II), 2-nitroimidazole (III) and triiodoimidazole (IV) have been adopted for evaluating thermodynamic feasibility. Figure 3 shows the detailed paths of MTNI (XVI) synthesis which comprises four main routes (R1 to R4) and three interlinked routes (R1′, R3′ and R1″). The detailed route description and involved reaction

Fig. 2 Isodesmic reaction scheme of XVI for the calculation of ΔH^0_f
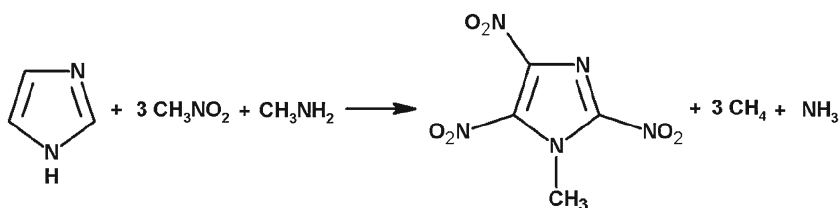
Table 1 Thermochemical information of reaction species from quantum chemical calculations

Reaction species	ΔH^0_f (kJ mol^{-1})	ΔS^0 (kJ mol^{-1} K^{-1})
Imidazole	137.0 (129.5)[a]	0.2701
Methyl imidazole	145.0	0.3115
2-Nitroimidazole	108.6	0.3290
2-Nitromethylimidazole	116.1	0.363
4-Nitroimidazole	105.2	0.3306
4-Nitromethylimidazole	109.5	0.3730
Tri-iodoimidazole	410.4	0.6756
Tri-iodomethylimidazole	415.9	0.4567
Nitric acid	−133.9	0.2668
Nitrogen pentaoxide	83.0	0.3504
NO$_2$BF$_4$	−1251.3	0.3691
Dimethyl sulfate	−687.0	0.3633
Diazomethane	215.0	0.2448
MTNI	128.8	0.4811

[a] Experimental value taken from ref. [32]

Table 2 Details about reaction routes and paths

Sl. no.	Route no. (RN)	Reaction path
1	R1	I-V-VI-VII-VIII-XVI
2	R2	II-IX-X-XVI
3	R3	III-XI-XII-XVI
4	R1′	I-V-IX-X-XVI
5	R3′	III-VII-VIII-XVI
6	R11′	III-VII-XII-XVI
7	R4	I-IV-XIII-XIV-XV-XVI

intermediates for a particular route has been given in Table 2. Novikov et al. [24] reported the synthesis scheme of XVI

containing series of nitration and methylation on imidazole (I). The preparation steps of intermediates 4-nitroimidazole (V), 1,4-dinitroimidazole (VI) and 2,4-dinitroimidazole (VII) were given by Bulusu et al. [25]. It contains nitration of I in mixed acid of 70 % nitric acid and concentrated sulfuric acid at reflux temperature to prepare V and further nitration in a mixture of acetic anhydride, fuming nitric acid and acetic acid for preparation of VI. 2,4-Dinitroimidazole (VII) was prepared from VI by thermal rearrangement with refluxing in chlorobenzene. Cho et al. [26] reported further nitration of intermediates and methylation by using
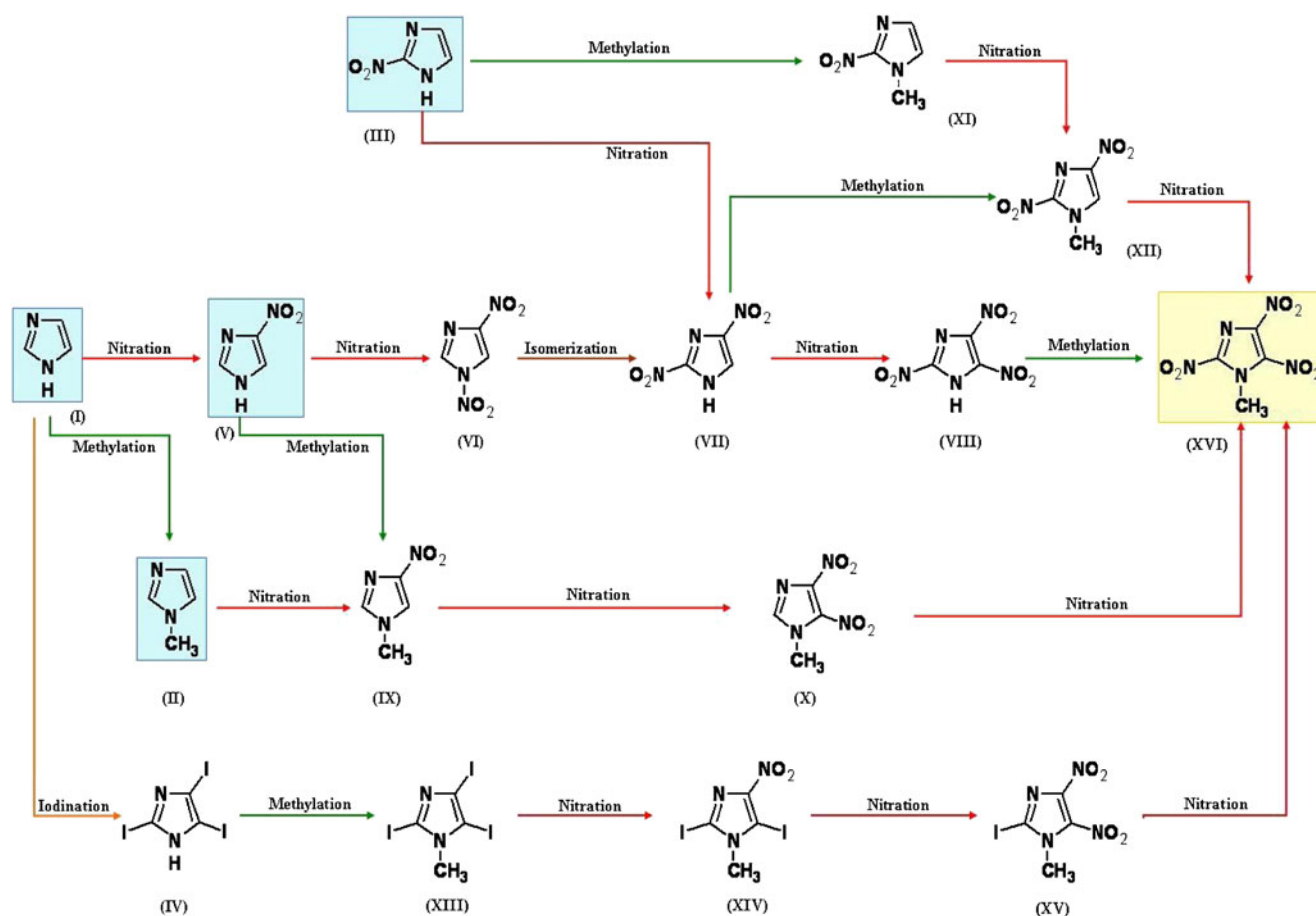
Fig. 3 Reaction scheme for MTNI synthesis

**Table 3** Nitration reaction heat (ΔH_r), entropy (ΔS_r), and free energy (ΔG_r) at 298.15 K

RN	Reaction path	ΔH_r (kJ mol^{-1})			ΔS_r (kJ mol^{-1} K^{-1})			ΔG_r (kJ mol^{-1})		
		HNO$_3$	N$_2$O$_5$	NO$_2$BF$_4$	HNO$_3$	N$_2$O$_5$	NO$_2$BF$_4$	HNO$_3$	N$_2$O$_5$	NO$_2$BF$_4$
R1	I-V	−139.7	−248.7	−189.4	−0.017	−0.023	0.119	−134.5	−241.8	−225.0
	V-VI	7.9	−101.1	−41.7	−0.016	−0.021	0.121	12.6	−94.7	−77.9
	VII-VIII	−76.7	−185.7	−126.5	−0.016	−0.022	0.121	−71.9	−179.3	−162.5
R2	II-IX	−143.4	−252.4	−193.1	−0.017	−0.022	0.120	−138.5	−245.8	−229.0
	IX-X	−97.1	−206.1	−146.7	−0.029	−0.036	0.107	−88.14	−195.5	−178.6
	X-XVI	−99.5	−208.4	−149.1	−0.018	−0.024	0.119	−94.1	−201.4	−184.6
R3	III-VII	−121.9	−230.9	−171.7	−0.019	−0.024	0.118	−116.4	−223.7	−206.9
	XII-XVI	−77.2	−186.2	−126.8	−0.018	−0.024	0.119	−71.7	−179.1	−162.3

diazomethane as methylating agent to synthesize MTNI. Methylation on VIII by using dimethyl sulfate was reported by Damavarapu et al. [27]. They have also worked out the feasibility of nitration on methyl imidazole by using a solid nitrating agent. Another route was reported by Jadhav et al. [28] which comprise iodination (IV) and methylation (XIII) of imidazole and consecutive nitrations (XIV and XV) to prepare XVI. It has been found that these reported routes involve multi-step reactions and result in low yield (about 30 %).

Effect of nitrating agents

In nitration reactions, selection of nitrating agent is always the crucial task. Several nitrating agents are cited in literature [29] and hence, it is hard for the chemist to choose which nitrating agent among them to maintain the balance between process, safety and economy. Initially, thermodynamic evaluation was carried out by using nitric acid as nitrating agent. It was found that, all nitration steps were highly exothermic in nature. However, entropy of reaction was found to be low (negative) which was not desirable. In

general, solid nitrating agents are essential to transform the entropy of reactions toward the higher (positive) side. In this study, N$_2$O$_5$ and NO$_2$BF$_4$ have been considered as promising solid nitrating agents and thermodynamic evaluations have been performed. Computed reaction heat (ΔH_r), entropy (ΔS_r) and free energy (ΔG_r) for nitration steps have been summarized in Table 3 at 298.15 K. It has been found that nitration reaction with N$_2$O$_5$ is highly exothermic and spontaneous in comparison with nitric acid and NO$_2$BF$_4$ for all steps. However, entropy of the reaction system has been reduced in comparison with nitric acid usage because the reaction product contains an equal molar quantity of nitric acid. Entropy of reaction for all nitration steps is higher (positive) by usage of NO$_2$BF$_4$ as nitrating agent. Entropy of the reaction system has been increased due to higher entropy reaction products (HF and BF$_3$). It has also been found that the moderate exothermic nature of nitration reactions are due to usage of NO$_2$BF$_4$ as nitrating agent. This thermodynamically favorable reaction condition needs to increase in free energy of reaction for all the temperatures in comparison to nitric acid and N$_2$O$_5$ usage. Hence, the study indicates that NO$_2$BF$_4$ is the appropriate candidate for carrying out nitration reaction of this scheme. Similar study could not be extended on R4 as these reactions involve complex halides.
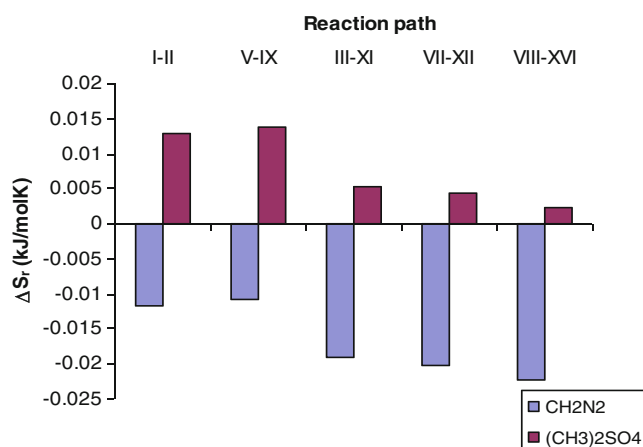
Fig. 4 Effect of methylating agent on reaction entropy

Table 4 Reaction free energy of methylation steps

Sl. no.	Reaction path	ΔG_r (kJ mol^{-1})	
		CH$_2$N$_2$	(CH$_3$)$_2$SO$_4$
1	I-II	−203.50	−269.8
2	V-IX	−207.53	−273.8
3	III-XI	−201.87	−268.2
4	VII-XII	−205.48	−271.8
5	VIII-XVI	−205.25	−271.6

Effect of methylating agents

Among the several methylating agents methyl iodide, diazomethane and dimethyl sulfate are widely used. In the present investigation, effect of diazomethane and dimethyl sulfate on reaction enthalpy, entropy and free energy have been evaluated. It has been found that heat of reaction in dimethyl sulfate reactions is higher than diazomethane reactions by 60 kJ mol^{-1}. Figure 4 shows the entropy change at various methylation reaction paths. Similar trend has been seen for free energy of reaction as reported in Table 4. Reaction entropy has also been improved due to usage of dimethyl sulfate in reactions. The present study reveals that dimethyl sulfate is a thermodynamically more feasible methylating agent for the proposed reaction scheme. It has also been noticed that entropy of methylation reaction decreases at later stages (VII-XII and VIII-XVI) of reaction routes. However, such effect has not been observed on reaction heat and free energy, which was found to be nearly constant at all the stages of reaction routes.

Role of substrate

Four different substrates (I, II, III and V) have been chosen for thermodynamic evaluation of various derived routes for MTNI synthesis. Studies have been carried out to understand the role of substrate for identifying a thermodynamically feasible route as well as exact sequence of nitration and methylation steps in it. While comparing nitration step of substrate I and II, it has been observed that nitration on II is

found to be highly exothermic and more spontaneous than nitration of I. Table 4 shows the improvement of reaction thermodynamic properties due to the methylated substrate (II) for nitration; hence it (II) may be preferred for preparation of IX effectively.

The effect of methylation on substrate III and V has shown the significant changes in reaction entropies for both the methylating agents. The reaction entropies of the reaction path V-IX (methylation of substrate V) and III-VII (methylation of substrate III) have been given in Table 4 which indicates that methylation on the substrate V is more spontaneous than substrate III. However, further nitration on XI is thermodynamically difficult (reaction path XI-XII) in comparison with nitration on III, V and IX. Thus methylation of III may not be thermodynamically feasible for further nitration steps on XI.

From this study, it has been found that route R2 is more thermodynamically feasible than other routes and involves only nitration reactions. It has also been found that routes R3′ and R11′ are equally feasible and do not show any significant effect on reaction enthalpies, entropies and free energy. Overall this thermochemical study resulted in an analysis of several routes for synthesis of MTNI and identified thermodynamically feasible routes.

Evaluation of nitration reactions

Nitration reaction is one of the most important ways to synthesize the nitro compounds. Figure 5 shows the $-Q_{NO2}$ of nitrating products. In unsaturated systems, including

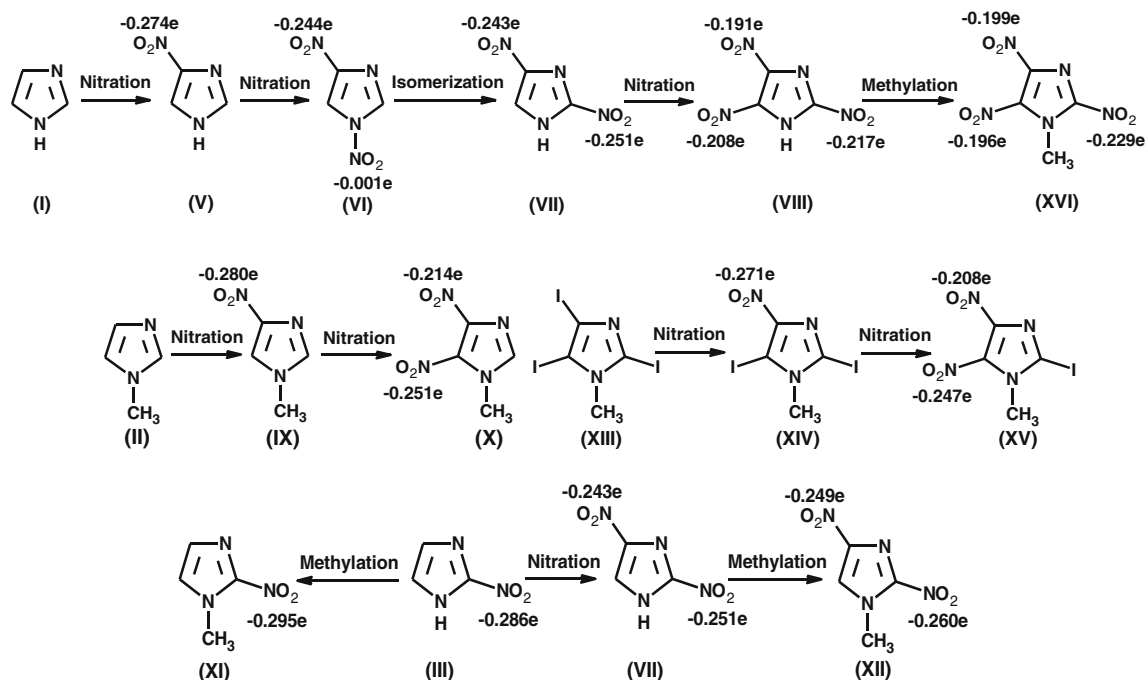Fig. 5 Charge on nitro groups ($-Q_{NO2}$) of the substrates

polynitroimidazoles, an interesting feature of many C-NO₂ bonds is the presence of a buildup of positive electrostatic potential above and below the bond region, and these positive buildups can serve as initial sites for nucleophilic attack [30, 31]. The $-Q_{NO2}$ is calculated using the natural bond orbital (NBO) analysis at B3LYP/3-21G** level. The magnitude of $-Q_{NO2}$ of products determines the degree of difficulty in nitration. The $-Q_{NO2}$ of XVI is much less in comparison with intermediate reaction products due to the strong electron withdrawing effect of three nitro groups, their space orientation and steric hindrance. Hence, difficulty is involved in its synthesis. The methylation of V to IX is found to be favorable, as this step enhances the $-Q_{NO2}$ of the corresponding nitro group. Similar trends are followed in cases of VII to XII and III to XI. $-Q_{NO2}$ of IX (−0.280e) is higher than V (−0.274e), this proves that nitration of II may be faster than I. The nitration of III to VII may yield better results than V to VII. III has a nitro group on C2 position of imidazole and may not reduce the electron density of C4. Nitration of V to VII involves the N-nitration product (VI) which on isomerization gives VII. This affects the electron density on the ring and reduces the charge on the nitro group. The 2,4,5-triiodo-1-methylimidazole (XIII) is a better substrate for the nitration because the iodo substituents can be replaced with nitro groups with different nitrating agents. Figure 5 summarizes that simultaneous addition of nitro groups on the substrate reduces the $-Q_{NO2}$ due to the electron withdrawing effect of the nitro group, which in turn reduces the reactivity and possible sites making further nitration more difficult.

Conclusions

Thermodynamic evaluation on various nitrating agents indicates that NO₂BF₄ is the suitable candidate for nitration and may not require stringent reaction conditions. Dimethyl sulfate is a more thermodynamically feasible agent for methylation than diazomethane. Computational evaluation revealed that the methyl imidazole (II) route is more feasible thermodynamically and contains only nitration steps. It may give better yield of MTNI by nitrating methyl imidazole under NO₂BF₄ environment and providing proper series–parallel reaction treatment. Routes R3′ and R11′ are equally feasible and have no effect of shifting of methylation steps. This thermodynamic study finds usefulness in analyzing several routes of MTNI synthesis and identifying the feasible routes. The charge on a nitro group was calculated and applied to investigate the nitrating reaction. The more negative charge on a nitro group corresponds to the easier and faster reaction, and the higher occurrence ratio.

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