

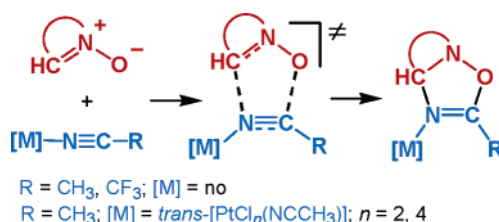
Theoretical Study of Reactant Activation in 1,3-Dipolar Cycloadditions of Cyclic Nitrones to Free and Pt-Bound Nitriles

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1,3-Dipolar cycloaddition of the cyclic nitrones $\text{CH}_2(\text{CH}_2)_2\text{CH}=\text{NO}$ (**N1**), $\text{CH}_2\text{CH}_2\text{OCH}=\text{NO}$ (**N2**), $\text{CH}_2\text{-OCH}_2\text{CH}=\text{NO}$ (**N3**), and $\text{O}(\text{CH}_2)_2\text{CH}=\text{NO}$ (**N4**) to organonitriles, RCN—both free (R = CH₃, CF₃) and ligated to Pt^{II} and Pt^{IV} (in the complexes *trans*-[PtCl₂(NCCH₃)₂] (**1**) and *trans*-[PtCl₄(NCCH₃)₂] (**2**))—was investigated extensively by theoretical methods at different levels of theory. The effectiveness of two types of dipolarophile activation (by introducing a strong electron-acceptor group R and by coordination to a metal center) was analyzed and compared. The influence of factors such as the nature of the cyclic nitron and the nature of the solvent on the reactions was also studied. The reactivity of dipoles and dipolarophiles increases along the series **N4** < **N1** ≈ **N3** < **N2** and CH₃CN < CF₃CN < **1** < **2**; the latter demonstrates that the coordination of RCN to a Pt center provides an even higher activation effect upon cycloaddition in comparison with the introduction of a strong electron-acceptor group R such as CF₃. A higher reactivity of the cyclic dipole **N1** in comparison with acyclic nitrones (e.g., CH₃CH=N(CH₃)O) is interpreted to be a result of its exclusive existence in a more strained and hence more reactive *E*-rather than *Z*-configuration. The activation and reaction energies have been calculated at different basis sets and levels of theory, up to MP4(SDTQ), CCSD(T), and CBS-Q. The activation energies are weakly sensitive to a change of the correlated methods. The consideration of the solvent effects results in the increase of the activation barriers, and such enhancement is less pronounced for the nonpolar or low polar solvents. The cycloadditions to CH₃CN and CF₃CN were found to be nearly synchronous, but these reactions involving **1** and **2** are clearly asynchronous. Moreover, the reaction of **N2** with **2** proceeds via a very early acyclic transition state, while for all other reactions the transition states have a cyclic nature.

Introduction

Cycloaddition (CA) reactions,¹ in general, and 1,3-dipolar cycloaddition (1,3-DCA),² in particular, are among the most important organic processes, allowing the synthesis of a significant number of ring systems, many of them with extended laboratory, industrial, and medical applications. Organonitriles (RC≡N), as representatives of dipolarophiles with a heteroatomic reaction site, are useful reagents, generating, after 1,3-

DCA, the C=N moiety in the resulting azoheterocycles. However, the usage of the nitriles is hampered because of their

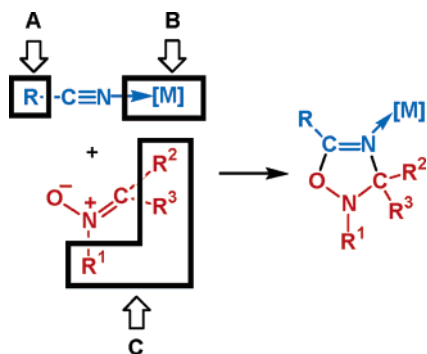
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SCHEME 1

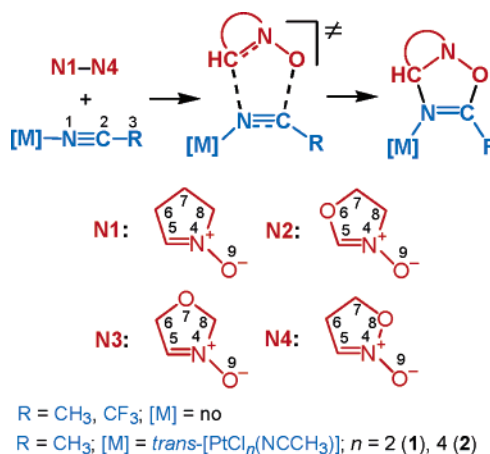


relative inertness in such reactions, for example, in reactions with nitrones, which represent one of the most common types of dipoles. Indeed, the nitriles with electron-donor substituent R do not typically react with nitrones even under harsh conditions. Hence, an additional activation of the reactants is required, and it can be reached either by affecting the nitrile (dipolarophile) or nitrone (dipole) or, in some instances, both of them.

In the majority of publications devoted to cycloaddition to nitriles, the dipolarophile exclusively underwent the activation³ via two principal routes: (i) modification of RCN by the introduction of an appropriate substituent (Scheme 1A) or (ii) coordination of the reactant to a Lewis acid (Scheme 1B). The first route is often applied in pure organic chemistry, and in the context of 1,3-DCA to RCN the use of electron-deficient nitriles such as CF_3CN or CCl_3CN leads to the isolation of corresponding substituted cycloaddition products.⁴ The second, less common, route of nitrile activation was investigated mostly for CA of azides by Purcell et al.,^{5a,b} Hay et al.,^{5c} and recently by Sharpless et al.⁶ and also for reactions with nitrones and nitrile oxides.⁷ Our experimental^{7a-d} and theoretical^{7f,g} results demonstrate that the coordination of RCN to platinum centers dramatically enhances the reactivity of the nitriles toward dipoles of allyl (nitrones; Scheme 1) and propargyl/allenyl anion (nitrile oxides) types in comparison with CA to free RCN.

The activation of nitrones as dipoles in 1,3-DCA to nitriles (Scheme 1C) by modification of the substituents has been the subject of limited works,^{8,9} while to the best of our knowledge studies of the *combined* activation of both reactants (i.e., using

SCHEME 2



highly reactive nitrones and transition metal-bound nitriles) are restricted to just two investigations.¹⁰ In the latter publications, RCN coordinated to the platinum center and cyclic nitrones were used (the transition from the acyclic nitrones to the cyclic ones may be considered, in principle, as an alteration of substituents at the C and N atoms of the dipole). Thus, the additional investigation of the *joint* activation of both nitriles and nitrones is necessary because this route seems to be the most comprehensive to control the reaction.

The *experimental* studies in this direction initiated recently¹⁰ are now extended to the *theoretical* methods which not only may interpret the synthetic results obtained thus far but also can be used for the investigation of the intimate mechanism of the reactions and for making some useful practical predictions. The main goal of this work is to investigate and compare the role, effectiveness, and driving forces of different types of reactants' activation in the reactions of nitrones with nitriles. Within this goal the following problems were raised: (i) interpretation of the experimentally observed higher reactivity of the *cyclic* nitrone **N1** (Scheme 2) toward nitriles in 1,3-DCA in comparison with the reactivity of *acyclic* systems, (i.e., $\text{RCH}=\text{N}(\text{R}')\text{O}$), (ii) analysis of the possibility of a further activation of dipoles on going from cyclic nitrones with purely hydrocarbon chain (**N1**) to those with the *O*-containing heteroatomic cycle (**N2**–**N4**), (iii) comparison of the relative roles of the platinum center, on one hand, and the strong acceptor substituent R in RCN, on the other hand, on the activation of nitriles, and (iv) solvent effect in these CAs.

In the current work, the detailed search of the reaction mechanisms and the estimates of energetic characteristics (at different levels of theory) have been performed for the cycloaddition of cyclic nitrones **N1**–**N4** to nitriles RCN, both free ($\text{R} = \text{CH}_3, \text{CF}_3$) and coordinated to Pt^{II} and Pt^{IV} centers in the complexes $\text{trans}[\text{PtCl}_n(\text{NCCH}_3)_2]$ ($n = 2, 4$). The influence of factors such as RCN complexation to the metal center, oxidation state of the latter, nature of organic groups R, nature of the cyclic nitrone, and nature of the solvent on the reaction is discussed. The calculations of the metal-mediated reactions were carried out for **N2** and **N4** as the *most* and the *least* reactive nitrones of the series.

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This article has the following structure. First, we describe the reactivity of nitrones and nitriles in terms of qualitative frontier molecular orbital (FMO) theory and discuss the structural features of the reactants and the final products. Second, the nature of gas-phase transition states and details of the reaction mechanisms are examined and includes the estimates of the activation and reaction energies and the comparative analysis of the reactivity of CH_3CN and activated nitriles as well as various cyclic nitrones. Third, the effects of solvation on the energetic characteristics of the reactions are discussed for variety of solvents. Fourth, the reasons for the higher activity of the cyclic nitrones versus acyclic ones are analyzed.

Computational Details

The full geometry optimization of all structures and transition states (TS) has been carried out with help of the Gaussian 98¹¹ program package. The structures of acetonitrile, nitron **N2**, final products of their cycloaddition, corresponding TSs, and orientation complexes (OC) have been optimized at the HF, DFT, and MP2¹² levels of theory using standard basis sets of Gauss functions 6-31G, 6-31G*, and 6-31+G**.¹³ The DFT calculations have been performed using the B3LYP functional.^{14,15} Single-point calculations of all these structures have been carried out at the HF, B3LYP, MP2, MP3, MP4(SDTQ), and CCSD(T)¹⁶ levels using 6-311++-G**,¹⁷ 6-31+G**, or 6-31G* basis sets as well as at the CBS-Q level.¹⁸ Due to the presence of the van der Waals orientation complexes which are formed at the initial steps of the reactions, counterpoise estimates of basis set superposition error (BSSE)¹⁹ were made for the reaction of **N2** with CH_3CN by performing calculations on the nitron and acetonitrile including basis functions

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from the other reactant, in the orientation complex geometries. Taking into account the fact that the activation parameters are only weakly sensitive to a change of the approximation (except the HF method), we do not discuss in the text the influence of the level of theory, basis set, and BSSE correction on the activation and reaction energies but consider it in the Supporting Information.

The structures of the other nitrones, CF_3CN , platinum complexes, corresponding final products, TSs, and OCs have been optimized at the B3LYP level, which was found to be the most reasonable one for the investigation of the nitron-to-nitrile cycloadditions (see Supporting Information). A quasi-relativistic Stuttgart pseudopotential described 60 core electrons, and the appropriate contracted basis set (8s7p6d)/[6s5p3d]²⁰ for the platinum atom and the 6-31G* basis set for other atoms were used. Further, this level is denoted as B3LYP/6-31G* even for the Pt complexes despite the usage of the other basis set on the Pt atom. Symmetry operations were not applied for all structures. For the stepwise mechanism, the calculations of possible dipolar and biradical intermediates and transition states of the Michael-type have been performed at the unrestricted approximations. The stability of the DFT solutions for selected equilibrium geometries was tested using the keyword STABLE in Gaussian 98.

The Hessian matrix was calculated analytically for all optimized structures to prove the location of correct minima (no “imaginary” frequencies) or saddle points (only one negative eigenvalue), and to estimate the thermodynamic parameters, the latter were calculated at 25 °C. The intrinsic reaction coordinates (IRC) were also calculated at the B3LYP/6-31G* level by the Gonzalez–Schlegel method.²¹ The structures of the orientation complexes found as a result of these calculations have been reoptimized at all above-mentioned levels.

The bonding nature in the TSs has been studied with the help of the AIM method of Bader.²² For the calculations of the electron density distribution $\rho(\mathbf{r})$, the gradient vector field $\nabla\rho(\mathbf{r})$, and its associated Laplacian $\nabla^2\rho(\mathbf{r})$, the programs GRIDV, GRDVEC, CONTOR, and EXT94B were used.²³ The Wiberg bond indices²⁴ for the transition states have been computed by using the natural bond orbital (NBO) partitioning scheme.²⁵ The synchronicity of the reactions has been calculated using the formula reported previously.^{26,27}

Solvent effects were taken into account for the estimate of the energetic characteristics of the reactions studied at the B3LYP/6-31G* level by using the polarizable continuum model²⁸ in the CPCM version²⁹ with a variety of solvents. For the reaction of **N2** with CH_3CN , the full geometry optimization of all structures involved in the reaction (except $\text{OC}_{\text{N}_2\text{-CH}}$) were performed with CH_2Cl_2 taken as a solvent. The geometry optimization at the CPCM level and the single-point CPCM calculations based on the gas-phase geometries led to very similar activation and reaction energies (with difference of 0.0–0.1 kcal/mol). Therefore, for all other

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reactions, only the single-point calculations of the solvent effects were carried out.

Results and Discussion

Cycloadditions of nitrones were the subject of intensive theoretical studies;³⁰ however, the vast majority of them dealt with alkenes^{27,31–37} or alkynes^{27,31} as dipolarophiles. These works include investigations of the reaction mechanism,^{27,31,32,34,36} the effects of Lewis acids (e.g., BH₃, BF₃)^{33,34} and solvents^{27b,34–36} on the mechanism and reaction energetic parameters, and the nature of the regio- and stereoselectivity.^{27b,31a,32d,34–37} At the same time, 1,3-DCA to nitriles was studied theoretically toward azides,^{6,38,39} and especially nitrile oxides^{7g} or nitrones^{7f} but only in a few publications.

For the cycloaddition reactions, two general mechanisms (i.e., concerted and stepwise) are recognized. The former includes only one TS and may be synchronous or asynchronous depending on whether the two new contacts between the reacting molecules in TS are formed simultaneously or not. The latter, consisting of several steps, starts from the one-end addition of a dipole to give a dipolar or diradical acyclic intermediate and ends up by the ring closure to give a final product. In the majority of publications,^{27,31,32a,34,36} the concerted mechanism was found to be preferred for thermal cycloadditions of nitrones. Our previous theoretical studies^{7f} indicated that acyclic nitrones couple with nitriles also concertedly even in case of the complex *trans*-[PtCl₄(NCCH₃)₂] taken as dipolarophile, while the stepwise routes are greatly disfavored. Thus, in our present study we focused only on the concerted mechanism, except the reaction of **N2** with *trans*-[PtCl₄(NCCH₃)₂], the most asynchronous process. For this reaction, the possibility of the stepwise cycloaddition was also investigated.

Equilibrium Structures and MO Composition of the Reactants. In the initial step, the equilibrium geometries of the reactants (i.e., the nitrones **N1–N4** and CF₃CN) have been calculated at different levels of theory and basis sets (see Computational Details and Table 1; the table with selected bond lengths of all calculated structures is given in the Supporting Information). The geometry optimization and calculations of

TABLE 1. Selected Bond Lengths (Å) for the Nitron **N2**, Starting Complexes **1** and **2**, the Products of the **N2** Cycloaddition, and the Transition States Calculated at the B3LYP/6-31G* Level^a

	N2	1	2	P_{N2-CH}	P_{N2-CF}	P_{N2-1}	P_{N2-2}
Pt–Cl	2.369	2.394				2.368–2.376	2.385–2.402
Pt–N(1)	1.963	1.975				2.027	2.052
N(1)–C(2)	1.152	1.148	1.275	1.268	1.290	1.290	1.301
C(2)–C(3)	1.455	1.454	1.493	1.517	1.488	1.488	1.487
N(4)–C(5)	1.303		1.513	1.515	1.505	1.505	1.486
C(5)–O(6)	1.355		1.419	1.409	1.398	1.398	1.406
O(6)–C(7)	1.458		1.428	1.432	1.435	1.435	1.432
C(7)–C(8)	1.537		1.532	1.531	1.532	1.532	1.530
N(4)–C(8)	1.495		1.480	1.482	1.485	1.485	1.476
N(4)–O(9)	1.277		1.472	1.477	1.476	1.476	1.483
C(2)–O(9)			1.360	1.347	1.334	1.334	1.328
N(1)–C(5)			1.449	1.459	1.470	1.470	1.483

	TS_{N2-CH}	TS_{N2-CF}	TS_{N2-1}	TS_{N2-2}
Pt–Cl			2.369–2.385	2.384–2.408
Pt–N(1)			1.980	1.979
N(1)–C(2)	1.195	1.194	1.192	1.167
C(2)–C(3)	1.477	1.494	1.482	1.466
N(4)–C(5)	1.342	1.333	1.318	1.301
C(5)–O(6)	1.336	1.327	1.319	1.324
O(6)–C(7)	1.461	1.465	1.468	1.468
C(7)–C(8)	1.534	1.536	1.537	1.539
N(4)–C(8)	1.480	1.480	1.479	1.483
N(4)–O(9)	1.326	1.326	1.328	1.307
C(2)···O(9)	1.927	1.828	1.772	2.101
N(1)···C(5)	2.128	2.265	2.474	3.087

^a For CH₃CN and CF₃CN, the calculated C≡N bond lengths are 1.160 and 1.158 Å, respectively.

the FMO composition of acetonitrile CH₃CN and the complexes *trans*-[PtCl₂(NCCH₃)₂] (**1**) and *trans*-[PtCl₄(NCCH₃)₂] (**2**) have been carried out and reported previously.^{7f,g,40} The structures **N1** and **N4** are not planar with the maximum torsion angle (CCCC or CCCO) of 19.8° and 23.5°, respectively, whereas the nitrones **N2** and **N3** are more flat (the maximum cyclic torsion angle is 12.3° and 6.9°, correspondingly). The structural parameters, calculated at the B3LYP/6-31G* level, are in a reasonable agreement with the X-ray experimental data for the nitrones H₃C(Ph)CCH₂CH(Ph)CH=NO,⁴¹ OCH(R)CH(Ph)C–{C(O)Ph}=NO (R = CH=CHC(O)OCH₃),⁴² and (H₃C)₂COCH₂–CR=NO (R = CHOC(CH₃)₂OCH₂).⁴³ The maximum deviation was found for the N(4)O(9) bond in **N1** and **N3** (0.027 Å), the N(4)O(8) bond in **N4** (0.044 Å), and the C(6)O(7) bond in **N3** (0.030 Å) and is not higher than 0.020 Å for the other bonds often appearing within the 3σ interval of the experimental data.

In accord with the classification by Sustmann,⁴⁴ for 1,3-DCA three main groups may be distinguished. Group I includes the processes controlled by the HOMO_{dipole}–LUMO_{dipolarophile} interaction (normal electron demand reactions), group III is formed by the processes with the HOMO_{dipolarophile}–LUMO_{dipole} predominant interaction (inverse electron demand reactions), and the intermediate group II collects the reactions with significant

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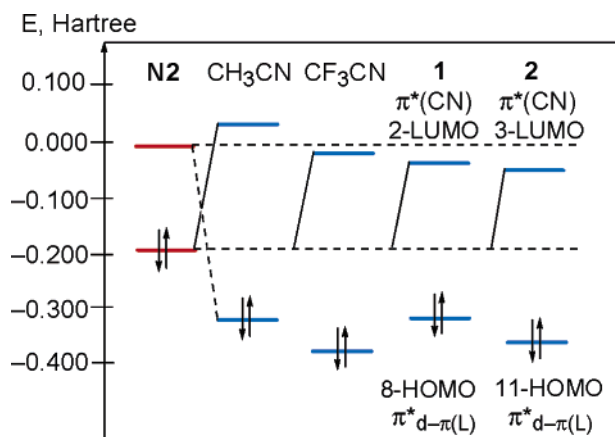
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SCHEME 3



involvement of both types of the HOMO–LUMO interactions. The cycloaddition of acyclic nitrones including that to free acetonitrile is usually attributed to group II.^{2b,7f} Calculations of the composition and energies of the frontier MOs showed that in case of the cyclic dipoles only the reactions of CH₃CN with N3 and N4 may be assigned to this type (the difference of two HOMO–LUMO energetic gaps $\Delta\Delta E$ is 1.16 and 1.31 eV, respectively). For all other processes (especially for CA to activated nitriles), the switch of the reaction type from the intermediate to normal electron demand occurs ($\Delta\Delta E = 2.08$ – 6.09 eV) (Scheme 3).⁴⁵

Comparison of the HOMO_{nitron}–LUMO_{nitrile} gaps leads also to the following qualitative conclusions: (i) the reactivity of the cyclic nitrones is predicted to increase along the row N4 < N3 < N1 < N2 and (ii) the activation of RCN by platinum (especially by Pt^{IV}) is predicted to be more effective than that by CF₃ group due to the greater lowering of the $\pi^*(\text{CN})$ MO energy. More accurate quantitative estimates of the energetic characteristics of the reactions are discussed below.

Equilibrium Structures of the Cycloaddition Products. In the next step of the study, calculations of the equilibrium geometries of products for the reactions of N1–N4 with CH₃CN (P_{N1-CH}–P_{N4-CH}) and CF₃CN (P_{N1-CF}–P_{N4-CF}) as well as of N2 and N4 with 1 and 2 (P_{N2-1}, P_{N4-1}, P_{N2-2}, P_{N4-2}) have been performed at the B3LYP/6-31G* level. The selected bond lengths of the products of N2 cycloadditions are given in Table 1, and the general view of all calculated structures is presented in the Supporting Information. The oxadiazoline

fragments NC(C)ONC are almost planar in all structures except P_{N2-2} and P_{N4-2}, where a displacement of the N(4) atom from the O(9)C(2)N(1)C(5) plane reaches 0.31 and 0.44 Å. The nitron rings are not planar in all cases, and the C(7) or O(7) atom is shifted by 0.22–0.61 Å from the plane X(6)C(5)N(4)X(8) (X = O, C), providing the general “bath” conformation of the bicyclic fragment. The dihedral angles formed by the planes N(1)C(2)O(9)N(4)C(5) and X(6)C(5)N(4)X(8) are in the range between 63.4° and 67.9°. For the Pt complexes, the plane of the oxadiazoline ring intersects the plane defined by the Pt, Cl, and N(1) atoms at an angle of 64.4° and 68.7° (P_{N2-1} and P_{N4-1}) or is situated between the Cl atoms (P_{N2-2} and P_{N4-2}).

To the best of our knowledge, there are no published X-ray structural data for oxadiazolines fused with a five-membered

(45) For complexes 1 and 2, the highest occupied MOs bearing the π -(CN) orbitals are the 8th and 11th, respectively, and the lowest unoccupied MOs with contribution of $\pi^*(\text{CN})$ orbitals are the 2nd and 3rd, respectively.

ring. However, taking into account the good agreement between the experimental and theoretical (at B3LYP/6-31G*) geometries for products of CA of acyclic nitrones to nitriles,^{7f} we hope that the calculations performed in this work predict reasonably the main structural features of the CA products.

Gas-Phase Transition States, apart from the Reaction of N2 with 2. For the concerted mechanism, one transition state was found for each of the reactions studied (TS_{N1-CH}–TS_{N4-CH}, TS_{N1-CF}–TS_{N4-CF}, TS_{N2-1}, TS_{N4-1}, TS_{N2-2}, and TS_{N4-2}), but in the case of TS_{N2-2}, the reaction profile and the nature of TS differ from those of the other processes, and they are discussed below.⁴⁶ One of the important characteristics of the concerted CAs is the degree of their synchronicity. Several criteria are usually used to estimate this parameter. First, it may be relative lengths of two newly formed contacts in the corresponding transition state. However, if the reacting atoms are of different types, the comparison of the Wiberg bond indices (WI) for these contacts, instead of the bond lengths, provides more reliable information about the synchronicity. Finally, the quantitative estimate of the synchronicity (S_y) can be obtained using the formula published previously,^{26,27} and in this definition all bonds directly involved in the reaction (five, in the case of 1,3-DCA) are considered.

The analysis of these criteria for the reactions studied suggests that the synchronicity decreases along the row of the nitriles CH₃CN > CF₃CN > 1 > 2 (i.e., the activation of RCN by platinum provides more asynchronous cycloaddition than by introducing the strong electron-acceptor substituent to the nitrile molecule). Indeed, the difference of the N(1)···C(5) and C(2)···O(9) contacts in TSs rises from 0.009 to 0.201 Å (for TS_{N-CH}) to 0.207–0.437 Å (TS_{N-CF}), 0.702 Å (TS_{N2-1}), 0.538 Å (TS_{N4-1}), and 0.749 Å (TS_{N4-2}). The difference in Wiberg bond indices $\Delta\text{WI} = \text{WI}(\text{C}\cdots\text{O}) - \text{WI}(\text{N}\cdots\text{C})$ has a positive value for all TSs (except TS_{N4-CH}) and enhances along the same sequence (Table 2). The negative magnitude of ΔWI for TS_{N4-CH} (–0.07) suggests that formation of the N···C contact slightly precedes the C···O one.

The high values of S_y for the reactions of nitrones N1–N4 with CH₃CN (0.92–0.95) indicate the almost *perfect synchronicity* of these processes, the situation similar to that found for the reactions of acyclic nitrones with acetonitrile^{7f} and also with ethylene and acetylene.²⁷ For the cycloadditions to CF₃CN, the S_y parameter is smaller but still significant (0.85–0.94) and demonstrates the rather high synchronicity of CA in these cases. The coordination of acetonitrile to Pt^{II} and particularly to Pt^{IV} results in the dramatic decrease of S_y value (0.74, 0.79, and 0.65 for the reactions N2 + 1, N4 + 1, and N4 + 2, respectively), and the corresponding processes can be clearly described as an asynchronous CA, which, nevertheless, remains concerted.⁴⁷

For the reactions of nitrones N1–N4 with one particular dipolarophile, the difference of the N···C and C···O distances

(46) The NPA charge transfer from the nitrones to CH₃CN upon formation of corresponding TS increases along the series CH₃CN < CF₃CN < 1 < 2 and N4 < N3 < N1 < N2 (Table 2). The “imaginary” frequencies of the TSs have small values (204i–481i) and decrease along the same sequences. These trends reflect the enhancement of electron deficiency of the nitrile and electron-richness of the dipole molecules and correlate with calculated activation energies and asynchronicity of TS (see Tables 2 and 3).

(47) The enhancement of the asynchronicity upon coordination of CH₃CN is determined by two factors: (i) the increase of the positive charge on the nitrile carbon atom from CH₃CN to the complexes⁴⁸ and (ii) the steric repulsion between the chloride ligands and the nitron molecule.

TABLE 2. Most Important Characteristics of the Transition States^a

	N1 + CH ₃ CN	N2 + CH ₃ CN	N3 + CH ₃ CN	N4 + CH ₃ CN
NPA	0.07	0.09	0.06	0.02
<i>ν</i> _i	448i	379i	448i	481i
ΔWI	0.04	0.06	0.02	-0.07
S _y	0.92	0.95	0.93	0.95
ρ(NC)	0.466	0.416	0.476	0.539
ρ(CO)	0.650	0.586	0.596	0.509
H _b (NC)	-0.084	-0.057	-0.089	-0.125
H _b (CO)	-0.160	-0.122	-0.126	-0.081
	N1 + CF ₃ CN	N2 + CF ₃ CN	N3 + CF ₃ CN	N4 + CF ₃ CN
NPA	0.18	0.20	0.16	0.12
<i>ν</i> _i	370i	287i	377i	432i
ΔWI	0.16	0.18	0.13	0.04
S _y	0.85	0.88	0.86	0.94
ρ(NC)	0.373	0.316	0.382	0.454
ρ(CO)	0.810	0.726	0.744	0.651
H _b (NC)	-0.039	-0.017	-0.043	-0.076
H _b (CO)	-0.279	-0.211	-0.223	-0.155
	N2 + 1	N4 + 1	N2 + 2	N4 + 2
NPA	0.31	0.24	0.21	0.35
<i>ν</i> _i	211i	359i	42i	204i
ΔWI	0.34	0.27	0.20	0.42
S _y	0.74	0.79	0.54	0.65
ρ(NC)	0.206	0.309	-	0.234
ρ(CO)	0.799	0.852	0.380	1.000
H _b (NC)	+0.007	-0.016	-	+0.003
H _b (CO)	-0.286	-0.333	-0.036	-0.524

^a NPA charge transfer from the nitron to nitrile (NPA, au), “imaginary” frequencies (*ν*_i), synchronicity (S_y), difference of the Wiberg bond indices (ΔWI), electron densities (ρ, e Å⁻³), and energy densities (H_b, Hartree Å⁻³) for the C··O and N··C contacts.

in TSs varies significantly, increasing along the row of dipoles **N4** < **N3** < **N1** < **N2**. The change of the ΔWI and S_y values is less pronounced, and the most synchronous CA (in terms of S_y) is realized in cases of the nitrones **N4** and **N2**. It is interesting to note that these nitrones represent two boundary examples, that is, the least and the most active dipole, respectively (see below).

The great difference between the N(1)··C(5) and C(2)··O(9) distances in **TS**_{N2-1}, **TS**_{N4-1}, and **TS**_{N4-2} and the long N(1)··C(5) contact raise the question: are these transition states cyclic or acyclic? A useful tool that can help to answer this question and to investigate additionally the nature of the transition states is the topological analysis of the electron density distribution. The contour line diagrams of the Laplacian distribution ∇²ρ(**r**) for two borderline cases (i.e., the most synchronous **TS**_{N4-CH} and the least synchronous **TS**_{N4-2}) are given in the Supporting Information (Figure 2S). The ring critical point for the oxadiazoline cycle and the bond critical points for the N··C and C··O contacts were found for all TSs indicating their *cyclic* nature. The electron density values ρ(**r**_b) at both bond critical points are similar for **TS**_{N-CH} (Table 2). For **TS**_{N-CF}, ρ(**r**_b) at the C··O contact becomes noticeably higher than that at the N··C contact, and this difference increases in **TS**_{N4-1}, **TS**_{N2-1}, and **TS**_{N4-2}, in agreement with enhancement of the asynchronicity. The negative values of the energy density H_b at the CO bond critical point suggest that this contact has some covalent contribution, which increases coherently with the asynchronicity of TS. The energy density for the CN contact generally has small negative magnitudes and is close to zero for **TS**_{N2-1} and **TS**_{N4-2}, thus demonstrating no covalent contribution. The small values of electron density at the CN bond critical point in

TS_{N2-1}, **TS**_{N4-1}, and **TS**_{N4-2} and significant asynchronicity of the corresponding reactions suggest that these processes should be considered partially as a nucleophilic addition with more facile formation of the CO bond in comparison with the CN one.

Intrinsic Reaction Coordinates. To investigate the reaction mechanism in more detail, the calculations of the IRC have been undertaken, starting from the transition states found (except the reaction of **N2** with **2**). Energy profiles and changes of the most important internuclear distances along the reaction path for two processes (i.e., **N4** + CH₃CN and **N4** + **2**) are shown in Figure 1. Results of the calculations suggest that the reactions start with formation of van der Waals orientation complexes (**OC**_{N1-CH-OC}_{N4-CH}, **OC**_{N1-CF-OC}_{N4-CF}, **OC**_{N2-1}, **OC**_{N4-1}, and **OC**_{N4-2}). The nitrile and nitron molecules in OCs have structural parameters similar to those for the isolated reactants, and the nitrile fragment is nearly linear. The total energies of the orientation complexes are, by 4.28–13.58 kcal/mol (B3LYP/6-31G*), lower than the sum of the reactants' energies (Figure 2A,B). However, the entropic contribution into the reaction energy is negative [ΔS = (-25.83) - (-45.68) cal/mol·K] and provides positive (or only small negative) Gibbs free energy differences for the formation of OC [ΔG = (-1.64) - (+5.51) kcal/mol] (Figure 2C,D), and the latter values correspond to the equilibrium constants which range from 16 to 9 × 10⁻⁵.

In the next step of the reaction, nitrile and nitron molecules further approach each other, giving the corresponding transition state. The N(1)C(2) and N(4)C(5) bond lengths are changed only slightly, whereas the N(1)C(5) and C(2)O(9) distances are reduced significantly, and the respective curves (Figure 1) have the point of inflection in the TS position. The subsequent transformation of the transition state into the final product is accompanied by creation of the new N(1)C(5) and C(2)O(9) bonds and weakening of the multiple CN bonds. The IRC calculations did not detect any intermediates, thus confirming that the mechanisms examined are truly concerted.

Mechanism of the Reaction N2 + 2. For the reaction between **N2** and Pt^{IV}-bound acetonitrile (**2**), all attempts to locate an extremum for transition state similar to that found for the other processes failed. Instead, the detailed analysis of the potential energy surface (PES) indicated the existence of a plateau on the reaction path that corresponds to the configuration with the C(2)O(9) and N(1)C(5) distances about 1.53 and 2.43 Å, respectively. Further investigations resulted in the location of very early transition state **TS**_{N2-2} and orientation complex **OC**_{N2-2}. Bond lengths of the nitron and nitrile fragments in **TS**_{N2-2} are close to those in the isolated molecules, but the reacting CH₃CN ligand is bent with CNPt and CCN angles of 158.6° and 157.4°. The C(2)O(9) and particularly N(1)C(5) contacts are very long (2.101 and 3.087 Å, respectively), the former is significantly shorter than the latter, and the ΔWI difference is 0.20. The low value for the parameter S_y (0.54) demonstrates that this reaction is the most asynchronous one among all discussed above.

The topological analysis of the electron density distribution for **TS**_{N2-2} showed that this transition state has *acyclic* nature insofar as no critical points for the N(1)C(5) bond and the oxadiazoline cycle were found, although the C(2)O(9) bond critical point was located (Figure 3). For the latter, the electron density and energy density have small values (0.380 e Å⁻³ and -0.036 hartree Å⁻³, respectively) that are determined by the long internuclear distance for this contact.

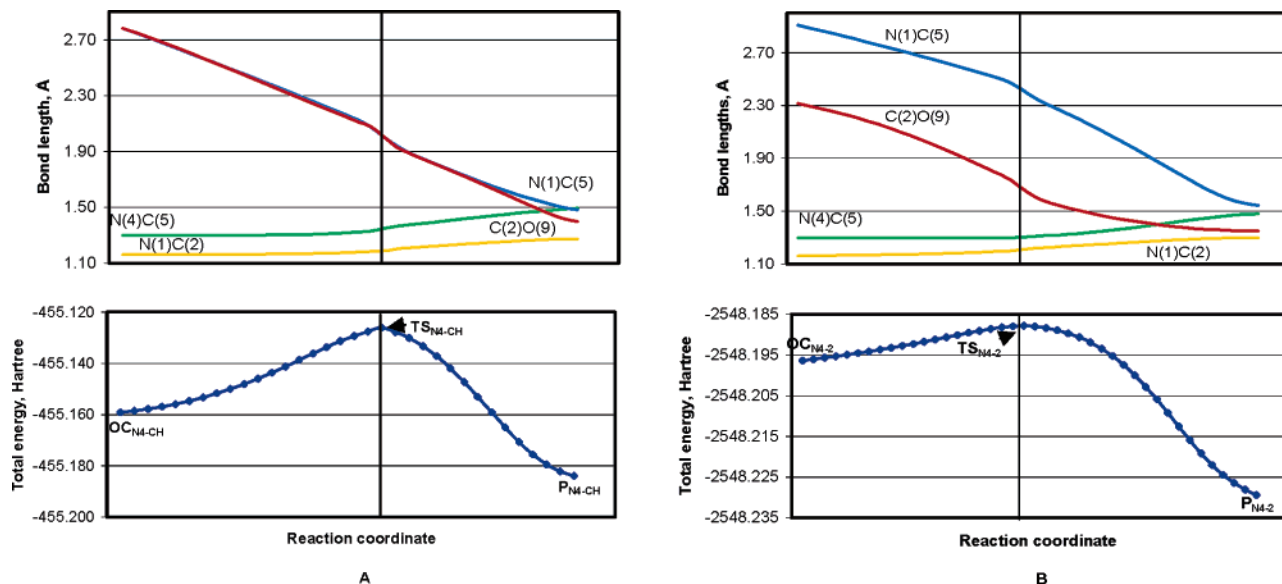


FIGURE 1. Calculated intrinsic reaction coordinates and change of selected internuclear distances along the reaction path for the CA of N4 to CH₃CN (A) and to **2** (B).

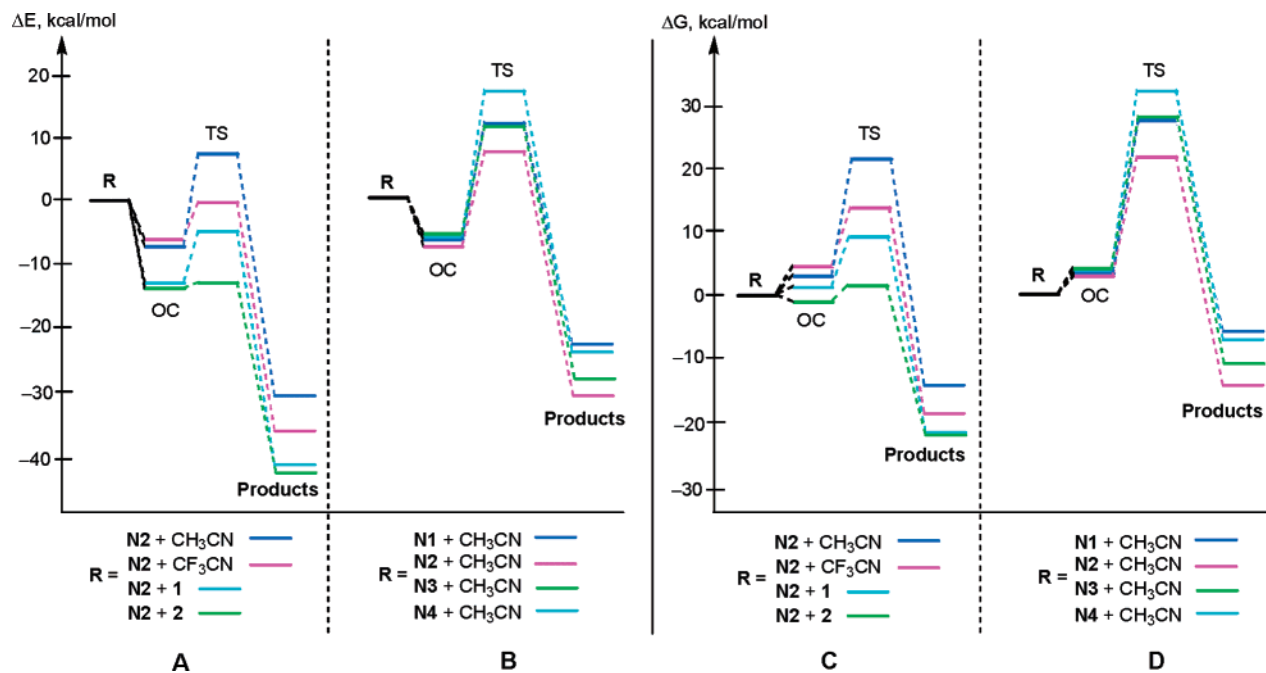


FIGURE 2. Energy profiles for the reactions of nitrones N1–N4 with nitriles in terms of ΔE (A, B) and ΔG (C, D) values.

The IRC calculations for this process could not be performed due to extremely flat potential surface near TS_{N2-2}. Actually, TS_{N2-2} has small “imaginary frequency” ($42i$), and maximum variations of the total energy from OC_{N2-2} to TS_{N2-2} and from TS_{N2-2} to the plateau on PES are 1.12 and 3.20 kcal/mol, respectively. At the same time, the overall change of the C(2)O(9) and N(1)C(5) distances is 1.088 and 1.806 Å, respectively. Nevertheless, for the extended search of PES, no other intermediates or transition states—dipolar or biradical ones—were found for this CA. Thus, the “almost barrierless” reaction of N2 with **2** is also concerted and proceeds via early acyclic transition state.

Activation and Reaction Energies. The location of the transition states and orientation complexes on PES allowed the estimate of the electronic activation energies (E_a), enthalpies, and Gibbs free energies of activation (ΔH^\ddagger and ΔG^\ddagger) for the

reactions studied (Table 3), and their inspection indicates the following. First, the cyclic nitrone N1 is more reactive toward CH₃CN than the acyclic analogue (CH₃)CH=N(CH₃)O^{7f} by 2.68 kcal/mol (i.e., by a factor of ca. 100). The reason for the higher reactivity of cyclic compared to acyclic nitrones in 1,3-DCA to nitriles is discussed below.

Second, the effect of insertion of the oxygen heteroatom into the nitrone ring strongly depends on the position of the O-center. Namely, the nitrone N2 is predicted to be the most reactive dipole (ca. 10⁴ times more reactive than N1) (Figure 2B,D). This fact could be explained in terms of the FMO theory as a result of the electron donation from the heteroatom to the dipole C=N⁺–O– site that leads to the rise of the HOMO energy and favors the normal electron demand of CA. The activity of N3 is similar to that of N1, obviously because the cyclic oxygen is far from the reacting C=N⁺–O– site and does not signifi-

TABLE 3. Energetic Characteristics (in kcal/mol) of the Cycloaddition Reactions of Nitrones N1–N4 to CH₃CN, CF₃CN and to the Complexes **1** and **2** Relative to Reactants (Plain Text) and to the Orientation Complex (Bold Text) for the B3LYP/6-31G* Level^a

reactants		E_a	ΔH^\ddagger	ΔG^\ddagger	ΔE	ΔH	ΔG
N1	CH ₃ CN	13.76 (16.45)	14.57	27.62	-22.00 (-19.35)	-19.64	-5.82
		20.45	19.94	24.38			
N2		7.79 (11.07)	8.74	21.84	-30.70 (-28.17)	-28.12	-13.94
		(10.97) ^b	(11.86) ^b	(25.13) ^b	(-28.17) ^b	(-25.69) ^b	(-11.55) ^b
N3		13.58 (17.02)	14.45	28.06	-27.64 (-25.56)	-24.93	-10.20
		19.30	18.84	24.12			
N4		18.09 (20.94)	18.72	31.62	-23.70 (-22.32)	-21.35	-7.55
		24.41	23.63	27.83			
N1	CF ₃ CN	5.19 (6.46)	6.01	19.29	-28.78 (-27.00)	-26.37	-12.62
		10.91	10.43	14.41			
N2		-0.62 (0.42)	0.37	13.75	-36.38 (-34.59)	-33.73	-19.45
		6.13	5.76	9.56			
N3		6.44 (7.68)	7.29	21.16	-33.49 (-32.52)	-30.76	-15.94
		11.63	11.21	15.65			
N4		12.43 (13.18)	13.09	26.14	-29.71 (-29.23)	-27.34	-13.60
		16.70	16.09	21.45			
N2	1	-4.89 (0.33)	-3.82	9.39	-41.18 (-35.11)	-38.32	-21.95
		7.98	8.13	7.72			
N4		9.39 (15.34)	10.01	25.01	-34.29 (-27.30)	-32.34	-15.53
		19.27	19.08	21.98			
N2	2	-12.46 (-4.18)	-10.89	1.44	-42.05 (-36.40)	-38.61	-22.61
		1.12	0.56	3.08			
N4		0.80 (7.54)	1.48	16.97	-36.51 (-29.81)	-33.16	-17.63
		11.23	10.51	15.02			
<i>E</i> -N _{acyc}	CH ₃ CN	11.17	12.03	25.41	-23.53	-21.05	-6.36
<i>Z</i> -N _{acyc}		16.11	16.89	30.30	-21.28	-16.89	-4.73

^a Single-point energies corrected on the solvent effects in parentheses. ^b Full geometry optimization at the CPCM-B3LYP/6-31G* level.

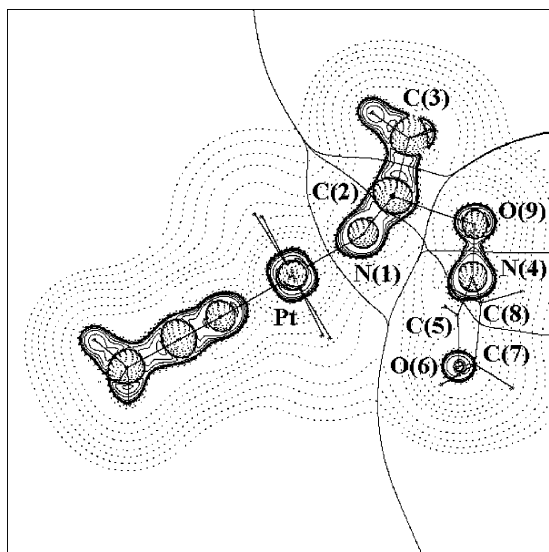


FIGURE 3. Contour line diagrams of the Laplacian distribution $\nabla^2\rho(r)$, bond paths, and selected zero-flux surfaces in the plane formed by the N(1), C(2), C(5), and O(9) atoms for **TS**_{N2-2}. Dashed lines indicate charge depletion ($\nabla^2\rho(r) > 0$), and solid lines indicate charge concentration ($\nabla^2\rho(r) < 0$).

cantly affect the reactivity. Finally, the usage of nitronates (**N4**) inhibits 1,3-DCA, and moreover, the activation barrier for the reaction **N4** + CH₃CN is even higher (by 1.32 kcal/mol) than that for CA of the acyclic nitrone (CH₃)CH=N(CH₃)O.

Third, the coordination of nitriles to a Pt center, especially if the latter is in a high oxidation state, provides an even higher activation effect in comparison with the introduction in RCN of a strong electron-acceptor substituent R such as CF₃. Indeed, the activation parameters considerably decrease along the series of dipolarophiles in the following order: CH₃CN > CF₃CN >

1 > **2** (Figure 2A,C). The lowering of ΔG^\ddagger from CH₃CN to CF₃CN taken as dipolarophiles is 5.48–8.33 kcal/mol that corresponds to enhancement of the reaction rate by a factor of 1×10^4 to 1.2×10^6 . Ligation of CH₃CN to Pt^{II} and Pt^{IV} decreases the activation barrier by 6.61–12.45 and 14.65–20.40 kcal/mol, respectively, and the reaction rate should increase by factors of 7×10^4 to 1.4×10^9 and 5.5×10^{10} to 9.1×10^{14} . Hence, the application of platinum as a Lewis acid is a more promising and effective route for enhancement of reactivity toward 1,3-DCA than the conventional activation of nitriles by electron-withdrawing groups.

It is interesting to note that the nitrile activation mainly affects the most reactive nitrones (i.e., **N2** and **N1**), whereas in the case of the nitronate **N4**, the lowering of the ΔG^\ddagger value on going from CH₃CN to CF₃CN, **1** or **2**, is much less pronounced. Nevertheless, the coordination of CH₃CN to a Pt^{IV} center reduces the activation barrier sufficiently even for the reaction with **N4** (to 16.97 kcal/mol), thus opening up a facile route for the making of fused bicyclic systems derived from nitronates.

As can be seen from Table 3, the reactions of **N2** with CF₃CN, **1**, and **2**, are characterized by negative E_a and ΔH^\ddagger values relative to reactants. However, considering the formation of the orientation complex along the reaction path, these energies become positive relative to OC. Such a situation was found previously for the CA of acyclic nitrones to complex **2**^{7f} as well as for the reactions of azomethine ylides with acrylonitrile⁴⁹ and of nitroethene with methyl vinyl ether in the presence of a Lewis acid.⁵⁰ The ΔG^\ddagger values are positive for all the reactions due to a strong decrease of the entropy from the reactants to OC and further to TS (Figure 2).

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TABLE 4. Absolute (ΔG_{solv}) and Relative to the Reactants ($\Delta\Delta G_{\text{solv}}^{\ddagger}$ and $\Delta\Delta G_{\text{solv}}$) Solvent Effects (in kcal/mol) for Structures Involved in the Reactions of the Nitron N2 in CH_2Cl_2 Solution^{a,b}

structure	EL	non-EL	ΔG_{solv}
N2	-5.16	-2.40	-7.56
CH ₃ CN	-2.88	-0.04	-2.92
CF ₃ CN	-0.88	+0.18	-0.70
1	-9.90	+3.23	-6.68
2	-11.32	+5.14	-6.19
TS _{N2-CH}	-4.84	-2.42	-7.26
TS _{N2-CF}	-5.67	-1.63	-7.29
TS _{N2-1}	-12.09	+2.71	-9.38
TS _{N2-2}	-11.22	+5.58	-5.64
P _{N2-CH}	-4.48	-3.49	-7.97
P _{N2-CF}	-4.18	-2.33	-6.51
P _{N2-1}	-10.30	+1.88	-8.42
P _{N2-2}	-11.42	+3.23	-8.19

dipolarophile	$\Delta\text{EL}^{\ddagger}$	$\Delta\text{non-EL}^{\ddagger}$	$\Delta\Delta G_{\text{solv}}^{\ddagger}$	ΔEL	$\Delta\text{non-EL}$	$\Delta\Delta G_{\text{solv}}$
CH ₃ CN	+3.20	+0.02	+3.22	+3.56	-1.05	+2.51
CF ₃ CN	+0.37	+0.59	+0.96	+1.86	-0.11	+1.75
1	+2.97	+1.88	+4.85	+4.76	+1.05	+5.81
2	+5.26	+2.84	+8.10	+5.06	+0.49	+5.55

^a The relative solvent effects are determined as $\Delta\Delta G_{\text{solv}}^{\ddagger} = \Delta G_{\text{solv}}(\text{TS}) - \sum \Delta G_{\text{solv}}(\text{reactants})$ and $\Delta\Delta G_{\text{solv}} = \Delta G_{\text{solv}}(\text{product}) - \sum \Delta G_{\text{solv}}(\text{reactants})$. ^b Electrostatic and nonelectrostatic components are denoted EL and non-EL, respectively.

The reaction energies (ΔE), enthalpies (ΔH), and Gibbs free energies (ΔG) have negative magnitudes for all processes (Table 3), indicating their strong exothermic and exoergonic character. Similar to the activation parameters, the ΔE , ΔH , and ΔG values (i) are more negative for CA of cyclic nitrones in comparison with acyclic ones, (ii) decrease along the sequence $\text{CH}_3\text{CN} > \text{CF}_3\text{CN} > \mathbf{1} > \mathbf{2}$, although such a drop is less pronounced than that for the activation energies, and (iii) decrease along the series $\text{N1} > \text{N4} > \text{N3} > \text{N2}$, that is, reactions of the nitron with a purely hydrocarbon chain are less exothermic and exoergonic than even those of the nitronate.

Solvent Effects. The CAs of nitrones to nitriles usually proceed in solutions,^{7b,d,10} and consideration of the solvent effects may be important for an estimate of the reliable energetic characteristics of these processes. To take these effects into account, first, we performed the calculations of the activation and reaction energies for all reactions studied using the self-consistent reaction field method based on the CPCM model with CH_2Cl_2 taken as a solvent. The results of these calculations (Table 3) demonstrate (i) the increase of the activation energies (by 0.75–8.28 kcal/mol) from the gas phase to the solution, (ii) the decrease, in absolute values, of the reaction energies (by 0.48–6.99 kcal/mol), and (iii) the highest solvation effect on the reactions with complexes **1** and **2** and the lowest effect for the CA to CF_3CN . Hence, the reactivity of **1** in solution becomes comparable or even lower than that of CF_3CN from both kinetic and thermodynamic viewpoints, although the ligation of the nitriles to the Pt^{IV} center (complex **2**) still provides the highest activation. All other trends found for the gas phase (see above) hold true for the solution.⁵¹

The calculated total solvent effect (ΔG_{solv}) may be decomposed into two main components: electrostatic (EL) and nonelectrostatic (non-EL) ones (Table 4; the complete version

of the table is given in the Supporting Information). The latter includes the cavitation, dispersion, and repulsion terms. The electrostatic component has the least negative magnitudes for CF_3CN and the most negative values for the metal-containing species. The positive overall nonelectrostatic term for the Pt complexes cannot fully compensate for the negative EL values, and the total solvent effect for these structures is noticeably negative. Thus, the general inhibition of CAs in the solution, which was predicted previously also for the reactions of nitrones with $\text{CH}_2=\text{CHOCH}_3$ ³⁴ and $\text{CH}_2=\text{CH}_2$,^{27b} is accounted for by a higher stabilization of the level of strongly polar reactants in comparison with the levels of TSs and products. The moderate solvent effect for the CA to CF_3CN is because the EL component provides only small stabilization of the nitrile's level and the non-EL component is the destabilizing one, or in terms of the relative solvent effects (see the second part of Table 4), it is due to the small $\Delta\text{EL}^{\ddagger}$ and ΔEL components for these reactions. The great solvent effect for the CA to the Pt complexes is determined by strongly negative EL values for **1** and **2** and, hence, highly positive $\Delta\text{EL}^{\ddagger}$ and ΔEL components.

Second, the influence of the solvent nature on the reactions of **N2** (as the most reactive nitron among those chosen for this work) was studied, and the results are listed in Table 5. The change of the solvent affects the activation and reaction energies only marginally for CAs to CH_3CN and CF_3CN with maximum variation of E_a and ΔE of 2.52 kcal/mol. These energies, however, become more sensitive to the solvent nature for the reactions of **N2** with **1** and, particularly, with **2**. The change of the E_a and ΔE magnitudes versus dielectric constant (ϵ) and E_T^{N} values (E_T^{N} reflects solvent polarity⁵²) of the solvent is shown in Figure 4. In general, there is an explicit, although nonlinear, tendency in the decrease of both activation and reaction energies with the concurrent decrease of the solvent polarity. Such a decrease of E_a reaches 6 kcal/mol for **N2** + **2** on going from water to benzene and corresponds to the enhancement of the reaction rate by a factor of 2.5×10^4 . The data obtained for the two solvents, acetonitrile and nitromethane, significantly deflect from the general dependence, and the corresponding energies have comparatively low values despite the considerable polar character of these solvents. Thus, the usage of nonpolar solvents or those with a low polarity should facilitate significantly the CAs to Pt-bound nitriles. Acetonitrile and nitromethane are good alternative solvents that, from the energetic viewpoints, could be employed if the poor solubility of the reagents does not allow the usage of nonpolar solvents.

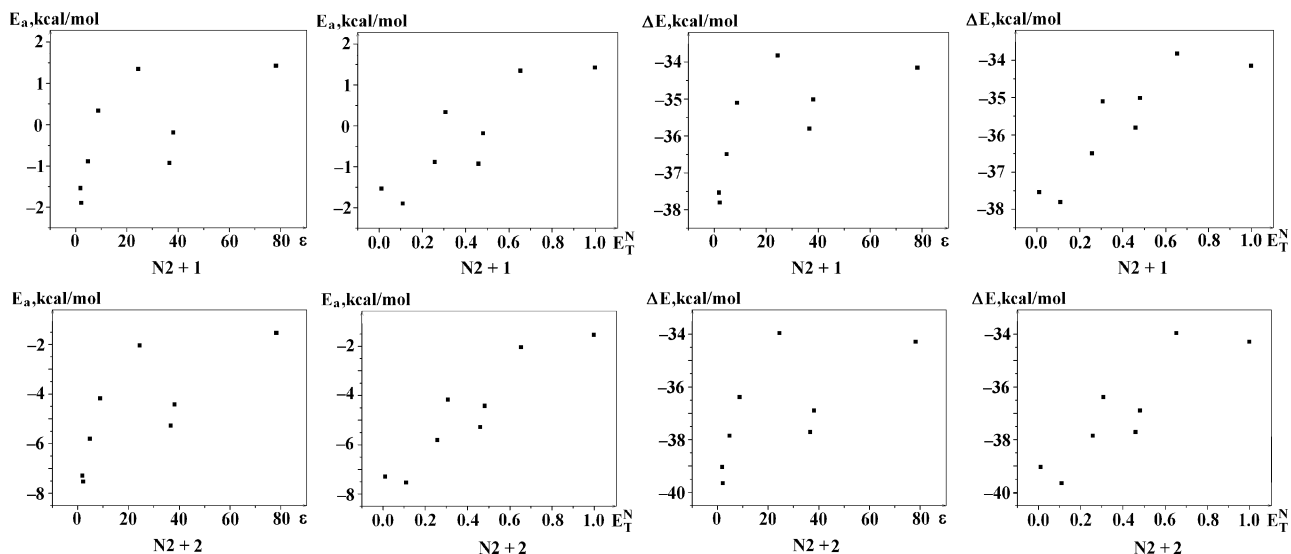
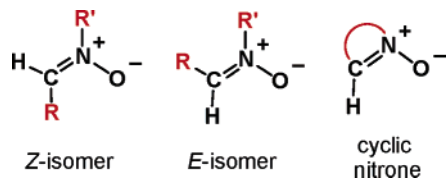
Comparison of the Reactivity of Cyclic and Acyclic Nitrones. The mono-C-substituted acyclic nitrones $\text{RCH}=\text{N}(\text{R}')\text{O}$, prepared by conventional methods,^{2a,53} predominantly exist in the more stable *Z*-configuration, that is, with the substituents R and R' on the opposite sides relative to the double CN bond (Chart 1), and particularly *Z*-nitrones, with rare exceptions,⁵⁴ are involved in 1,3-DCAs.⁵⁵ In contrast, the cyclic nitrones exhibit exclusively the *E*-configuration, when the non-hydrogen atoms forming the ring are situated on the same side

(52) Reichardt, C. *Chem. Rev.* **1994**, *94*, 2319.(53) (a) *Methoden der Organischen Chemie*; Houben Weyl; Thieme Verlag: Stuttgart, Germany, 1990; Vol. E14b. (b) Murahashi, S.-I.; Shiota, T. *Tetrahedron Lett.* **1987**, *28*, 2383. (c) Murahashi S.-I.; Mitsui, H.; Shiota, T.; Tsuda, T.; Watanabe, S. *J. Org. Chem.* **1990**, *55*, 1736. (d) Ballistreri, F. P.; Chiacchio, U.; Rescifina, A.; Tomaselli, G. A.; Toscano, R. M. *Tetrahedron* **1992**, *48*, 8677.(51) As a result of the geometry optimization at the CPCM level, $\text{TS}_{\text{N2-CH}}$ becomes more asynchronous: the difference of the $\text{N}(1)\text{C}(5)$ and $\text{C}(2)\text{O}(9)$ distances increases from 0.201 Å for the gas phase to 0.264 Å for the solution, and the difference of the corresponding Wiberg bond indices increases from 0.06 to 0.10, respectively.

TABLE 5. Activation and Reaction Energies (E_a and ΔE) (in kcal/mol) Relative to the Reactants for the Cycloadditions of N_2 in Solutions with Different Solvents^a

dipolarophile	H ₂ O $\epsilon = 78.39$ $E_T^N = 1.000$		CH ₃ NO ₂ $\epsilon = 38.20$ $E_T^N = 0.481$		CH ₃ CN $\epsilon = 36.64$ $E_T^N = 0.460$		C ₂ H ₅ OH $\epsilon = 24.55$ $E_T^N = 0.654$		CH ₂ Cl ₂ $\epsilon = 8.93$ $E_T^N = 0.309$		CHCl ₃ $\epsilon = 4.90$ $E_T^N = 0.259$		C ₆ H ₆ $\epsilon = 2.25$ $E_T^N = 0.111$		heptane $\epsilon = 1.92$ $E_T^N = 0.012$	
	E_a	ΔE	E_a	ΔE	E_a	ΔE	E_a	ΔE	E_a	ΔE	E_a	ΔE	E_a	ΔE	E_a	ΔE
CH ₃ CN	11.86	-27.96	10.84	-28.32	10.38	-28.80	11.89	-27.61	11.07	-28.17	10.21	-29.03	9.88	-29.01	9.37	-29.70
CF ₃ CN	0.24	-35.43	-0.18	-34.94	-0.67	-35.52	0.33	-35.26	0.42	-34.59	-0.18	-35.38	-0.61	-35.69	0.03	-35.38
1	1.42	-34.16	-0.19	-35.02	-0.93	-35.81	1.34	-33.83	0.33	-35.11	-0.89	-36.50	-1.90	-37.81	-1.54	-37.54
2	-1.55	-34.30	-4.43	-36.90	-5.28	-37.72	-2.05	-33.97	-4.18	-36.40	-5.81	-37.86	-7.54	-39.65	-7.30	-39.04

^a Dielectric constant and E_T^N parameter of the solvents are indicated.

**FIGURE 4.** Dependencies of the activation and reaction energies (E_a and ΔE) on the dielectric constant (ϵ) and E_T^N parameter for the reactions of N_2 with **1** and **2**.**CHART 1**

relative to the C=N bond. Existence of the cyclic nitrones only in the “chemically frozen” *E*-configuration may be a reason for the higher reactivity of the cyclic nitrones in comparison with acyclic ones. To check this hypothesis, the activation and reaction energies for the CA of *Z*- and *E*-*N*,*C*-dimethyl nitronium (*Z*-/*E*-CH₃CH=N(CH₃)O, *Z*-/*E*-**N**_{acyc}) to CH₃CN were calculated (the reaction of the *Z*-isomer was studied previously by us^{7f}).

As was expected, the *E*-nitronium was found to be less stable by 4.46 kcal/mol (ΔG scale, B3LYP/6-31G*) than the *Z*-nitronium, and such a destabilization of the reactant may be a result of the steric repulsion between the two methyl groups of the planar CCN(C)O framework. The energies of the *E*- and *Z*-transition states (*E*-/*Z*-**TS**_{acyc}) are very close in their values, and *E*-**N**_{acyc} appears to be more reactive (by 4.89 kcal/mol) than the

corresponding *Z*-isomer (Table 3). The absence of any destabilization at the TS level may be accounted for by the deviation of the CCNC fragment from planarity (the corresponding torsion angle in *E*-**TS**_{acyc} is 23.8°) that decreases the methyl–methyl interaction. The energy level of the products is destabilized (by 2.83 kcal/mol) on going from the *Z*- to *E*-configuration, although this effect is less pronounced than that for the reactants, and the reaction of *E*-**N**_{acyc} is by 1.63 kcal/mol more exoergic than the CA of the *Z*-isomer.

Considering the cyclic nitrones, the similar relative destabilization of the reactants' level occurs due to operating ring strains. In the course of the reaction, the double C=N bond is transformed to a single C–N bond, and the ring strains become weaker. Therefore, the relative energetic levels of the transition state and the product are not destabilized or they do it faintly. Thus, the fixation of ring dipoles in the *E*-configuration, more strained and hence more reactive than the *Z*-isomer of acyclic nitronium, should be responsible for the activation discussed.

Conclusion

An effect of the concurrent activation of both dipoles and dipolarophiles in reactions of cycloaddition of nitrones to organonitriles opens a facile route for the synthesis of poorly explored types of five-membered heterocycles such as Δ^4 -1,2,4-oxadiazolines. The present work directed at the study of theoretical aspects of this effect is the first attempt, to the best of our knowledge, to give a theoretical background for the CA of jointly activated nitrones and nitriles, to interpret scarce

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experimental results in this area, and to give some predictions that can be useful from a practical viewpoint.

Our results demonstrate that (i) the nitrile complexation to Pt^{II} and, especially, to Pt^{IV} centers results in a higher activation of RCN in comparison with the introduction of a strong electron-acceptor group R such as CF_3 , (ii) experimentally observed higher reactivity of the cyclic nitrones with purely hydrocarbon chain versus acyclic nitrones may be interpreted as a result of their existence exclusively in the more strained and hence more reactive *E*- rather than *Z*-configuration, and (iii) O-heterocyclic nitrones with the oxygen atom at the 6th position of the ring (e.g., **N2**) are predicted to be even more reactive than **N1** in the reactions with nitriles from both kinetic and thermodynamic viewpoints. Thus, the usage of cyclic nitrones of the **N2**-type on one hand, and the metal-bound nitriles on the other hand, is the most efficient and promising way for the acceleration of the nitrono-to-nitrile CA reactions. On the contrary, the nitronate **N4** is shown to be less reactive toward nitriles than the acyclic nitrones. Nevertheless, the coordination of CH_3CN to a Pt^{IV} center should allow even this type of cycloaddition.

The detailed investigation of the solvent effects undertaken in this work indicates that solvation inhibits the reactions in comparison with the gas phase that is the most pronounced for CAs to Pt-bound nitriles. Nevertheless, the usage of nonpolar solvents or solvents with a low polarity should minimize such inhibition.

The mechanistic studies showed that the synchronicity of the concerted CA decreases along the sequence of dipolarophiles $\text{CH}_3\text{CN} > \text{CF}_3\text{CN} > \mathbf{1} > \mathbf{2}$. The CA to CH_3CN and CF_3CN is highly synchronous, although the interaction of nitrones with **1** and especially with **2** is clearly asynchronous. For all reactions (except **N2** + **2**), the respective transition states have a five-membered cyclic nature. The mechanism of CA of the most reactive nitrono **N2** to the most activated nitrile (in complex **2**) is quite different from that for the other reactions. Being "almost barrierless" and concerted rather than stepwise, it includes very

early *acyclic* transition state. Such features of the mechanism, of the $\text{TS}_{\text{N2-2}}$ transition state nature as well as the extremely flat potential energy surface near this TS suggest that the chemical behavior of **N2** and **2** toward each other should also be different in comparison with the other investigated reactions. This difference may be related to a possibility of other processes in the **N2** + **2** system; for example, spontaneous N–O bond cleavage and formation of a ketoimino complex $\text{trans-}[\text{PtCl}_4\{\text{RC}(=\text{O})\text{N}=\text{CN}(\text{H})\text{CH}_2\text{CH}_2\text{O}\}_2]$. The complexes of the latter type were obtained recently, in the single-pot reactions between the cyclic nitrono $\text{C}(\text{CH}_3)_2\text{CH}_2\text{CH}_2\text{CH}=\text{NO}$ and the Pt–nitrile complexes $\text{trans-}[\text{PtCl}_2(\text{N}\equiv\text{CR})_2]$ (R = $\text{CH}_2\text{CO}_2(\text{CH}_3)$, $\text{CH}_2\text{-Cl}$), where the nitrile is activated by coordination to the metal center and also by the strong electron-withdrawing group R.^{10b} Although the reactants used in this case are different from **N2** and **2**, there is a common characteristic of these two processes (i.e., extremely high overall activation of the reagents). Thus, it seems that such a "hyperactivation" may even negatively affect the nitrono-to-nitrile CA facilitating formation of secondary products. Obviously, additional investigations of this effect are necessary, and the corresponding experimental and theoretical studies are under way in our groups.

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Supporting Information Available: Discussion of the influence of the level of theory and basis set on the activation and reaction energies, general view of all equilibrium structures, tables with the calculated bond lengths, HOMO–LUMO gaps, total energies, enthalpies, Gibbs free energies, absolute and relative solvent effects, contour line diagrams of the Laplacian distribution, bond paths, and selected zero-flux surfaces for $\text{TS}_{\text{N4-CH}}$ and $\text{TS}_{\text{N4-2}}$. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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