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The Boekelheide Rearrangement of Pyrimidine *N*-oxides as a Case Study of Closed or Open Shell Reactions - Experimental and Computational Evidence for the Participation of Radical Intermediates

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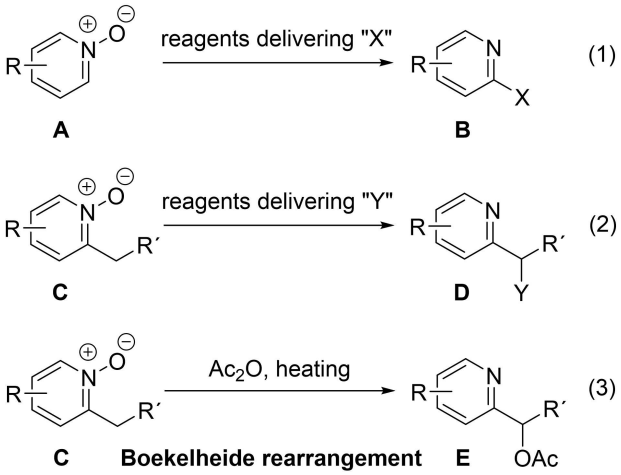
Dedicated to Prof. Dr. Herbert Mayr on the occasion of his 75th birthday.

Abstract: In a case study, the acetic anhydride-promoted reaction of a model pyrimidine *N*-oxide to the corresponding 4-acetoxymethyl-substituted pyrimidine derivative (Boekelheide rearrangement) was investigated in detail by experiment and quantum chemical calculations. The reaction conditions were varied and several side products formed in low to moderate yields were identified. These experiments indicate that a (pyrimidin-4-yl)methyl radical is one of the key species of the rearrangement. This interpretation was supported by the fact that rearrangements performed in solvents which can easily lose hydrogen atoms, afford considerable quantities of products incorporating the solvent. With TEMPO the key radical could be trapped. Other carboxylic acid anhydrides confirm the conclusion that the Boekelheide rearrangement of the model pyrimidine *N*-oxide proceeds, at least in part, via radical intermediates. The high level closed and open shell quantum chemical calculations show that concerted [3,3]-sigmatropic rearrangements or stepwise processes, either via ion pairs or via radicals, are energetically feasible.

Introduction

N-Oxides of nitrogen containing heterocycles, in particular of pyridine and pyrimidine derivatives, are important and versatile intermediates in organic synthesis since the *N*-oxide function allows selective functionalization in its proximity.[1] Two major pathways are relevant for the synthetic usage of *N*-oxides as shown in Scheme 1 with pyridine *N*-oxides as substrates: functionalization of the CH group next to the *N*-oxide moiety (**A** to **B**, Equation (1))[2] or functionalization of an alkyl group in this position (**C** to **D**, Equation (2)).[3] Very different reagents and conditions can be applied to achieve these processes and as a consequence diverse reaction mechanisms are involved. A long known reaction belonging to the second category employs carboxylic acid anhydrides such as acetic anhydride which converts compounds **C** into acetoxy-substituted products **E** (Equation (3)). According to one of the pioneers of this type of *N*-oxide usage the reaction is called Boekelheide rearrangement.[4] Remarkably, the mechanism of this useful process is not fully understood so far. It was proposed that the



Scheme 1. Typical reactions of pyridine *N*-oxides of general structure **A** or **C** leading to products **B**, **D**, or **E**.

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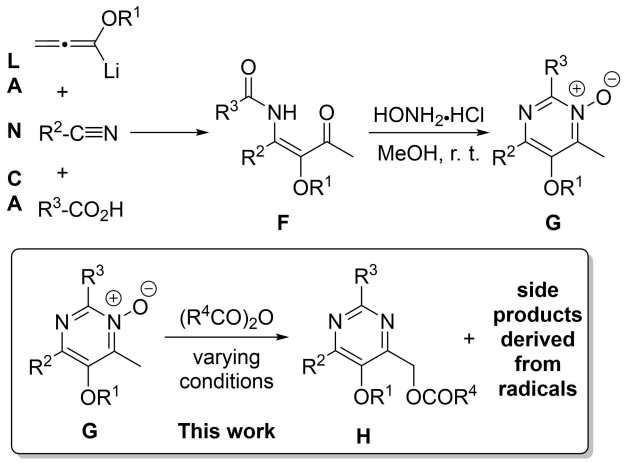
reaction proceeds as concerted [3,3]-sigmatropic rearrangement in the crucial step, but in several reports the participation of charged intermediates or of radicals was also discussed.[5]

During our studies on the use of alkoxyallenes as building blocks for the synthesis of heterocycles[6] we discovered a new three-component reaction of lithiated alkoxyallenes (**LA**) with nitriles (**N**) and carboxylic acids (**CA**) furnishing β-alkoxy-β-ketoenamides **F** (Scheme 2).[7] This LANCA approach to intermediates **F** is very flexible with respect to the substitution pattern. Subsequent condensation reactions of **F** led to compound libraries of highly substituted pyridine,[8] oxazole,[9] pyrimidine,[10] and quinoxaline[11] derivatives. The reaction of β-alkoxy-β-ketoenamides **F** with hydroxylamine hydrochloride proceeded particularly smoothly and directly afforded pyrimidine *N*-oxides **G** in good yields and in a regioselective manner.[12]

Subsequently, we examined Boekelheide rearrangements of these useful intermediates employing acetic anhydride and found that the expected 4-acetoxymethyl-substituted pyrimidine derivatives **H** (R^4 = Me) were usually formed in good to excellent yields (Scheme 2).[13] However, it was also observed that side products were formed in several reactions in varying quantities. The product composition was apparently dependent on the applied reaction conditions. These puzzling results and the structure of the side products indicated a possible involvement of radical intermediates. For this reason, we started a more systematic investigation under variation of the reaction conditions and a careful product analysis. In addition, a computational study of the reaction pathways of the employed model compound was undertaken.

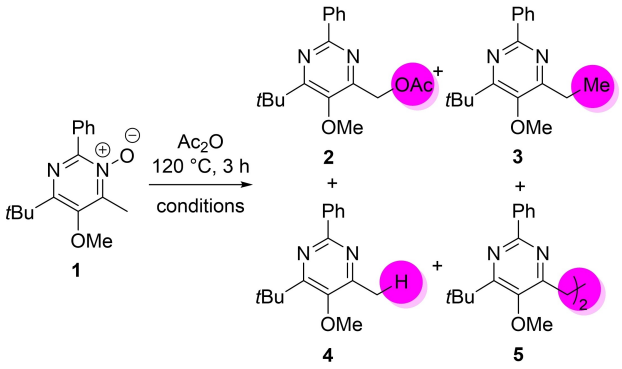


Scheme 2. LANCA route to β-alkoxy-β-ketoenamides **F**, conversion into pyrimidine *N*-oxides **G** and subsequent Boekelheide rearrangement to **H**.

Results and Discussion

Experimental facts

As model compound for the mechanistic studies we selected pyrimidine *N*-oxide **1** which is available in almost quantitative yield from the corresponding β-alkoxy-β-ketoenamide.[13] When this compound was treated with acetic anhydride at 120 °C under different reaction conditions we obtained the expected 4-acetoxymethyl-substituted pyrimidine derivative **2** in yields of up to 75 % and, depending on the reaction conditions, the side products **3**, **4**, and **5** in varying quantities (Scheme 3 and Table 1). Entry 1 presents the result of an already published experiment,[13] where "standard conditions" were applied, i.e., neat acetic anhydride, 120 °C for several hours, air atmosphere (no exclusion of oxygen, water or light). Compound **2** was



Scheme 3. Boekelheide rearrangement of pyrimidine *N*-oxide **1** with acetic anhydride leading to the expected product **2** and side products **3**, **4**, and **5** (for conditions and product ratios, see Table 1).

Table 1. Reaction of pyrimidine *N*-oxide **1** with acetic anhydride under various conditions; also see Scheme 3.

Entry	Conditions[a]	Yield of **2**	Yield of **3**	Yield of **4**[b]	Yield of **5**[b]
1[13]	Standard	69 %	3 %	–	–
2	Standard	39–74 %	3–34 %	0–3 %	0–1 %
3	O_2 atmosphere	75 %[c]	25 %[c]		
4	Ar atmosphere	94 %[c]	6 %[c]		
5	Light exclusion	99 %[c]	1 %[c]		
6	Standard 0.1 equiv. $(BzO)_2$	35 %	37 %		
7	Standard 0.1 equiv. AIBN	40 %	36 %	2 %	2 %
8	Standard 1.05 equiv. Bu_3SnH	39 %	7 %	50 %	
9	Standard 2.0 equiv. KO*t*Bu	51 %[c]	42 %[c]	2 %[c]	3 %[c]
10	Standard in DMSO	41 %	29 %	1 %	2 %
11	Standard in benzene	52 %	28 %	1 %	3 %

[a] Standard conditions: air atmosphere, Ac_2O, no solvent. [b] In most cases side products **4** and **5** were isolated in mixtures; they were identified by comparison of the NMR spectra of independently prepared samples. [c] Ratio determined for the crude product.

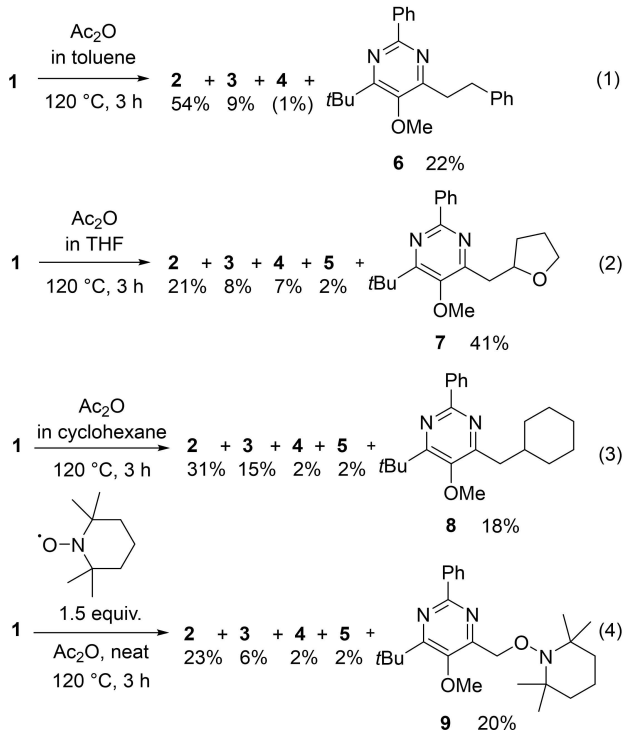
isolated as major product in 69% yield and ethyl-substituted side product **3** in 3% yield. However, when we repeated this experiment (entry 2), scattering product ratios were observed and together with **2** and **3** the new side products **4** and **5** were detected. In order to identify the reason for this unsatisfying low reproducibility we deviated from the standard conditions.

When the Boekelheide rearrangement of **1** was performed under an atmosphere of oxygen the crude product analysis showed a 75:25 ratio of products **2** and **3** (entry 3), whilst the experiment under an argon atmosphere resulted in a 94:6 ratio of the two compounds (entry 4). Standard conditions under light exclusion provided even a 99:1 ratio of **2** and **3** in the crude product (entry 5). These conditions seem to be optimal to receive high yields of acetoxymethyl-substituted pyrimidine derivatives such as **2**, but they were not examined with other substrates.[14] For the current mechanistic investigation it was more relevant to study the influence of other parameters.

The formation of the side-products indicated the participation of a (pyrimidin-4-yl)methyl radical and hence we also studied the Boekelheide rearrangement of **1** in the presence of 0.1 equiv. of radical initiators such as benzoyl peroxide [$(BzO)_2$] (entry 6) or azobisisobutyronitrile (AIBN) (entry 7). Remarkably, the quantity of compound **2** was reduced and the formation of the ethyl-substituted pyrimidine derivative **3** was significantly enhanced in both entries. The two compounds were isolated as major products in both experiments in quite similar yields of ca. 35%. On the other hand, when the hydrogen atom donor reagent tributyltin hydride was employed as additive the production of **3** was strongly reduced (7%) whereas the methyl-substituted pyrimidine derivative **4** was now the major product which was isolated in 50% yield (entry 8).

The generally discussed mechanism of the Boekelheide rearrangement involves a shift of a proton of the 4-methyl group to provide an *exo*-methylene group (see discussion below). Therefore, the influence of a base such as potassium *tert*-butoxide was examined (Table 1, entry 9). The product ratio of the crude product shows a relatively high content of the ethyl-substituted pyrimidine derivative **3** and only small amounts of side products **4** and **5**. The presence of the polar solvent DMSO (entry 10) or of the nonpolar solvent benzene (entry 11) did not change much and resulted in mixtures that are similar to those obtained under the standard conditions (entry 2).

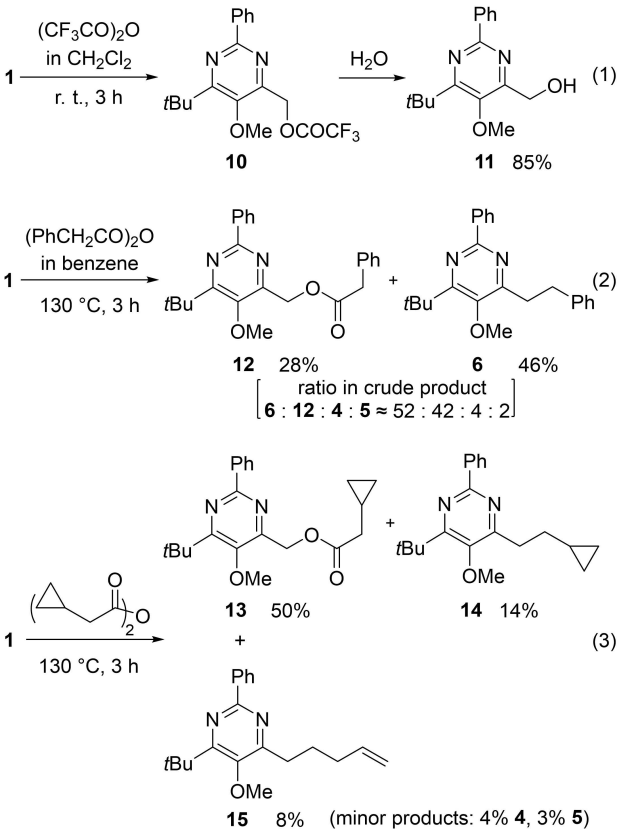
Solvents known to easily lose a hydrogen atom behave different. In toluene as solvent the Boekelheide rearrangement of **1** with acetic anhydride furnished **2** as product in 54% yield and a mixture containing 2-phenylethyl-substituted pyrimidine derivative **6** and compound **3** (calculated yields 22% and 9%, respectively). (Scheme 4, Equation (1)), clearly showing that a benzyl radical derived from the solvent was incorporated into this product. Traces of compound **4** (ca. 1%) were detected in the crude product but were not isolated after column chromatography. An even higher degree of solvent participation was observed with tetrahydrofuran as solvent (Equation (2)). The (tetrahydrofur-2-yl)methyl-substituted pyrimidine derivative **7** was the major product formed in 41% yield; compounds **2**–**5** were also identified. A similar experiment in



Scheme 4. Boekelheide rearrangement of pyrimidine *N*-oxide **1** with acetic anhydride in different solvents or in the presence of a radical trapping reagent.

cyclohexane as solvent gave (cyclohexyl)methyl-substituted compound **8** in 18% yield together with **2**–**5** (Equation (3)). The presence of a (pyrimid-4-yl)methyl radical was further confirmed by an experiment employing (2,2,6,6-tetramethylpiperidin-1-yl)oxyl (TEMPO) as radical trapping reagent (Equation (4)). Besides compounds **2**–**5** the expected product **9** was isolated in 20% yield. All these experiments clearly demonstrate that radical intermediates derived from **1** and in part from the solvents are involved in the Boekelheide rearrangement.

Finally, we examined the influence of the carboxylic acid anhydride component on the outcome of the Boekelheide rearrangement of pyrimidine *N*-oxide **1** (Scheme 5). The reaction with trifluoroacetic anhydride[15] was already part of our previous publication.[13] We were pleased that the very mild conditions provided high yields, but observed spontaneous hydrolysis of the sensitive trifluoroacetic ester **10** during work-up and purification. The corresponding hydroxymethyl-substituted pyrimidine derivative **11** was isolated in high yield (Scheme 5, Equation (1)). Although unknown side-products were isolated in small quantities, we have no clear evidence that compounds derived from radicals are formed during this transformation.[16] In contrast, the reactions of compound **1** with phenylacetic acid anhydride and with cyclopropylacetic acid anhydride furnished again product mixtures which indicate the intermediacy of radicals (Eqs. (2) and (3)). The involvement of benzyl radicals is clearly demonstrated by the relatively high yield of the 2-phenylethyl-substituted pyrimidine derivative **6** (46%) whereas the rearrangement product **12** was formed in



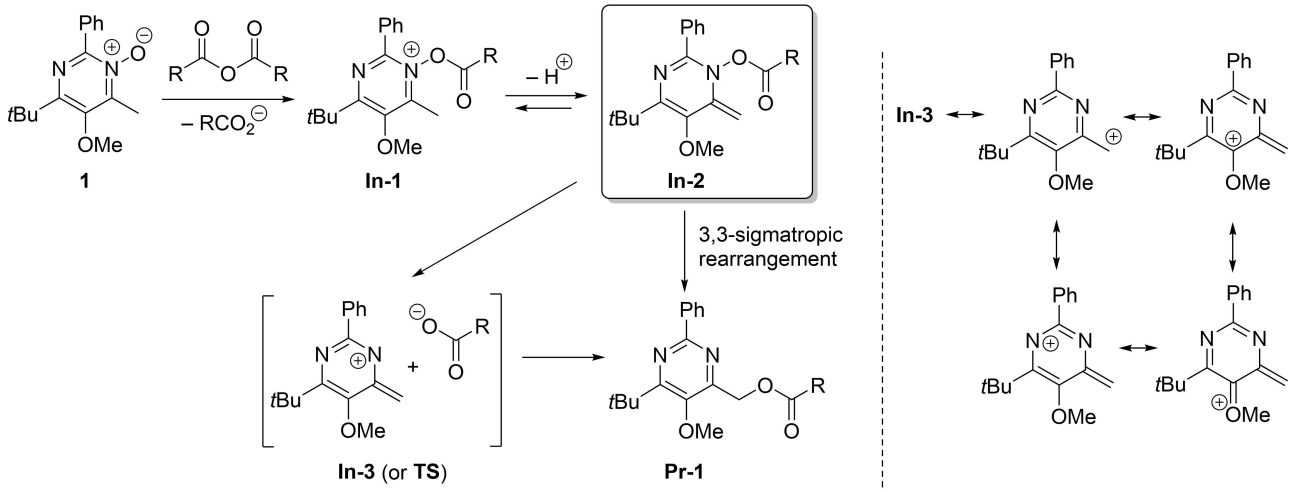
Scheme 5. Boekelheide rearrangement of pyrimidine *N*-oxide **1** with different carboxylic acid anhydrides.

lower quantities (28%). In the crude product of this experiment, we could even identify small amounts of the benzyl radical dimerization product 1,2-diphenylethane together with side products **4** and **5** (Eq. (2)). Reaction of **1** with cyclopropylacetic acid anhydride gave the expected product **13**, but also compounds **14** and **15** containing either a cyclopropylethyl or a 4-penten-1-yl group (Eq. (3)). The reversible ring-opening of cyclopropylmethyl radicals is a well-known process.[17,18]

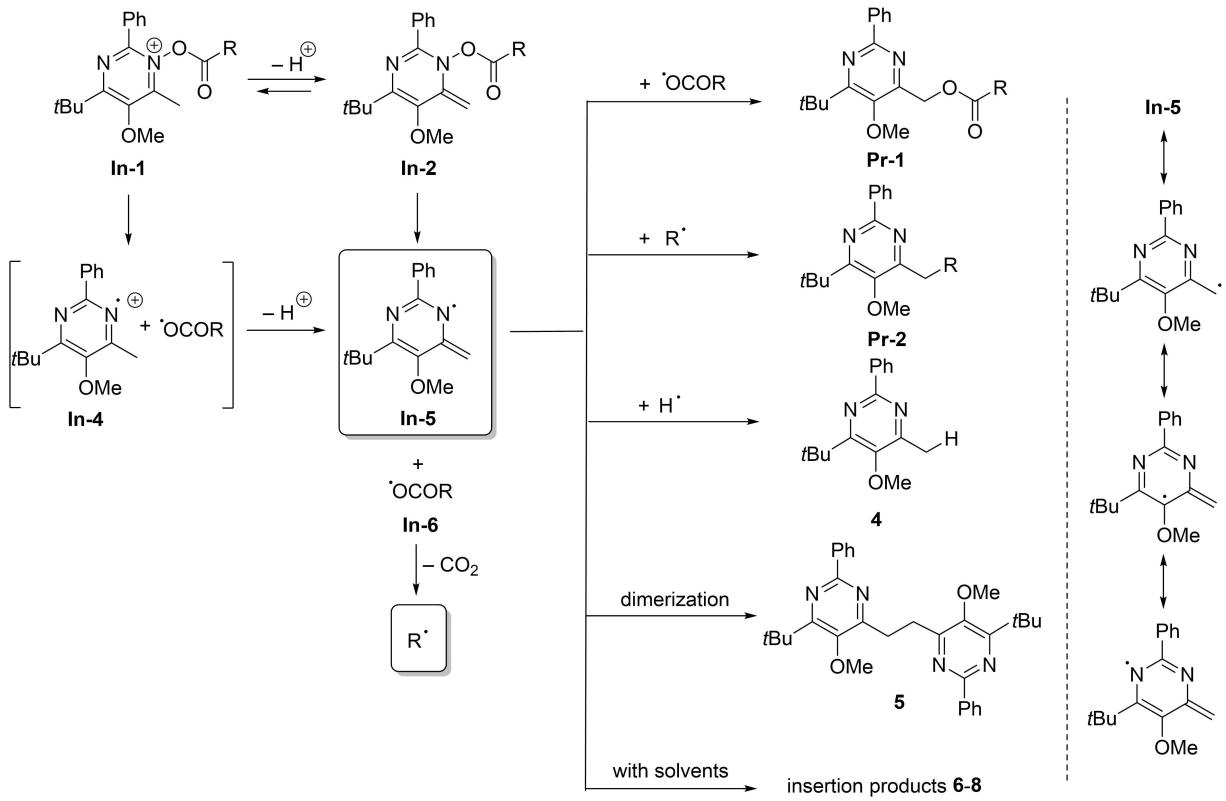
Mechanistic Interpretation

As mentioned above, the Boekelheide rearrangement of heterocyclic *N*-oxides is generally discussed on the basis of concerted and/or stepwise processes.[5] Scheme 6 presents the concerted mechanism which involves a primary O-acylation of the *N*-oxide moiety by the carboxylic acid anhydride and a subsequent (reversible) deprotonation of intermediate **In-1** to the *exo*-methylene species **In-2** which is regarded as the key intermediate of the overall process. It can undergo a [3,3]-sigmatropic rearrangement under cleavage of the weak N–O bond directly providing product **Pr-1**. However, it is also possible that **In-2** first dissociates to the ion pair **In-3** which recombines to the rearranged compound **Pr-1**. Although the drawn formula of **In-3** with a positive charge at a nitrogen center appears to be unfavorable the depicted Lewis structures indicate good stabilization of this benzyl cation type intermediate, in particular by the 5-methoxy group. Therefore, this dissociation pathway cannot be ruled out a priori. But it is also possible that the charge distribution in the transition state of the concerted reaction of **In-2** to **Pr-1** is reflected by the formula **In-3**.

The experimental data unequivocally indicate that under certain reaction conditions radical intermediates are involved and that the (pyrimidin-4-yl)methyl radical **In-5** seems to be the key species. The formation of this radical and its possible reactions are illustrated in Scheme 7. A homolytic cleavage of the weak N–O bond of **In-2** can directly provide the two radicals **In-5** and an acyloxy radical **In-6**. Alternatively, the O-acylated pyrimidine *N*-oxide **In-1** may first undergo a homolytic fragmentation to the acyloxy radical and the radical cation **In-4** which is subsequently deprotonated to deliver the crucial (pyrimidin-4-yl)methyl radical **In-5** which is highly stabilized as demonstrated by the Lewis structures (Scheme 7, right part).



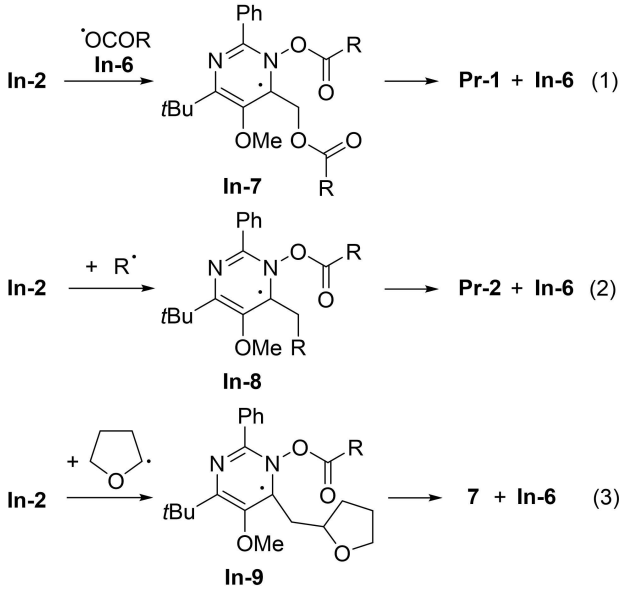
Scheme 6. Concerted and ionic pathways of pyrimidine *N*-oxide **1** to product **Pr-1** via stabilized intermediate **In-2**.



Scheme 7. Possible radical pathways of O-acylated pyrimidine *N*-oxides **In-1** with (pyridimin-4-yl)methyl radical **In-5** as key intermediate.

This intermediate has a manifold of options to react with other components. Recombination with the acyloxy radical **In-6** furnishes the "normal" Boekelheide rearrangement product **Pr-1**, but since acyloxy radicals suffer fast decarboxylation to radicals the recombination can also provide products of type **Pr-2** with an incorporation of R• the carboxylic acid substituent. These reactions may occur within the solvent cage and hence may not be as unfavorable as other radical-radical recombinations. Several hydrogen atom donors may be responsible for the formation of the methyl-substituted compound **4**: the solvent, the carboxylic acid anhydride, precursor **1** or **In-1** to list the most probable hydrogen sources. It is evident that an additive such as tributyltin hydride strongly increases the amount of side product **4** (Table 1, entry 8). Dimerization of radical **In-5** is certainly responsible for the generation of compound **5**.

The recombination of two radicals is not a very favorable process if their stationary concentrations are low. Therefore, radical chain reactions of intermediate radicals with *exo*-methylene species **In-2** may even be more likely (Scheme 8). The acyloxy radical **In-6** or the radical R• may also add to **In-2** (Eqs. (1) and (2)) to furnish new stabilized radicals **In-7** or **In-8**, which after homolytic N–O bond cleavage provide products **Pr-1** or **Pr-2** under regeneration of **In-6**. The dimerization product **5** may also be formed via a similar pathway if (pyrimidin-4-yl)methyl radical **In-5** adds to **In-2** (not shown). Similarly, abstraction of a hydrogen from a solvent such as tetrahydrofuran by a present radical species (e.g., R•) generates a new radical



Scheme 8. Chain reactions of *exo*-methylene compound **In-2** with different radicals leading to products **Pr-1**, **Pr-2**, or **7**.

which adds to **In-2** to produce via intermediate **In-9** (tetrahydrofur-2-yl)methyl-substituted pyrimidine derivative **7** (Eq. (3)). With toluene or cyclohexane as solvents likewise processes can be assumed whereas benzene seems to be inert under the applied conditions. It is evident that radical starters such as

$(BzO)_2$ or AIBN can promote these processes by delivering the corresponding starting radicals.

The influence of oxygen on the product composition is not fully understood at the moment. In the presence of light moderate oxygen concentration as present in air atmosphere (standard conditions) can possibly produce species which start the radical chain reactions. Depending on the individual experiment this may lead to irreproducible amounts of the observed side products. A pure oxygen atmosphere strongly reduces the quantity of these side products which may be due to fast quenching of the starter radicals by molecular oxygen. Whereas this interpretation is speculative, it is evident that light exclusion (even in the presence of oxygen) has a very positive influence on a clean rearrangement reaction leading selectively to the "normal" Boekelheide product. In order to identify potential light absorbing intermediates the UV-Vis spectra of **In-1b** and of **In-2b** were calculated by the B3LYP/def2TZVP + PCM (dichloromethane) method (for details see Supporting Information). Only the *exo*-methylene intermediate **In-2b** shows an absorption reaching the visible part of the spectrum, with a broad band ranging from 320–500 nm (maximum at 385 nm). It is therefore very likely that intermediate **In-2b** can be excited by visible light and hence its homolytic cleavage to the radical pair **In-5**/**In-6** (Scheme 7) may be induced.[19]

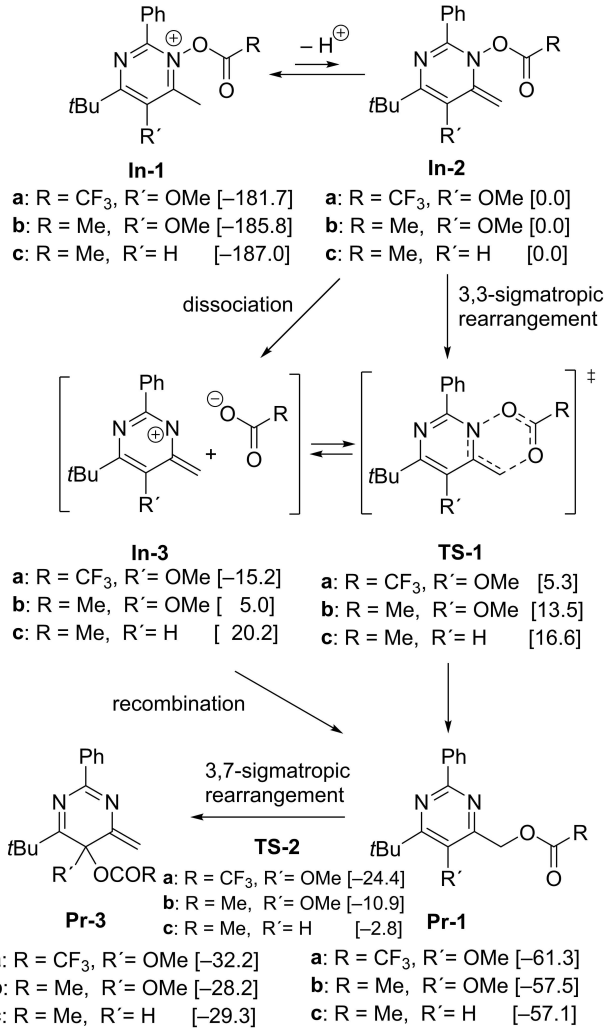
Summarizing the experimental facts, it is evident that the mechanistic scenario of the Boekelheide rearrangements of model compound **1** is quite complex. Depending on the conditions, the reaction can occur cleanly affording the expected rearrangement products, e.g., compound **2**, essentially without side products. But other reaction conditions apparently promoted the formation of initiating radical species which led to additional products. In order to distinguish between concerted, ionic or radical processes and to identify the most probable reaction mechanisms we compared these possible pathways by computational chemistry.

Computational Study

In the following section, the observed experimental results will be discussed on the basis of the Gibbs free energy surface as investigated by a comprehensive quantum chemical study. Thus, mechanistic details, for example, intermediates and reaction barriers via transition states, and the respective thermodynamic and kinetic data will be in the center of the investigation.

On the basis of optimized DFT geometries for the gas phase using the hybrid functional B3LYP/6-31G(d)[20,21] + GD3BJ[22,23] geometry optimizations were performed using the hybrid functional PBE1PBE/def2TZVP[24–28] including Grimme dispersion GD3BJ and the PCM solvent sphere of dichloromethane.[29] In accordance with the experimental findings, closed shell as well as open shell calculations (radicals and radical cations) under the applied experimental reaction conditions were performed (room temperature, no irradiation). Then, double hybrid functional (U)B2PLYPD3/def2TZVP-optimizations[30] including the PCM solvent sphere of dichloromethane were done for all species discussed here. In the following section, we discuss differences in Gibbs free energies (ΔG_{298}) (kcal/mol) (see also Supporting Information for details). For comparison of the ionic (Scheme 9) versus radical pathways (Scheme 10) additionally single point CCSD(T)/def2TZVP-calculations including the PCM solvent sphere of dichloromethane [31–36] were performed using a smaller model system (without *t*-butyl and phenyl groups compared to **In-2b**). All calculations were done using the Gaussian 16 package of programs.[37]

In Scheme 9 we summarize the calculations of closed shell pathways, i.e., the concerted process via a 3,3-sigmatropic reaction and the possible ionic pathway via a heterolytic N–O bond cleavage are compared. As acyl groups a trifluoroacetyl substituent (series **a**) was compared with the generally used acetyl substituent (series **b** and **c**). Although no experimental data are available for this series, we also included the compounds and intermediates without substituent at C-5



Scheme 9. Energetics of closed shell pathways of Boekelheide rearrangements of pyrimidine *N*-oxides with intermediates **In-2a–c** as key precursor leading to products **Pr-1a–c** at B2PLYPD3/def2TZVP//B2PLYPD3/def2TZVP + PCM (CH_2Cl_2) level of theory (all values in kcal/mol).

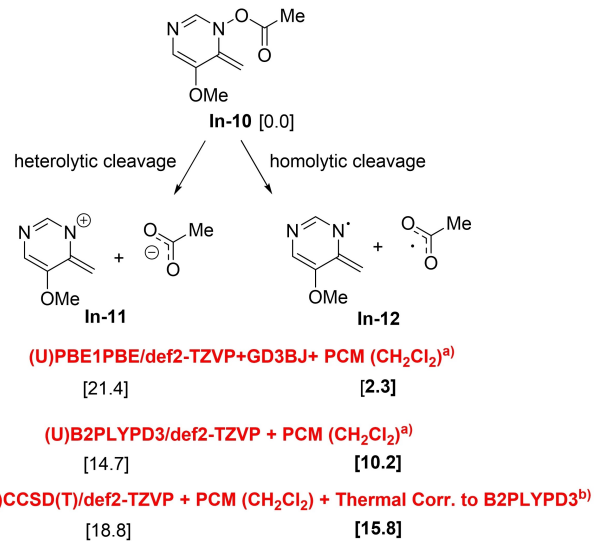
instead of a methoxy group (series **c**) to reveal the effect of the strongly electron-donating methoxy group.

The calculated protonation reaction of **In-2** to give **In-1** indicates the enormous basicity of **In-2**. Its calculated gas phase basicity is close to that of DBU (1,8-diazabicyclo[5.4.0]undec-7-ene) (pK_s of the protonated form about 12) and reveals the importance of the aromaticity of precursor **In-1** compared to intermediate **In-2**. For all three series we found that the final rearrangement products **Pr-1a–c** are energetically strongly favored with respect to the preceding *exo*-methylene compounds **In-2a–c** (−61.3 to −57.1 kcal/mol). On the other hand, the transition states **TS** of the 3,3-sigmatropic rearrangements leading directly from **In-2a–c** to **Pr-1a–c** differ considerably. In excellent agreement with the experimental results (rearrangement at room temperature) the trifluoroacetyl-substituted system has the lowest barrier of only 5.3 kcal/mol, whereas the two acetyl-substituted cases have higher barriers of 13.5 and 16.6 kcal/mol, respectively. These two results show that the 5-methoxy group has moderately decreased the energy of the transition state. Hence the charge distributions within the transition states **TS** resemble the situation of ion pairs **In-3a–c** which are generated by heterolytic bond cleavage of **In-2a–c**. The dissociation of **In-2a** to **In-3a** with trifluoroacetate as anion is even exergonic (−15.2 kcal/mol) and the difference of systems **b** and **c** follows the expected influence of substituents (compare Lewis structures depicted on the right side of Scheme 6).

A conceivable subsequent 3,7-sigmatropic rearrangement of products **Pr-1a–c** leading to compounds **Pr-3a–c** was also calculated. The transition states **TS** show that this process should be possible under the applied conditions, however, the products **Pr-3a–c** are roughly 30 kcal/mol higher in energy than **Pr-1a–c**. It can therefore not be expected that this rearrangement of the aromatic heterocycles **Pr-1a–c** to non-aromatic systems can be experimentally observed. In summary, the Gibbs free energies (ΔG_{298}) values compiled in Scheme 9 clearly reveal the high thermodynamic driving force of the Boekelheide rearrangement. They also demonstrate that the closed-shell pathways are kinetically possible, however, a clear decision for a concerted process or a dissociative process via **In-3** is not possible.

Since the experimental data clearly indicate that radicals are participating, either on the main reaction pathway or as competing processes, a comprehensive comparison of the thermodynamics of the heterolytic cleavage versus the homolytic cleavage was undertaken. In order to limit the computational efforts a simplified model *exo*-methylene compound **In-10** (instead of **In-2b**) was investigated at different levels of theory (Scheme 10). Thus, DFT-calculations using the double hybrid PBE-functional and the B2PLYPD3 were used for complete geometry optimizations including dichloromethane as solvent (PCM). Additionally, CCSD(T)-single point calculations on the B2PLYPD3-geometries were performed to describe the radical character as good as possible.

The results compiled in Scheme 10 reveal that in all cases the homolytic cleavage leads to energetically more favorable intermediates. However, at the most reliable level of theory

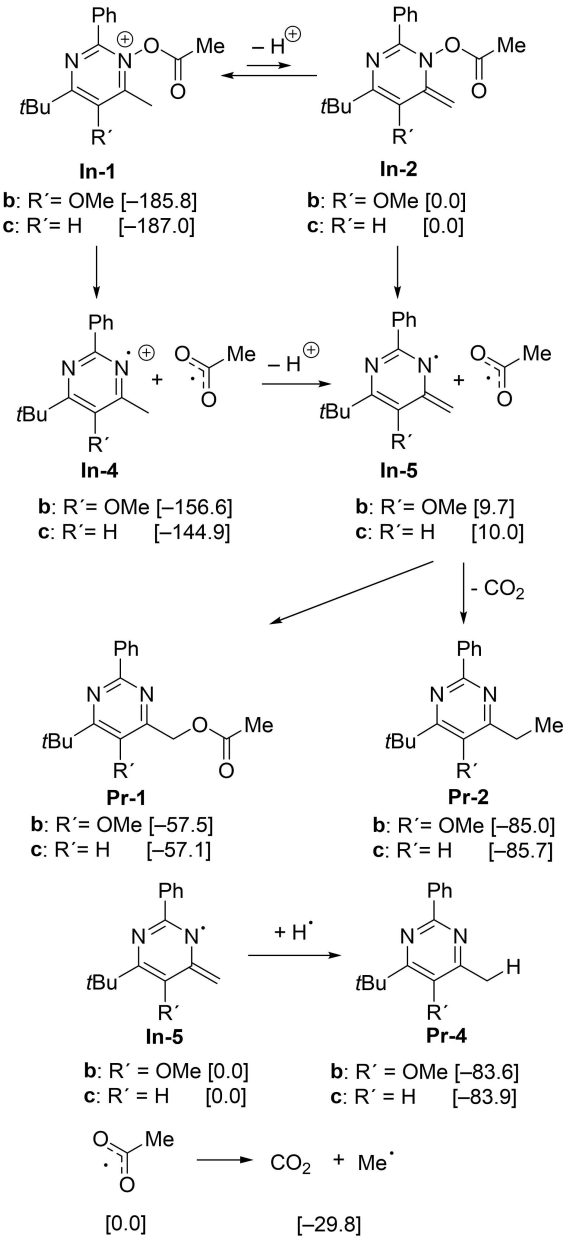


Scheme 10. Comparison of energetics of heterolytic and homolytic Boekelheide rearrangements of a simplified intermediate **In-10** to ion pair **In-11** and radical pair **In-12** at different levels of theory (kcal/mol). a) Fully optimized at the indicated level; b) single points using the (U)B2PLYPD3 geometries + thermal correction to Gibbs free energy from (U)B2PLYPD3/def2TZVP + PCM (CH_2Cl_2).

(CCSD(T)) the difference of the Gibbs free energies is only 3 kcal/mol suggesting a possible competition of both pathways, homolysis and heterolysis under experimental conditions. However, for entropical reasons, a combination of radicals is less likely compared to a concerted rearrangement. From these data it can be extrapolated that with a trifluoroacetyl group the heterolytic cleavage is favored, which agrees with the absence of radical derived products in this case (see Scheme 5, Equation (1)). The calculation of transition states of homolytic reactions could not be performed within this project, since the barriers leading from **In-10** to **In-11** or **In-12** cannot be determined computationally at the appropriate high level.

In Scheme 11 the thermodynamics of radical pathways were presented employing the (U)B2PLYPD3-level of theory as used for the closed shell reactions. For the trifluoroacetyl acetic-induced Boekelheide rearrangement the radical pathways are less likely and therefore we restricted the calculations to series **b** and **c**. The formation of **In-5b–c**/acetyloxy radical pairs is energetically feasible since their Gibbs energies are only approximately 10 kcal/mol higher than those of the precursor compounds **In-2b–c**. It is remarkable that the methoxy group has almost no effect on the stability of **In-5b**.

The alternative pathway to the **In-5b–c**/acetyloxy radical pairs, which comprises in a primary homolytic cleavage of the N–O bond of the protonated O-acylated pyrimidine *N*-oxides **In-1b–c** to provide the radical cations **In-4b–c** and the acetyloxy radical followed by a deprotonation to **In-5b–c**, was also calculated. This route seems less favorable since the homolytic bond cleavages leading to **In-4b–c** require at least approximately 29 or 42 kcal/mol, respectively. In this case the 5-methoxy group leads to the expected stabilization of the radical



Scheme 11. Energetics of open shell pathways of Boekelheide rearrangements **In-5b–c**/acetyloxy radical pairs leading to products **Pr-1b–c Pr-2b–c** and **4b–c** at (U)B2PLYPD3/def2TZVP//B2PLYPD3/def2TZVP + PCM (CH_2Cl_2) level of theory (all values in kcal/mol).

cation **In-4b**. Abstraction of the proton from radical cations **In-4b–c** leads to the **In-5b–c**/acetyloxy radical pairs.

The decarboxylation of the acetyloxy radical to furnish the methyl radical is exergonic by ca. 30 kcal/mol.[38] The combinations of radicals **In-5b–c** with the acetyloxy, the methyl radical or a hydrogen atom lead in strongly exergonic reactions to products **Pr-1b–c**, **Pr-2b–c** or **Pr-4b–c**. The calculated reaction enthalpies reflect the respective stability of the radicals involved. Overall, the calculated values presented in Scheme 11 clearly reveal that the assumed radical processes are energetically feasible and can establish competing pathways to the concerted or ionic mechanisms.

Conclusion

Our experiments unequivocally demonstrated that the Boekelheide rearrangements of model pyrimidine *N*-oxide **1** with carboxylic acid anhydrides can involve radical intermediates. The extend of products formed via radicals strongly depends on the reaction conditions, hence indicating that initiating radicals are required. As a unique reagent, trifluoroacetic anhydride does not give products derived from radicals. The experimental results indicate that concerted [3,3]-sigmatropic rearrangements and radical initiated processes may occur as parallel reactions. This was confirmed by comprehensive closed and open shell quantum chemical calculations which demonstrate the energetic feasibility of all pathways. The closed shell rearrangement can also proceed via a heterolytic N–O bond cleavage leading to an ion pair instead of the concerted sigmatropic process. The exceptional behavior of trifluoroacetic anhydride as reagent is also confirmed by the calculations. The different scenarios for the radical processes are sketched. It is most likely that they occur as radical chain reactions started by radicals which are introduced either via impurities such as oxygen or by initiators; alternatively, they are generated by thermal or light-induced processes.

Experimental Section

For general information, other experimental and analytical details as well as computational details see Supporting Information.

General procedure for the Boekelheide rearrangements: In an ACE sealed tube equipped with a stir bar, pyrimidine *N*-oxide **1** was dissolved in acetic anhydride (or another carboxylic acid anhydride) and the solution was heated at reflux at 120 °C for 3 h under air atmosphere. After cooling to room temperature, the excess of anhydride was removed under reduced pressure. Purification of the crude product by column chromatography (silica gel, hexanes/EtOAc) provided the rearranged product **2** and other by-products.

(6-*tert*-Butyl-5-methoxy-2-phenylpyrimidin-4-yl)methyl acetate (2): (data from Ref. [13]) colorless solid, M. P. 59–61 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta = 1.48$ (s, 9 H, *t*-Bu), 1.41 (s, 9 H, *t*-Bu), 2.22 (s, 3 H, Me), 3.84 (s, 3 H, OMe), 5.32 (s, 2 H, OCH_2), 7.43–7.62, 8.40–8.43 (2 m, 2 H, 3 H, Ph). ^{13}C{^{1}H} NMR ($CDCl_3$, 100.5 MHz): $\delta = 20.9$ (q, Me), 29.2, 38.4 (q, s, *t*-Bu), 61.7 (t, OCH_2), 62.6 (q, OMe), 128.0, 128.3, 129.9, 137.7 (3 d, s, Ph), 150.4, 156.6, 157.8, 169.2 (4 s, C-2, C-4, C-5, C-6), 170.8 (s, C=O). IR (ATR): $\nu = 2960–2865$ (=C–H, C–H), 1750 (C=O), 1550 (C=C), 1450 cm^{-1} (C=N). HRMS (ESI): *m/z* $[M+Na]^+$ calcd for $C_{18}H_{22}N_2NaO_3$ 337.1528, found: 337.1540.

(4-*tert*-Butyl-6-ethyl-5-methoxy-2-phenylpyrimidine (3): (data from Ref. [13]) pale yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta = 1.55$ (t, $J = 7.5$ Hz, 3 H, Me), 1.58 (s, 9 H, *t*-Bu), 2.93 (q, $J = 7.5$ Hz, 2 H, CH_2), 3.80 (s, 3 H, OMe), 7.45–7.56, 8.58–8.62 (2 m, 2 H, 3 H, Ph). ^{13}C{^{1}H} NMR ($CDCl_3$, 125.8 MHz): $\delta = 12.3$ (q, Me), 25.2 (t, CH_2), 29.6, 38.3 (q, s, *t*-Bu), 61.8 (q, OMe), 128.2, 128.5, 129.8, 138.5 (3 d, s, Ph), 150.6, 157.6, 164.7, 167.9 (4 s, C-2, C-4, C-5, C-6). IR (ATR): $\nu = 3090–2870$ (=C–H, C–H), 1545 (C=C), 1445 cm^{-1} (C=N). HRMS (ESI): *m/z* $[M+H]^+$ calcd. for $C_{17}H_{24}N_2O_2$ 271.1810, found: 271.1791.

Independent synthesis of 6-*tert*-Butyl-5-methoxy-6-methyl-2-phenylpyrimidine (4): According to a literature procedure,[10b] (*E*)-*N*-(4-methoxy-2,2-dimethyl-5-oxohex-3-en-3-yl)benzamide (0.137 g, 0.500 mmol)[8c] and NH_4OAc (0.278 g, 7.97 mmol) were placed in an

ACE sealed tube. The mixture was dissolved in MeOH (3 mL) and stirred for 3 d at 65 °C. After addition of water and CH_2Cl_2 (5 mL each) the layers were separated and the aqueous layer was extracted with CH_2Cl_2 (4×5 mL). The combined organic layers were dried with Na_2SO_4, filtered and concentrated. Column chromatography (silica gel, hexanes/ethyl acetate = 10:1) provided **4** (0.063 g, 49%) as pale yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.47 (s, 9 H, *t*-Bu), 2.58 (s, 3 H, Me), 3.90 (s, 3 H, OMe), 7.38–7.43, 8.39–8.45 (2 m, 3 H, 2 H, Ph). ^{13}C{^{1}H} NMR ($CDCl_3$, 101.8 MHz): δ = 19.9 (q, Me), 29.2, 38.1 (q, s, *t*-Bu), 60.9 (q, OMe), 128.0, 128.3, 129.7, 138.1 (3 d, s, Ph), 150.9, 157.4, 160.3, 167.8 (4 s, C-2, C-4, C-5, C-6). IR (ATR): ν = 3060–2835 (=C–H, C–H), 1585 (C=C), 1445 cm^{-1} (C=N). HRMS (ESI): *m/z* $[M+H]^+$ calcd for $C_{16}H_{21}N_2O$ 257.1648, found: 257.1638. Anal. Calcd for $C_{16}H_{20}N_2O$ (256.3): C 74.97, H 7.86, N 10.93, found: C 74.76, H 7.79, N 10.67.

Independent synthesis of 1,2-Bis[6-(*tert*-butyl)-5-methoxy-2-phenylpyrimidin-4-yl]ethane (5): To a solution of compound **11** (0.220 g, 0.966 mmol) in THF (5 mL) were added at 0 °C mesyl chloride (75 µL, 0.809 mmol) and triethylamine (141 µL, 1.02 mmol) and the mixture was stirred at r.t. After 1 h, NaI (0.528 g, 3.52 mmol) in THF (5 mL) was added and the mixture was stirred for additional 1.5 h at r.t. After addition of water and diethyl ether (5 mL each) the layers were separated and the aqueous layer was extracted with diethyl ether (3×10 mL). The organic layer was washed with 10% aq. Na_2SO_3 solution (10 mL) and brine (10 mL) and dried (Na_2SO_4) filtered and concentrated. Column chromatography (silica gel, hexanes/ethyl acetate 20:1) provided *4-(tert-butyl)-6-(iodomethyl)-5-methoxy-2-phenylpyrimidine* (0.249 g, 67%) as pale yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.47 (s, 9 H, *t*-Bu), 3.93 (s, 3 H, OMe), 4.53 (s, 2 H, CH_2), 7.41–7.50, 8.42–8.47 (2 m, 3 H, 2 H, Ph). ^{13}C{^{1}H} NMR ($CDCl_3$, 101.8 MHz): δ = 0.2 (t, CH_2), 29.2, 38.7 (q, s, *t*-Bu), 61.6 (q, OMe), 128.2, 128.6, 130.2, 137.6 (3 d, s, Ph), 149.5 (s, C-5), 158.0, 159.9, 170.0 (3 s, C-6, C-4, C-2). IR (ATR): ν = 3060–2855 (=C–H, C–H), 1545–1530 cm^{-1} (C=C, C=N). HRMS (ESI): *m/z* $[M+H]^+$ calcd. for $C_{16}H_{20}IN_2O$ 383.0614, found: 383.0620.

The compound obtained from the reaction described above (0.115 g, 0.300 mmol) in THF (5 mL) at −78 °C was treated with *t*-BuLi (0.25 mL, 1.6 M in hexanes, 0.400 mmol) and the solution was stirred for 10 min at this temperature. After quenching with aq. satd. NH_4Cl solution (5 mL), diethyl ether (10 mL) was added and the aqueous phase was extracted with diethyl ether (2×10 mL). The combined organic phases were dried (Na_2SO_4), filtered and all volatiles were removed in vacuo. The crude product was purified by column chromatography (silica gel, hexanes/EtOAc, 20:1) to provide a 1:1 mixture of **4** and **5** (0.045 g, calculated yields 20% each).

Data assigned to compound **5**: ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.43 (s, 18 H, *t*-Bu), 3.52 (s, 4 H, CH_2), 3.81 (s, 6 H, OMe), 7.39–7.49, 8.44–8.49 (2 m, 6 H, 4 H, Ph). ^{13}C{^{1}H} NMR ($CDCl_3$, 101.8 MHz): δ = 29.4, 38.3 (q, s, *t*-Bu), 33.0 (t, $PyrCH_2$), 62.1 (q, OMe), 128.0, 128.5, 129.7, 138.4 (3 d, s, Ph), 151.6 (s, C-5), 156.9, 162.5, 168.4 (3 s, C-6, C-4, C-2). IR (ATR): ν = 3070–2840 (=C–H, C–H), 1595–1545 cm^{-1} (C=C, C=N). HRMS (ESI): *m/z* $[M+H]^+$ calcd for $C_{32}H_{39}N_4O_2$ 511.3068, found: 511.3038.

Reaction of pyrimidine *N*-oxide 1 with acetic anhydride in toluene: According to the general procedure, pyrimidine *N*-oxide **1** (0.182 g, 0.669 mmol), and acetic anhydride (1.5 mL) in toluene (3 mL) afforded after purification by flash chromatography (silica gel, hexanes/EtOAc, 10:1 to 8:1) compound **2** (0.113 g, 54%) as colorless crystals and a mixture of compounds **3** and **6** (0.070 g, 9% **3**, 22% **6**).

Data assigned to **4-*tert*-butyl-5-methoxy-6-phenethyl-2-phenylpyrimidine (6)**: ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.46 (s, 9 H, *t*-Bu), 3.13–3.23 (m, 4 H, CH_2), 3.73 (s, 3 H, OMe), 7.17–7.23, 7.26–7.32, 7.40–7.50, 8.39–8.51 (4 m, 2 H, 3 H, 3 H, 2 H, Ph). ^{13}C{^{1}H} NMR ($CDCl_3$, 125.8 MHz): δ = 29.2, 38.2 (q, s, *t*-Bu), 33.6, 33.8 (2 t, CH_2Ph, 6-CH_2), 61.7 (q, OMe), 126.0, 128.0, 128.35, 128.4, 128.5, 129.8, 138.1, 141.8 (6 d, 2 s, Ph), 150.5 (s, C-5), 157.4, 162.5, 167.3 (3 s, C-6, C-4, C-2). IR (ATR): v = 3060–2850 (=C–H, C–H), 1605–1545 cm^{-1} (C=C, C=N). HRMS (ESI): *m/z* $[M+H]^+$ calcd for $C_{23}H_{27}N_2O$ 347.2118, found: 347.2131.

Reaction of pyrimidine *N*-oxide 1 with acetic anhydride in THF: According to the general procedure, pyrimidine *N*-oxide **1** (0.183 g, 0.672 mmol), and acetic anhydride (1.5 mL) in THF (3 mL) afforded after purification by flash chromatography (silica gel, hexanes/EtOAc, 10:1) compound **3** (0.015 g, 8%) as colorless oil, a mixture of **4** and **5** (0.016 g, 7% **4**, 2% **5**), compound **7** (0.016 g, 7%) as pale yellow oil, and a mixture of **2** and **7** (0.119 g, 21% **2**, 34% **7**).

4-*tert*-Butyl-5-methoxy-2-phenyl-6-[(tetrahydrofuran-2-yl)methyl]-pyrimidine (7): ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.46 (s, 9 H, *t*-Bu), 1.67–1.75, 1.88–2.01, 2.10–2.19 (3 m, 1 H, 2 H, 1 H, CH_2), 2.89 (dd, *J* = 6.7, 14.4 Hz, 1 H, 6-CH_2), 3.26 (dd, *J* = 6.5, 14.4 Hz, 1 H, 6-CH_2), 3.73–3.80, 3.88–3.97 (2 m, 1 H each, CH_2), 3.82 (s, 3 H, OMe), 4.61 (m_c, 1 H, OCH), 7.38–7.48, 8.39–8.45 (2 m, 3 H, 2 H, Ph). ^{13}C{^{1}H} NMR ($CDCl_3$, 125.8 MHz): δ = 25.7 (t, CH_2), 29.3, 38.4 (q, s, *t*-Bu), 31.5, 37.7 (2 t, CH_2), 62.0 (q, OMe), 67.8 (t, OCH_2), 77.8 (d, OCH), 127.9, 128.2, 129.6, 138.1 (3 d, s, Ph), 150.8 (s, C-5), 157.2, 161.0, 168.2 (3 s, C-6, C-4, C-2). IR (ATR): ν = 3090–2850 (=C–H, C–H), 1585–1545 cm^{-1} (C=C, C=N). HRMS (ESI): *m/z* $[M+H]^+$ calcd for $C_{20}H_{27}N_2O_2$ 327.2067, found: 327.2066.

Reaction of pyrimidine *N*-oxide 1 with acetic anhydride in cyclohexane: According to the general procedure, pyrimidine *N*-oxide **1** (0.182 g, 0.669 mmol), and acetic anhydride (1.5 mL) in cyclohexane (3 mL) afforded after purification by flash chromatography (silica gel, hexanes/EtOAc, 8:1) compound **2** (0.064 g, 31%) as colorless crystals, a mixture of **3** and **8** (0.070 g, 15% **3**, 17% **8**) and a mixture of **4**, **5** and **8** (0.010 g, 2% **4**, 2% **5**, 1% **8**).

Data assigned to **4-*tert*-butyl-5-methoxy-6-[(cyclohexyl)methyl]-2-phenylpyrimidine (8)**: ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.49 (s, 9 H, *t*-Bu), 1.10–1.37, 1.65–1.78 (2 m, 6 H, 4 H, CH_2), 2.06–2.15 (m, 1 H, CH), 2.76 (d, *J* = 7.1 Hz, 2 H, $PyrCH_2$), 3.78 (s, 3 H, OMe), 7.41–7.50, 8.46–8.51 (2 m, 3 H, 2 H, Ph). ^{13}C{^{1}H} NMR ($CDCl_3$, 125.8 MHz): δ = 25.1, 26.3, 26.5 (3 t, CH_2), 29.3, 38.2 (q, s, *t*-Bu), 33.4 (t, CH_2), 37.0 (d, CH), 61.8 (q, OMe), 128.0, 128.3, 129.6, 138.3 (3 d, s, Ph), 151.1 (s, C-5), 157.2, 163.0, 167.8 (3 s, C-6, C-4, C-2). IR (ATR): ν = 3035–2850 (=C–H, C–H), 1585–1545 cm^{-1} (C=C, C=N). HRMS (ESI): *m/z* $[M+H]^+$ calcd for $C_{22}H_{31}N_2O$ 339.2431, found: 339.2411.

Reaction of pyrimidine *N*-oxide 1 with acetic anhydride in the presence of TEMPO: According to the general procedure, pyrimidine *N*-oxide **1** (0.647 g, 2.37 mmol), TEMPO (0.545 g, 3.49 mmol) and acetic anhydride (3 mL) afforded after purification by flash chromatography (silica gel, hexanes/EtOAc, 15:1 to 8:1) compound **3** (0.038 g, 6%) as colorless oil, a mixture of **4**, **5** and **9** (0.225 g, 2% **4**, 2% **5**, 20% **9**) and compound **2** (0.174 g, 23%) as colorless crystals.

4-(*tert*-Butyl)-5-methoxy-2-phenyl-6-{[(2,2,6,6-tetramethylpiperidin-1-yl)oxy]methyl}pyrimidine (9): ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.15 (s, 6 H, Me), 1.30–1.65 (m, 12 H, CH_2, Me), 1.43 (s, 9 H, *t*-Bu), 3.93 (s, 3 H, OMe), 5.03 (s, 2 H, 6-CH_2), 7.39–7.50, 8.45–8.52 (2 m, 3 H, 2 H, Ph). ^{13}C{^{1}H} NMR ($CDCl_3$, 101.8 MHz): δ = 17.1 (t, CH_2), 20.3 (q, Me), 29.2, 38.3 (q, s, *t*-Bu), 33.1 (q, Me), 40.0 (t, CH_2), 60.2 (s, N*C*Me_2), 63.5 (q, OMe), 75.4 (t, 6-CH_2), 128.0, 128.3, 129.7, 138.0 (3 d, s, Ph), 151.0 (s, C-5), 157.4, 158.2, 169.1 (3 s, C-6, C-4, C-2). IR (ATR): v = 3075–2815 (=C–H, C–H), 1585–1545 cm^{-1} (C=C, C=N). HRMS (ESI): *m/z* $[M+H]^+$ calcd for $C_{22}H_{29}N_3O_2$ 412.2934, found: 412.2958.

(6-*tert*-Butyl-5-methoxy-2-phenylpyrimidin-4-yl)methyl 2-phenyl acetate (12): According to the general procedure, pyrimidine *N*-oxide **1** (0.181 g, 0.665 mmol) and 2-phenylacetic anhydride (0.528 g, 2.07 mmol) afforded after purification by flash chromatography (silica gel, hexanes/EtOAc, 10:1 to 4:1) compound **12** (0.072 g, 28%) as pale yellow oil and **6** (0.107 g, 46%, contaminated with traces of **4** and **5**). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.48 (s, 9 H, *t*-Bu), 3.77 (s, 3 H, OMe), 3.82 (s, 2 H, C*H*$_2$Ph), 5.35 (s, 2 H, 4-CH_2), 7.25–7.39, 7.42–7.48, 8.34–8.41 (3 m, 5 H, 3 H, 2 H, Ph). ^{13}C{^{1}H} NMR ($CDCl_3$, 101.8 MHz): δ = 29.2, 38.2 (q, s, *t*-Bu), 33.6 (t, *C*H$_2$Ph), 33.8 (t, 4-CH_2), 61.7 (q, OMe), 126.0, 128.0, 128.35, 128.4, 128.5, 129.8, 138.1, 141.8 (6 d, 2 s, Ph), 150.5 (s, C-5), 157.4, 162.5, 167.3 (3 s, C-6, C-4, C-2). IR (ATR): ν = 3160–2870 (=C–H, C–H), 1740 (C=O), 1600–1545 cm^{-1} (C=C, C=N). HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{24}H_{27}N_2O_3$ 391.2016, found: 391.2052.

(6-(*tert*-Butyl)-5-methoxy-2-phenylpyrimidin-4-yl)methyl 2-cyclopropyl acetate (13): According to the general procedure, pyrimidine *N*-oxide **1** (0.080 g, 0.294 mmol) and 2-cyclopropylacetic anhydride (0.7 mL) afforded after purification by flash chromatography (silica gel, hexanes/EtOAc, 8:1 to 4:1) compound **13** (0.049 g, 50%) as colorless oil, a mixture of **14** and **15** (0.070 g, 14% **14**, 2% **15**) and a mixture of **4**, **5** and **15** (0.010 g, 4% **4**, 3% **5**, 6% **15**). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 0.15–0.25, 0.56–0.61 (2 m, 4 H each, Cp), 1.14–1.30 (m, 1 H, CH), 1.48 (s, 9 H, *t*-Bu), 2.40 (d, *J* = 7.1 Hz, 2 H, $COCH_2$), 3.86 (s, 3 H, OMe), 5.35 (s, 2 H, 4-CH_2), 7.41-7.48, 8.40–8.45 (2 m, 3 H, 2 H, Ph). ^{13}C{^{1}H} NMR ($CDCl_3$, 125.8 MHz): δ = 4.4, 6.8 (t, d, Cp), 29.1, 38.4 (q, s, *t*-Bu), 39.3 (t, CH_2), 61.7 (t, CH_2O), 62.5 (q, OMe), 128.0, 128.3, 129.9, 137.7 (3 d, s, Ph), 150.3 (s, C-5), 156.7, 157.8, 169.1 (3 s, C-6, C-4, C-2), 172.9 (s, CO). IR (ATR): ν = 3090–2865 (=C–H, C–H), 1740 (C=O), 1585–1535 cm^{-1} (C=C, C=N). HRMS (ESI): *m/z* $[M + Na]^+$ calcd for $C_{21}H_{25}NaN_2O_3$ 377.1836, found: 377.1833. Anal. calcd. for $C_{21}H_{26}N_2O_3$ (354.5): C 71.16, H 7.39, N 7.90; found: C 71.16, H 7.44, N 7.93.

Analytical data of **4-(*tert*-Butyl)-6-[(2-cyclopropyl)ethyl]-5-methoxy-2-phenylpyrimidine (14)**: ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 0.08–0.14, 0.42–0.48 (2 m, 4 H each, Cp), 0.77–0.89 (m, 1 H, CH), 1.48 (s, 9 H, *t*-Bu), 1.70–1.82 (m, 2 H, CH_2), 2.83–2.95 (m, 2 H, 6-CH_2), 3.78 (s, 3 H, OMe), 7.38–7.48, 8.38–8.47 (2 m, 3 H, 2 H, Ph). ^{13}C{^{1}H} NMR ($CDCl_3$, 125.8 MHz): δ = 4.6, 11.1 (t, d, Cp), 29.1, 38.4 (q, s, *t*-Bu), 31.8, 33.1 (2 t, CH_2), 61.8 (q, OMe), 128.0, 128.3, 129.9, 138.3 (3 d, s, Ph), 150.7 (s, C-5), 156.7, 163.7, 168.0 (3 s, C-6, C-4, C-2). IR (ATR): ν = 3080–2840 (=C–H, C–H), 1585–1545 cm^{-1} (C=C, C=N). HRMS (ESI): *m/z* $[M + H]^+$ calcd for $C_{20}H_{27}N_2O$ 313.2274, found: 313.2265.

NMR data assigned to **4-(*tert*-Butyl)-5-methoxy-6-(pent-4-en-1-yl)-2-phenylpyrimidine (15)**: ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.47 (s, 9 H, *t*-Bu), 1.85–2.02, 2.15–2.20 (2 m, 2 H each, CH_2), 2.80–2.87 (m, 2 H, 6-CH_2), 3.72 (s, 3 H, OMe), 4.97–5.09, 5.50–5.90 (2 m, 2 H, 1 H, HC=CH_2), 7.23–7.33 (m, 3 H, Ph). ^{13}C{^{1}H} NMR ($CDCl_3$, 125.8 MHz): δ = 29.2, 38.2 (q, s, *t*-Bu), 27.1, 31.2, 33.7 (3 t, CH_2), 61.7 (q, OMe), 115.0 (t, =CH_2), 128.3, 129.6, 138.2 (2 d, s, Ph), 138.5 (d, =CH), 150.8 (s, C-5), 157.2, 162.6, 168.0 (3 s, C-6, C-4, C-2).

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Conflict of Interest

The authors declare no conflict of interest.

Data Availability Statement

The data that support the findings of this study are available in the supplementary material of this article.

Keywords: heterocycles · quantum chemical calculations · radicals · rearrangement · reaction mechanism

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