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Hydrogen Abstraction from Cyclic Amines by the Cumyloxyl and Benzyloxyl Radicals. The Role of Stereoelectronic Effects and of Substrate/Radical Hydrogen Bonding

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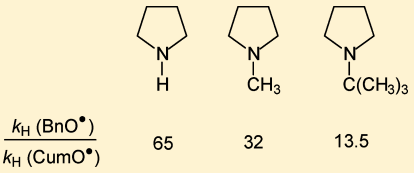
Supporting Information

ABSTRACT: A kinetic study on the hydrogen abstraction reactions from cyclic amines and diamines (pyrrolidines, piperidines, morpholines, and piperazines) by the cumyloxyl (CumO$^\bullet$) and benzyloxyl (BnO$^\bullet$) radicals was carried out. The reactions with CumO$^\bullet$ were described in all cases as *direct* hydrogen abstractions. The differences in the hydrogen abstraction rate constant (k_H) were explained in terms of the different number of abstractable hydrogen atoms, the operation of stereoelectronic effects, and, with the morpholines, on the basis of polar effects. Significantly higher k_H values were measured for the reactions of the amines with BnO$^\bullet$. This behavior was explained on the basis of a mechanism that proceeds through the rate-determining formation of a hydrogen bonded pre-reaction complex between the radical α-C−H and the nitrogen lone pair followed by hydrogen abstraction within the complex. A decrease in k_H was observed going from secondary to tertiary amines and, with tertiary amines, on increasing steric hindrance at nitrogen, pointing toward the important role of steric and electronic effects on pre-reaction complex formation. These results expand previous findings contributing to a detailed mechanistic description of the reactions of alkoxyl radicals with amines, showing that structural effects in both the substrate and the radical can play a dramatic role and providing new information on the role of substrate/radical interactions on these processes.

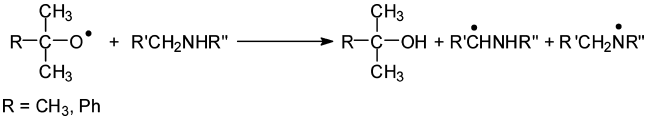


INTRODUCTION

Alkoxyl radicals are an important class of oxygen centered radicals that are involved in a variety of chemical and biological processes.[1−4] Hydrogen abstraction represents one of the most important reactions of these radicals, and accordingly, a large number of studies have been devoted to the mechanistic investigation of these processes.[5−15] Among the hydrogen atom donors employed in these studies, aliphatic amines have attracted great interest. These substrates are characterized by electron-rich α-C−H bonds and undergo hydrogen abstraction by electron-poor radicals such as alkoxyls,[16] with relatively high rate constants ($k_H \sim 10^8$ M^{-1} s^{-1} at room temperature in acetonitrile solution). Accordingly, a rather detailed description of the role of structural and solvent effects on hydrogen abstraction reactions from alkylamines by alkoxyl radicals has been provided, limited however to the reactions of two tertiary alkoxyl radicals: the *tert*-butoxyl ((CH$_3$)$_3$CO$^\bullet$, *t*BuO$^\bullet$) and cumyloxyl (PhC(CH$_3$)$_2$O$^\bullet$, CumO$^\bullet$) radicals.[17−25] These studies have shown that hydrogen abstraction reactions from the α-C−H bonds of alkylamines are generally entropy controlled,[19] and that the reaction is most rapid when the α-C−H bond being broken can be eclipsed with the nitrogen lone pair, indicating that stereoelectronic effects play an important role in these reactions.[19,20,24] With primary and secondary alkylamines, competition between α-C−H and N−H abstraction to give α-aminoalkyl and aminyl radicals, respectively, is generally observed as described in Scheme 1.[20−24]

The greater importance of the former pathway as compared to the latter one has been explained on the basis of the significantly higher BDE of a N−H bond as compared to α-C−H bonds.

Scheme 1



In order to obtain information on the role of alkoxyl radical structure on these processes, we have recently carried out detailed time-resolved kinetic studies in acetonitrile solution on the hydrogen abstraction reactions from primary, secondary, and tertiary alkylamines by CumO$^\bullet$ with comparison to the primary alkoxyl radical benzyloxyl (PhCH$_2$O$^\bullet$, BnO$^\bullet$).[26−28] With all the amines investigated, an increase in reactivity has been observed on going from CumO$^\bullet$ to BnO$^\bullet$, as measured by the rate constant ratios (k_H(BnO$^\bullet$)/k_H(CumO$^\bullet$)) that varied between 2.8 for the reactions of the two radicals with a relatively hindered amine such as triisobutylamine (TIBA), and 3380 for the reactions with *tert*-octylamine (TOA). Quite importantly, the highest (k_H(BnO$^\bullet$)/k_H(CumO$^\bullet$)) ratios have been observed with amines that undergo relatively slow hydrogen abstraction by CumO$^\bullet$, namely 1,4-diazabicyclo-[2,2,2]octane (DABCO), 1-azabicyclo[2,2,2]octane (ABCO), 2,2,6,6-tetramethylpiperidine (TMPPD), and TOA

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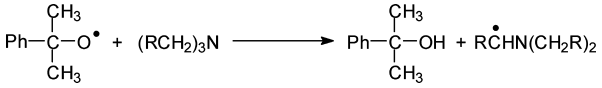
((k_H(BnO$^\bullet$)/k_H(CumO$^\bullet$) = 1094, 2027, 1182, and 3380, respectively). The lower rate constants measured for the reactions of CumO$^\bullet$ with ABCO and DABCO have been explained on the basis of a stereoelectronic effect, because in these substrates, the α-C−H bonds are held with a dihedral angle of ca. 60°, in a conformation that does not allow efficient overlap with the nitrogen lone pair.[19,20,24] With TMPPD and TOA, hydrogen abstraction can only occur from the N−H bond, a feature that, as mentioned above, accounts for the low k_H values measured for their reactions with CumO$^\bullet$ (k_H = 3.13 × 10^6, and 1.34 × 10^6 M^{-1} s^{-1}, respectively).[26] Along these lines, the very high (k_H(BnO$^\bullet$)/k_H(CumO$^\bullet$) ratios observed for the reactions of ABCO, DABCO, TMPPD, and TOA clearly indicate that stereoelectronic effects and N−H BDEs play a negligible role in the reactions of these substrates with BnO$^\bullet$.

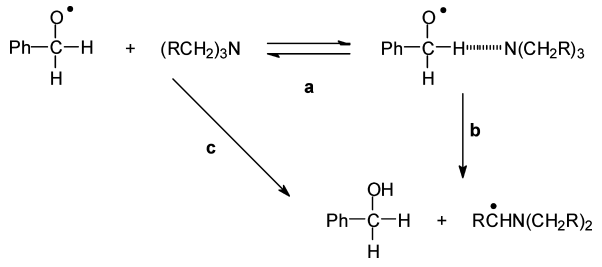
The large differences in reactivity observed for the reactions of CumO$^\bullet$ and BnO$^\bullet$ with alkylamines have been explained on the basis of two different mechanisms. The reactions with CumO$^\bullet$ have been described in terms of a *direct* hydrogen abstraction mechanism, indicative of a reaction that proceeds through the interaction of the radical center with the amine α-C−H and/or N−H bond, in line with previous studies,[18−24] as described in Scheme 2 for a generic tertiary amine.

Scheme 2



The reactions of BnO$^\bullet$ have been instead described in terms of a mechanism that proceeds through the rate determining formation of a pre-reaction complex, where the BnO$^\bullet$ α-C−H engages in hydrogen bonding with the amine lone pair, followed by hydrogen abstraction within the complex (Scheme 3, paths **a**−**b**). Evidence in favor of this mechanistic picture has also been provided through computational studies.[26,28]

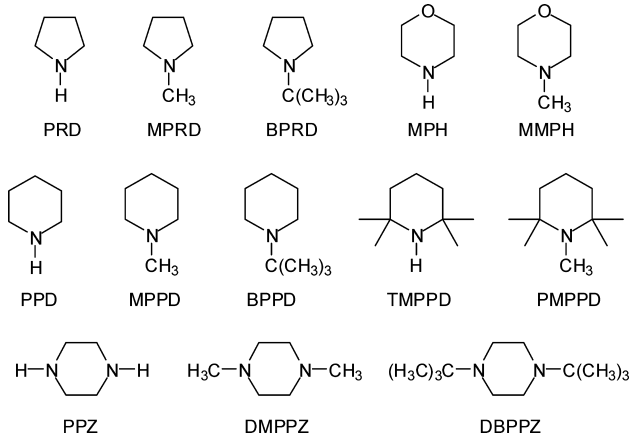
Scheme 3



Efficient complex formation is possible only for relatively unhindered amines. With TIBA, steric hindrance prevents the formation of a sufficiently stable complex, and its reaction with BnO$^\bullet$ has been described as a *direct* hydrogen abstraction (Scheme 3, path **c**, R = CH(CH$_3$)$_2$).[28]

In view of the relevance of these processes, and in order to develop a deeper mechanistic understanding of the role of structural effects on the hydrogen abstraction reactions from amines by alkoxyl radicals, in particular for what concerns the role of stereoelectronic effects and of substrate−radical hydrogen bond interactions, we have extended the kinetic studies to the reactions of CumO$^\bullet$ and BnO$^\bullet$ with a series of secondary and tertiary cyclic amines and diamines, namely, pyrrolidine (PRD), *N*-methylpyrrolidine (MPRD), *N*-*tert*-butylpyrrolidine (BPRD), piperidine (PPD), *N*-methylpiperidine (MPPD), *N*-*tert*-butylpiperidine (BPPD), morpholine (MPH), *N*-methylmorpholine (MMPH), piperazine (PPZ), and 1,4-di-*tert*-butylpiperazine (DBPPZ), whose structures are displayed in Chart 1. Also included are the structures of the

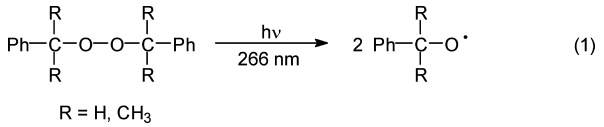
Chart 1



previously investigated substrates 2,2,6,6-tetramethylpiperidine (TMPPD), 1,2,2,6,6-pentamethylpiperidine (PMPPD), and 1,4-dimethylpiperazine (DMPPZ).[26,27]

RESULTS

The reactions of CumO$^\bullet$ and BnO$^\bullet$ with the amines displayed in Chart 1 have been studied using the laser flash photolysis (LFP) technique. The alkoxyl radicals have been generated by 266 nm LFP of nitrogen-saturated acetonitrile solutions (T = 25 °C) containing the parent peroxides, according to eq 1.



(1)

CumO$^\bullet$ and BnO$^\bullet$ are characterized by a broad absorption band in the visible region of the spectrum that, in acetonitrile solution, is centered at 485 and 460 nm, respectively.[29,30] Under the experimental conditions employed, the most important decay pathway of CumO$^\bullet$ is represented by C−CH$_3$ β-scission,[12,29] while the decay of BnO$^\bullet$ is mainly attributed to hydrogen abstraction from the solvent.[31]

The kinetic studies have been carried out by LFP in acetonitrile solution following the decay of the CumO$^\bullet$ and BnO$^\bullet$ visible absorption bands at 490 and 460 nm, respectively, as a function of the amine concentration. The reactions of MPPD and MMPH with CumO$^\bullet$ have also been studied in 2,2,4-trimethylpentane (isooctane) solution.

Excellent linear relationships have been obtained when the observed rate constants (k_{obs}) have been plotted against substrate concentration. The second-order rate constants for hydrogen abstraction from the substrates (k_H) by the alkoxyl radicals have been obtained from the slopes of these plots. As an example, Figure 1 shows the plots of k_{obs} vs [PPD] for the reactions of this amine with CumO$^\bullet$ (filled circles) and BnO$^\bullet$ (open circles) for measurements carried out in acetonitrile solution at T = 25 °C.

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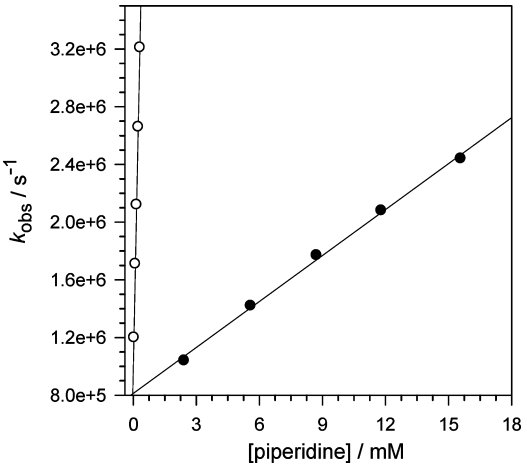

Figure 1. Plots of the observed rate constant (k_{obs}) against [piperidine] for the reactions of the cumyloxyl radical (CumO•, filled circles) and benzyloxyl radical (BnO•, open circles), measured in nitrogen-saturated acetonitrile solution at T = 25 °C by following the decay of CumO• and BnO• at 490 and 460 nm, respectively. From the linear regression analysis: CumO• + PPD: intercept = 8.13×10^5 s^{-1}, $k_H = 1.06 \times 10^8$ M^{-1} s^{-1}, $r^2 = 0.9975$; BnO• + PPD: intercept = 9.60×10^5 s^{-1}, $k_H = 7.04 \times 10^9$ M^{-1} s^{-1}, $r^2 = 0.9982$.

Additional plots for the hydrogen abstraction reactions by CumO• and BnO• from the other amines are displayed in the Supporting Information (Figures S1−S20). All the kinetic data thus obtained are collected in Table 1 together with the pertinent k_H(BnO•)/k_H(CumO•) ratios. Also included in Table 1 are the rate constants obtained previously under analogous experimental conditions for the reactions of CumO• and BnO• with TMPPD,[26] PMPPD, and DMPPZ.[27]

Table 1. Second-Order Rate Constants (k_H) for the Reactions of the Cumyloxyl (CumO•) and Benzyloxyl (BnO•) Radicals with Secondary and Tertiary Cyclic Amines and Diamines

	k_H/M^{-1} s^{-1}[a]		
substrate[b]	CumO•	BnO•	k(BnO•)/k(CumO•)
PRD	$1.24 \pm 0.05 \times 10^8$	$8.03 \pm 0.03 \times 10^9$	65
MPRD	$1.91 \pm 0.01 \times 10^8$	$6.2 \pm 0.2 \times 10^9$	32
BPRD	$3.0 \pm 0.1 \times 10^8$	$4.05 \pm 0.09 \times 10^9$	13.5
PPD	$1.07 \pm 0.01 \times 10^8$	$7.00 \pm 0.04 \times 10^9$	65
MPPD	$1.22 \pm 0.04 \times 10^8$	$5.61 \pm 0.08 \times 10^9$	46
	$2.38 \pm 0.04 \times 10^8$[c]		
BPPD	$1.26 \pm 0.05 \times 10^8$	$3.1 \pm 0.3 \times 10^9$	25
TMPPD[d]	$3.13 \pm 0.02 \times 10^6$	$3.7 \pm 0.1 \times 10^9$	1182
PMPPD[e]	$1.71 \pm 0.02 \times 10^8$	$4.26 \pm 0.07 \times 10^9$	25
MPH	$5.0 \pm 0.2 \times 10^7$	$5.69 \pm 0.05 \times 10^9$	114
MMPH	$4.32 \pm 0.06 \times 10^7$	$5.1 \pm 0.2 \times 10^9$	118
	$9.6 \pm 0.1 \times 10^7$[c]		
PPZ	$2.26 \pm 0.01 \times 10^8$	$9.5 \pm 0.1 \times 10^9$	42
DMPPZ[e]	$1.16 \pm 0.04 \times 10^8$	$8.0 \pm 0.1 \times 10^9$	69
DBPPZ	$1.32 \pm 0.02 \times 10^8$	$5.8 \pm 0.1 \times 10^9$	44

[a]Measured in N_2-saturated acetonitrile solution at T = 25 °C by 266 nm LFP, [dicumyl peroxide] = 10 mM or [dibenzyl peroxide] = 8 mM. k_H values were determined from the slope of the k_{obs} vs [substrate] plots, where in turn k_{obs} values were measured following the decay of the CumO• or BnO• visible absorption bands at 490 and 460 nm, respectively. Average of at least two determinations. [b]For substrate structures, see Chart 1. [c]Measured in isooctane solution. [d]Ref 26. [e]Ref 27.

DISCUSSION

Starting from the reactions of CumO•, the kinetic data displayed in Table 1 show that, within the pyrrolidine, piperidine, and piperazine series, the k_H values vary in a limited range, between 1.07×10^8 M^{-1} s^{-1} for piperidine (PPD) and 3.0×10^8 M^{-1} s^{-1} for *N*-*tert*-butylpyrrolidine (BPRD). In this comparison, it is, however, important to take into account that these substrates are characterized by different numbers of α-C−H bonds, i.e., of the hydrogen atoms that are known to be preferentially abstracted by alkoxyl radicals.[17−25]

With PRD and PPD, our measured k_H values for reaction with CumO• are in good agreement with the literature values for the corresponding reactions with *t*BuO• ($k_H = 9.5 \times 10^7$ and 7.9×10^7 M^{-1} s^{-1}, respectively, at T = 22 °C, in benzene/di-*tert*-butylperoxide 1:2),[24] in line with the very similar hydrogen abstraction reactivities generally displayed by *t*BuO• and CumO•.[20,32−34]

Lower k_H values have been measured for the reactions of CumO• with morpholine (MPH) and *N*-methylmorpholine (MMPH) ($k_H = 5.0 \times 10^7$ and 4.32×10^7 M^{-1} s^{-1}, respectively). These values are between 2 and 3 times lower than the values measured for the corresponding reactions of PPD and *N*-methylpiperidine (MPPD), where the observed decrease in reactivity clearly reflects the replacement of the CH_2 in position 4 of the piperidine ring with an oxygen atom (see later).

Previous studies on the hydrogen abstraction reactions from tertiary amines by *t*BuO• and CumO• have clearly shown that these reactions can be described in terms of the *direct* hydrogen abstraction mechanism displayed in Scheme 2, with the reaction that is most rapid when the α-C−H bond is collinear with the nitrogen lone pair, thus allowing the best orbital overlap.[19,20,24] This overlap determines a decrease in the α-C−H BDE and a corresponding stabilization of the α-aminoalkyl radical formed after hydrogen abstraction. Along these lines, a *direct* hydrogen abstraction mechanism can also be applied for the description of the reactions of CumO• with the cyclic amines and diamines displayed in Chart 1, where the differences in reactivity observed for the reactions with the pyrrolidines, piperidines, and piperazines can be conveniently explained on the basis of the different number of abstractable hydrogen atoms and of the contribution of stereoelectronic effects.

In the pyrrolidine series, the increase in k_H observed on going from PRD to MPRD reasonably reflects the increased number of α-C−H bonds (4 for PRD and 7 for MPRD), taking in particular into account that with tertiary alkoxyl radicals significantly higher rate constants have been measured for hydrogen abstraction reactions from α-C−H bonds as compared to N−H bonds ($k_{C-H} = 1.71 \times 10^8$ M^{-1} s^{-1}, for the reaction of CumO• with 1,2,2,6,6-pentamethylpiperidine (PMPPD),[27] as compared to $k_{N-H} = 3.13 \times 10^6$ M^{-1} s^{-1} for the corresponding reaction with 2,2,6,6-tetramethylpiperidine (TMPPD);[26] see Table 1). Accordingly, when corrected for the different number of abstractable α-C−H hydrogens, very similar rate constant values are observed for the reactions of PRD and MPRD with CumO•: $k_{H(corr)} = 3.1 \times 10^7$ and 2.7×10^7 M^{-1} s^{-1}, respectively.

Quite interestingly, an increase in k_H has been observed on going from PRD and MPRD to BPRD (where hydrogen

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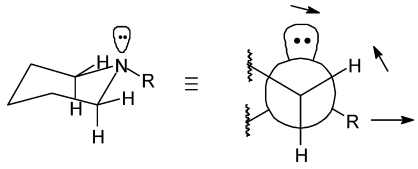
abstraction can only occur from the ring carbons), despite the same number of α-C−H bonds in PRD and BPRD, and of the decreased number of α-C−H bonds on going from MPRD to BPRD. These results show that, as compared to PRD and MPRD, BPRD is activated toward hydrogen abstraction by CumO•, indicating a peculiar role for the *tert*-butyl substituent and pointing toward the operation of stereoelectronic effects. It is reasonable to propose that in BPRD the bulkyness of the *tert*-butyl group favors a conformation that allows a higher degree of overlap between an α-C−H bond and the nitrogen lone pair, as compared to PRD and MPRD, leading to the observed increase in rate constant.

As compared to the pyrrolidine series, smaller differences in reactivity have been observed for the piperidine and piperazine series. Almost identical k_H values have been measured for the reactions of CumO• with PPD, MPPD, and BPPD, whereas a decrease in k_H has been observed on going from PPZ and DMPPZ to DBPPZ. These results can be reasonably explained on the basis of the contribution of the two factors discussed above (number of abstractable hydrogen atoms and stereoelectronic effects) within these series, where however the relative importance of these contributions is very difficult to establish. On a per hydrogen basis, PPD and PPZ undergo hydrogen abstraction from the ring α-C−H bonds with almost identical rate constants ($k_{H(corr)}$ = 2.7 × 10^7 and 2.8 × 10^7 M^{-1} s^{-1}, respectively). Comparison between the k_H value measured for PMPPD, that as mentioned above can only undergo hydrogen abstraction from the *N*-methyl group,[26] and those measured for MPPD and DMPPZ, clearly shows a decrease in hydrogen abstraction reactivity from the *N*-methyl groups on going from the former substrate to the latter ones. For PMPPD and DMPPZ, this behavior has been previously explained in terms of the operation of stereoelectronic effects. Calculations have shown that it is easier for PMPPD than DMPPZ to orient its *N*-methyl α-C−H bond so that it is properly aligned with the nitrogen lone pair in the most suited conformation for hydrogen atom abstraction.[27] A similar explanation will reasonably account for the decrease in reactivity observed on going from PMPPD to MPPD.

Comparison between the k_H values measured for PMPPD, PPD, MPPD, PPZ, and DMPPZ also indicates that the presence of *N*-methyl groups leads to a significant decrease in the reactivity of the ring α-C−H bonds. With PPD, MPPD, PPZ, and DMPPZ, optimal overlap between the ring α-C−H bonds and the nitrogen lone pair requires a certain degree of ring distortion, and the attainment of such conformation is expected to be energetically more costly for MPPD and DMPPZ as compared to PPD and PPZ.

Along these lines, the very small increase in k_H observed in the piperidine and piperazine series on going from the *N*-methyl substituted substrates to the *N*-*tert*-butyl substituted ones indicates that, also with six-membered ring substrates, the presence of *N*-*tert*-butyl substituents activates the ring α-C−H bonds toward hydrogen abstraction by CumO•. An explanation for this behavior can be put forward on the basis of the well-known stretching of six-membered rings induced by the presence of bulky substituents,[35] that, as compared to the *N*-methyl substituted substrates, makes easier the attainment of the most suited conformation for hydrogen abstraction, as shown in Scheme 4 (R = Me, *t*-Bu), where ring stretching determined by the replacement of the *N*-methyl by *tert*-butyl is expected to increase the degree of overlap between the equatorial α-C−H bonds and the nitrogen lone pair.

Scheme 4



Quite interestingly, the observation of significantly higher k_H values for the reactions of BPPD and DBPPZ with CumO• as compared to those measured for the corresponding reactions of ABCO and DABCO (for which k_H = 3.7 × 10^6 and 9.6 × 10^6 M^{-1} s^{-1}, respectively),[20] where as mentioned above the α-C−H bonds are held in a conformation that does not allow efficient overlap with the nitrogen lone pair,[19,20,24] clearly indicates that, despite the presence of bulky substituents on nitrogen, the six-membered ring of these substrates is still sufficiently flexible to achieve efficient overlap between the equatorial α-C−H bonds and the nitrogen lone pair.

As mentioned above, among the different substrates the lowest k_H values have been measured for the reactions of CumO• with MPH and MMPH. Replacement of the CH_2 group in position 4 of the piperidine ring with oxygen leads to a substantial decrease in basicity (the protonated forms of MPH and PPD are characterized by pK_a values in DMSO (water) of 9.15 (8.49) and 10.85 (11.12), respectively),[36] and is also expected to decrease the electron density at the nitrogen α-C−H bonds. Along this line, the decrease in hydrogen abstraction reactivity observed on going from the piperidines to the morpholines can be reasonably explained on the basis of polar effects, because the electrophilic radical CumO• will abstract an hydrogen atom more rapidly from the former substrates as compared to the latter ones.[16]

We have also investigated whether these differences in reactivity may be a consequence of the interaction of the solvent with the oxygen lone pairs of the morpholine substrates. On the basis of the hypothesis that this interaction may influence the conformational equilibrium leading to a decrease in reactivity of the morpholines as compared to the corresponding piperidines, we have studied the reactions of CumO• with MPPD and MMPH in the noncoordinating solvent isooctane. The kinetic data displayed in Table 1 show a very similar behavior for the two substrates, with comparable increases in the k_H value on going from acetonitrile to isooctane ($k_{H(isooctane)}/k_{H(MeCN)}$ = 1.95 and 2.22, for MPPD and MMPH, respectively). These results clearly indicate that the hypothesis of a specific solvent effect on the conformational equilibria of the morpholine substrates can be discarded. A similar kinetic effect has been previously observed for the corresponding reactions of CumO• with triethylamine ($k_{H(isooctane)}/k_{H(MeCN)}$ = 1.45).[17,27] This behavior has been explained on the basis of a hydrogen bond interaction between the nitrogen center and the solvent that decreases the degree of overlap between the α-C−H bond and the nitrogen lone pair in the transition state for hydrogen abstraction leading to a decrease in reactivity. Hydrogen bonding can take place only with acetonitrile that is a relatively weak hydrogen bond donor (HBD), as measured by Abraham's α_2^H parameter (α_2^H = 0.09),[37] and not with isooctane for which α_2^H = 0.00. The same explanation reasonably holds for the kinetic solvent effects observed in the reactions of CumO• with MPPD and MMPH.

The data displayed in Table 1 show that the k_H values measured for the reactions of BnO• with the cyclic amines and

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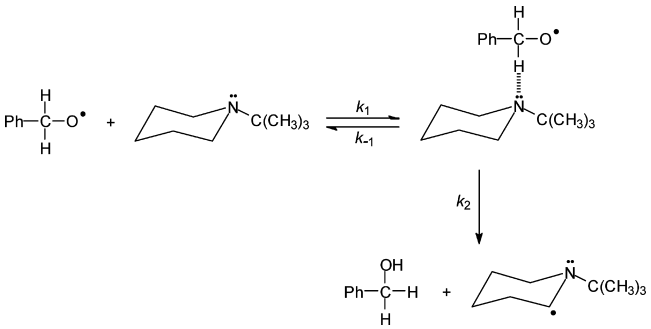
diamines are in all cases between 1 and 2 orders of magnitude higher than those measured for the corresponding reactions of CumO•, as quantitatively indicated by the rate constant ratios (k_H(BnO•)/k_H(CumO•)) that vary between 13.5 for the reactions with BPRD and 118 for the reactions with MMPH. These differences are similar to those observed previously for the reactions of these two radicals with a variety of alkylamines,[26−28] and can be explained accordingly, on the basis of the two mechanisms described in Schemes 2 and 3. As mentioned above, the reactions of the cyclic amines and diamines with CumO• can be described in all cases in terms of the *direct* hydrogen abstraction mechanism shown in Scheme 2 for a generic tertiary amine.

The reactions of BnO• proceed instead through the rate-determining formation of a hydrogen-bonded substrate−radical pre-reaction complex between the nitrogen lone pair and the radical α-C−H wherein fast hydrogen abstraction occurs, as described in Scheme 5 for BPPD, in close analogy to the mechanism described above for the reactions of BnO• with acyclic alkylamines (Scheme 3, paths **a**−**b**).

Scheme 5



In Scheme 5, k_1 and k_{-1} represent the rate constants for the formation and dissociation of the hydrogen-bonded pre-reaction complex, while k_2 is the rate constant for hydrogen abstraction within the complex. On the basis of our previous studies on the reactions of BnO• with alkylamines,[26−28] also for the cyclic amines and diamines employed in the present study $k_2 \gg k_{-1}$ reasonably applies. Accordingly, the reaction rate can be expressed as $v = k_1$ [substrate][BnO•], where the rate constant for complex formation k_1 corresponds to the k_H values displayed in Table 1 for the reactions of BnO• with the three substrates. These results provide additional information on the important role played by specific substrate−radical interactions in these processes, suggesting in particular that with BnO• the presence of a relatively strong hydrogen bond acceptor (HBA) site in the hydrogen atom donor promotes complex formation and preorganizes the reactants for hydrogen abstraction leading to large rate enhancements as compared to the corresponding reactions of radicals that cannot act as HBDs such as CumO•.

In the different series, a decrease in k_H is observed in all cases on going from the secondary to the tertiary amines, and, within the tertiary amines, on going from the *N*-methyl to the *N*-*tert*-butyl substituted amine, i.e., by increasing the steric hindrance of the substituent. A similar trend has been observed for the reactions of acyclic alkylamines with BnO•, where a decrease in k_H has been observed along different series on going from the primary to the secondary and tertiary amine.[26] This behavior has been explained on the basis of the combination of steric and electronic effects, and a common explanation can be put forward in the present study. The replacement of hydrogen by an alkyl group increases the steric hindrance around the nitrogen atom, decreasing in the same time the substrate HBA ability (as measured by Abraham's β_2^H parameter: β_2^H = 0.69−0.73 for primary and secondary amines, and 0.58−0.62 for tertiary amines (0.67 for triethylamine)).[38] Both factors will affect rate and efficiency of pre-reaction complex formation contributing to the observed kinetic behavior.

The importance of steric effects in the reactions BnO• with the amines is also evidenced by the slightly higher k_H values measured for the reactions of the unsubstituted and *N*-alkyl substituted pyrrolidines, piperidines, and piperazines as compared to the values measured for the corresponding reactions of secondary and tertiary acyclic alkylamines,[26,27] in line with the observation that the nitrogen lone pairs of these cyclic amines are expected to be more easily accessible to BnO• than those of the acyclic amines.

The slight decrease in reactivity observed on going from the piperidines to the morpholines can again be explained on the basis of the inductive effect of the oxygen atom. Replacement of a CH_2 group with an oxygen atom decreases the substrate HBA ability leading to lower rate constant for pre-reaction complex formation for the morpholines as compared to the piperidines.

In conclusion, the results presented above provide new information on the role of structural and electronic effects in both the radical and the substrate on hydrogen abstraction reactions from amines by alkoxyl radicals, expanding previous findings and leading to a very detailed mechanistic picture for the reactions of CumO• and BnO•. The reactions of CumO• with the cyclic amines and diamines can be described in all cases on the basis of a *direct* hydrogen atom abstraction mechanism where stereoelectronic effects play an important role. With BnO•, the reactions can be instead described in terms of the rate determining formation of a hydrogen-bonded substrate−radical pre-reaction complex followed by fast hydrogen abstraction. In these reactions, a major role is played by substrate HBA ability and by the accessibility of the nitrogen lone pair.

EXPERIMENTAL SECTION

Materials. Spectroscopic-grade acetonitrile and 2,2,4-trimethylpentane (isooctane) were used in the kinetic experiments. Pyrrolidine (PRD), *N*-methylpyrrolidine (MPRD), piperidine (PPD), *N*-methylpiperidine (MPPD), morpholine (MPH), *N*-methylmorpholine (MMPH), and piperazine (PPZ) were of the highest commercial quality available (≥99%) and were further purified prior to use by filtration over neutral alumina. The purity of the substrates was checked by GC prior to the kinetic experiments and was in all cases >99.5%.

N-*tert*-Butylpyrrolidine (BPRD), *N*-*tert*-butylpiperidine (BPPD), and 1,4-di-*tert*-butylpiperazine (DBPPZ) were prepared according to previously described procedures. BPRD and BPPD were prepared by reaction of *tert*-butylamine with 1,4-dibromobutane and 1,5-dibromopentane, respectively, in absolute ethanol in the presence of potassium carbonate.[39] DBPPZ was prepared by a slight modification of this procedure, by reaction of *N*,*N*′-di-*tert*-butylethylenediamine with 1,2-dibromoethane, where ethanol was replaced by DMSO. BPRD, BPPD, and DBPPZ were identified by ^{1}H NMR, showing spectral data in full agreement with the literature.[39,40]

^{1}H NMR ($CDCl_3$). BPRD: δ 2.64 (m, 4H), 1.77 (m, 4H), 1.09 (s, 9H). BPPD: δ 2.51 (m, 4H), 1.58 (m, 4H), 1.43 (m, 2H), 1.06 (s, 9H). DBPPZ: δ 2.56 (s, 4H, CH_2), 1.00 (s, 9H).

The purity of BPRD, BPPD, and DBPPZ used in the kinetic experiments was checked by GC and was in all cases >99.5%.

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Dicumyl peroxide was of the highest commercial quality available and was used as received. Dibenzyl peroxide was prepared in small portions by reaction of KO_2 with benzyl bromide in dry benzene, in the presence of 18-crown-6 ether, according to a previously described procedure.[30,41]

Laser Flash Photolysis Studies. LFP experiments were carried out with a laser kinetic spectrometer using the fourth harmonic (266 nm) of a Q-switched Nd:YAG laser, delivering 8 ns pulses. The laser energy was adjusted to ≤10 mJ/pulse by the use of the appropriate filter. A 3.5 mL Suprasil quartz cell (10 mm × 10 mm) was used in all experiments. Nitrogen-saturated solutions of dicumyl and dibenzyl peroxide (10 and 8 mM, respectively) were employed. These concentrations were chosen in order to ensure, in the presence of amines, prevalent absorption of the 266 nm laser light by the precursor peroxides. All the experiments were carried out at $T = 25 \pm 0.5$ °C under magnetic stirring. The observed rate constants (k_{obs}) were obtained by averaging 3−5 individual values and were reproducible to within 5%.

Second-order rate constants for the reactions of the cumyloxyl and benzyloxyl radicals with the amines were obtained from the slopes of the k_{obs} (measured following the decay of the cumyloxyl and benzyloxyl radical visible absorption bands at 490 and 460 nm, respectively) vs [amine] plots. Fresh solutions were used for every amine concentration. Correlation coefficients were in all cases >0.992. The given rate constants are the average of at least two independent experiments, with typical errors being ≤5%.

■ ASSOCIATED CONTENT

Supporting Information

Plots of k_{obs} vs amine concentration for the reactions of $CumO^{\bullet}$ and $BnO^{\bullet}$. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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