Articles

tert-Butylation of Quinolinium Cations and Quinoline *N*-Oxides by *tert*-Butylmercury Halides[1]

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In the presence of *t*-BuHgCl/KI the radical cations formed by the addition of *tert*-butyl radicals to C-2 of the quinolinium cation react in Me_2SO by proton loss followed by one-electron oxidation (**1a**, R = H, Me, Cl). For the *N*-methyl, or *N*-methoxyquinolinium cations proton loss is not observed and the radical cations react by one-electron reduction (**1b**, R = Me, Cl; **1c**, R = Me). With quinoline *N*-oxide and its 4-substituted derivatives the C-2 adduct radicals (**1d**, R = H, Me, Cl) are deprotonated by DABCO to yield after one-electron oxidation the 2-*tert*-butylquinoline *N*-oxides. The adduct radical cations formed by *t*-Bu• addition at the C-4 of quinolinium ions **2** seldom lose the C-4 proton but react by reduction, hydration, or in the case of 2-chloroquinoline *N*-oxide, dimerization. The loss of the proton from the 2-adducts **1** but not from the 4-adducts **2** seems to be stereoelectronic in origin. With *N*-methylquinolinium cation the addition of *t*-Bu• occurs selectively (>90%) at C-4 in contrast to the low selectivity observed in addition to quinolinium ion itself. However, with *N*-methoxyquinolinium perchlorate the major reaction products (70–90%) result from the addition of *t*-Bu• at C-2.

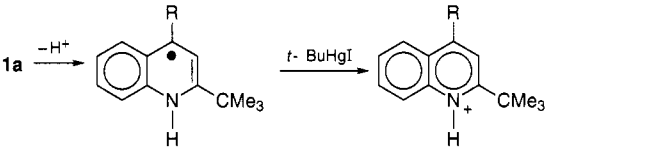
Introduction

The system *t*-BuHgCl/KI not only generates *t*-Bu• upon photolysis in Me_2SO but will serve as an oxidizing (*t*-BuHgI + e^- → *t*-Bu• + Hg^0 + I^-) or reducing (*t*-$BuHgI_2^-$ − e^- → *t*-Bu• + HgI_2) agent toward easily oxidizable or reducible radicals or radical ions.[2] Thus, in the presence of *t*-BuHgCl/KI the adduct radical cations formed by the addition of *t*-Bu• to a quinolinium cation can undergo either reduction or proton loss followed by oxidation. Previous work has demonstrated that the 2- and 4-*tert*-butylquinolinium adduct radical cations **1a** and **2a** with

1 **2**

a: X = H
b: X = Me
c: X = OMe
d: X = O⁻

R = H, Me, or Cl show quite different reactivities in the presence of *t*-BuHgI/KI in Me_2SO.[3] The adducts **1a** lose a proton to form an easily oxidized quinolinyl radical, reaction 1, while the adducts **2a** undergo electron transfer (reaction 2) with I^- or *t*-$BuHgI_2^-$ to form the 1,4-dihydroquinoline derivatives. These observations have been interpreted in terms of the rate of proton loss from **1a** or **2a**.[3] The argument was advanced that **2a** exists in a conformation that places H(4) in a quasi-equatorial position in the plane of the π-system of the radical cation.



For steric and stereoelectronic reasons this proton is lost slowly. On the other hand, **1a** would be expected to have a conformation with H(2) in a quasi-axial position. A large dihedral angle between the C(2)–H bond and the plane of the amine radical cation favors rapid proton loss. However, another explanation can be advanced. In **2a** there would not be much hindrance to the approach of *t*-$BuHgI_2^-$ to the amine radical cation center, and electron transfer would be expected to be fast. For **1a** this approach might be sterically hindered. Since **1a** might not be readily reduced, proton loss could occur leading to the observed substitution product. On the other hand, since **1a** is a more localized radical cation than **2a**, one might expect **1a** to undergo one-electron reduction more readily if steric effects are not important.

With certain radical cations **2a** where reduction does not occur readily, other reaction channels become operative. Thus, with R = *t*-Bu reductive electron transfer to **2a** is apparently sterically hindered and hydration of the radical cation becomes important (Scheme 1, R = *t*-Bu) leading to the stable 2,4-di-*tert*-butylquinoline hydrate, **3**.[3,4]

1,4-Dihydroquinolines without substituents at C-2 can react further with *t*-BuHgI/KI/*hν* to form tetrahydroquinolines, Scheme 2 (R = *t*-Bu), a process previously observed in the *tert*-butylation of the quinolinium ion.[3]

⊗ Abstract published in *Advance ACS Abstracts,* July 15, 1995.

(1) Electron Transfer Processes. 60.

(2) Russell, G. A.; Yao, C.-F.; Rajaratnam, R.; Kim, B. H. *J. Am. Chem. Soc.* **1991**, *113*, 373.

(3) Russell, G. A.; Rajaratnam, R.; Wang, L.; Shi, B. Z.; Kim, B. H.; Yao, C. F. *J. Am. Chem. Soc.* **1993**, *115*, 10596.

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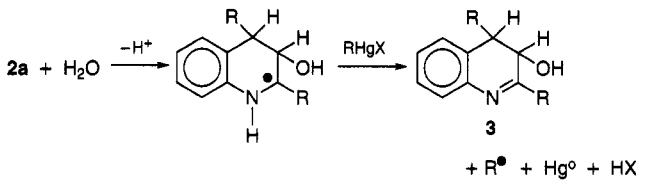
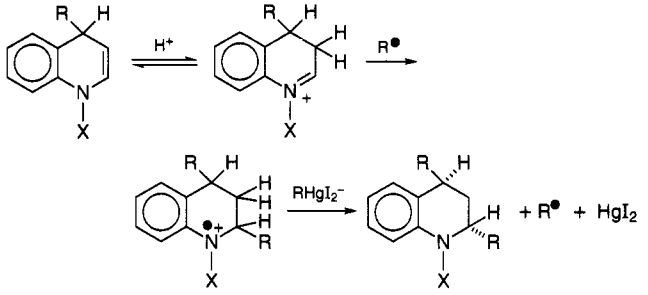
Scheme 1



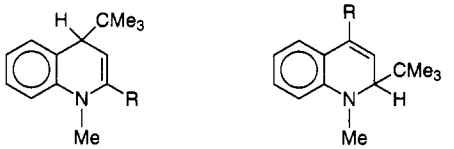
Scheme 2



In an attempt to understand the factors that control the reaction products derived from **1** and **2**, we have studied the *tert*-butylation of three additional series of quinoline derivatives, the *N*-methyl, and *N*-methoxyquinolinium salts and the quinoline *N*-oxides, substrates which could potentially produce **1b-d** and **2b-d**. The present results demonstrate that in iodide-promoted reactions, proton loss from **1** does not always occur in preference to reduction. Thus, we find that **1b** with R = Cl or Me undergoes reduction to form the isolable 1,2-dihydroquinoline derivatives while with **2b** (R = H) reduction leads to the 1,4-dihydroquinoline derivative which reacts further by Scheme 2 to form **4b**. The products observed are also most consistent with **1c** undergoing reduction with R = H or Me. However, in these cases further reactions result in the loss of the X substituent with aromatization of the quinoline ring. With quinoline *N*-oxides proton loss from the 2-adducts (**1d**) can be observed in the presence of DABCO. However, for the 4-adducts (**2d**) this process is not important.

Results and Discussion

***N*-Methylquinolinium Salts.** *N*-Methylquinaldinium iodide has been previously reported to yield **5b** in 90% yield upon photolysis with *t*-BuHgCl/KI in Me_2SO solution.[3] Sunlamp photolysis of *N*-methyllepidinium



iodide with 4 equiv of *t*-BuHgCl and 0–8 equiv of KI in Me_2SO for 2 h produced the 1,2-dihydroquinoline derivative **6b** in 85–90% yield. The adduct radical cation **1b** with R = Me is reduced by I^- and/or *t*-BuHgI_2^- without loss of the proton at C-2. The low acidity of the adduct radical cation may be connected with an expected increase in strain from the vicinal *t*-Bu and Me interactions upon deprotonation.

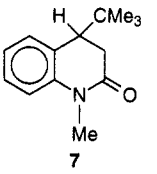
Table 1. Reaction of *N*-Methylquinolinium Iodide with 4 Equiv of *t*-BuHgCl in Me_2SO[a]

molar equiv			% yield[b]	
KI	PTSA	time, h	**5a**	**4b**
0	0	2	10	tr
4	0	0.5	86[c]	8
4	0	4	10	80
8	0	4	7	82
8	4	0.5	0	84

[a] 0.5 mmol in 10 mL of Me_2SO irradiated with a 275 W fluorescent sunlamp at 35–40 °C. [b] By ^1H NMR with an internal standard following basic aqueous $Na_2S_2O_3$ workup and CH_2Cl_2 extraction. [c] A mixture of two isomers in a 3.5:1 ratio.

Photolysis of 4-chloro-*N*-methylquinolinium iodide with 4 equiv of *t*-BuHgCl for 2 h produced only 7% of **6c** and 37% of the demethylated product, 2-*tert*-butyl-4-chloroquinoline. Since **6c** is relatively stable under the reaction conditions, the major reaction course apparently was demethylation to form 4-chloroquinoline followed by substitutive *tert*-butylation. In the presence of 8 equiv of KI the yield of **6c** increased to 89% with only 7% of the demethylated product. The presence of I^- not only increases the reducing ability of *t*-BuHgCl but also increases the rate of photochemical formation of *t*-Bu$^\bullet$.[5] Thus, in the presence of KI a fast free radical alkylation replaces the slow demethylation observed in its absence.

2-Chloro-*N*-methylquinolinium iodide when subjected to the workup conditions of aqueous $Na_2S_2O_3$ underwent hydrolysis to form 1-methyl-2(1*H*)-quinolinone. Photolysis of the quinolinium salt with 4 equiv of *t*-BuHgCl and 8 equiv of KI for 2 h produced after workup 4-*tert*-butyl-3,4-dihydro-1-methyl-2(1*H*)-quinolinone (**7**) in 44% yield and 1-methyl-2(1*H*)-quinolinone in 30% yield.



Continuing the reaction for 16 h did not increase the yield of **7** but reduced the yield of 1-methyl-2(1*H*)-quinolinone to 7%. The most reasonable interpretation is that the reaction with *t*-BuHgCl/KI forms **5c** which is hydrolyzed to **7** upon workup.

N-Methylquinolinium iodide initially produces **5a** (and possibly its 1,2-dihydro isomer). Further reaction converts **5a** into a single stereoisomer **4b** in a process which occurs more readily in the presence of PTSA, Table 1. Scheme 2 is apparently being followed. The attack of *t*-Bu$^\bullet$ upon quinolinium ion is not selective, and nearly equal amounts of attack occur at C-2 and C-4.[3] However, with the *N*-methyl derivative attack occurs selectively at C-4, undoubtedly for steric reasons.

***N*-Methoxyquinolinium Salts.** In most cases photolysis of the perchlorate salts with *t*-BuHgCl/KI in Me_2SO gave demethoxylated alkylation products. In general, it appears that *tert*-butylation precedes demethoxylation.

(4) We previously ascribed the formation of **3** to the oxidation of 2,4-di-*tert*-butyl-1,4-dihydroquinoline because workup with $NaBH_4$ formed *cis*-2,4-di-*tert*-butyl-1,2,3,4-tetrahydroquinoline.[2] Further work has shown that **3** as well as 1,4-dihydroquinolines are reduced by $NaBH_4$ to yield the *cis*-2,4-disubstituted tetrahydroquinolines. There is no evidence (^1H NMR, GCMS) that 2,4-di-*tert*-butyl-1,4-dihydroquinoline is formed from the 2-*tert*-butylquinolinium ion or that the 1,4-dihydroquinoline is a precursor to **3**.

(5) Russell, G. A.; Hu, S.; Herron, S.; Baik, W. Ngoviwatchai, P.; Jiang, W.; Nebgen, M.; Wu, Y.-W. *J. Phys. Org. Chem.* **1988**, *1*, 299.

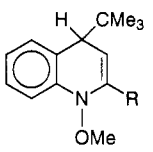
Table 2. Reaction of Quinaldinium and *N*-Methoxyquinaldinium Perchlorates with 4 Equiv of *t*-BuHgCl in Me_2SO[a]

	molar equiv			% yield[c]		
reactant[b]	KI	PTSA	time, h	Qa[b]	4-*t*-BuQa[b]	**10**
Qa	0	0	1	88		6
Qa	4	0	1	30	10	45
N-MeOQa	0	0	2	19	69	0
N-MeOQa	0	4	0.5	38	37	0
N-MeOQa	4	0	0.5	9	14	26
N-MeOQa	8	0	0.25			55[d]
N-MeOQa	8	0	0.5		4	38

[a] Photolysis of 0.2 mmol of the salt in 4 mL of Me_2SO by a 275 W fluorescent sunlamp at 35–40 °C. [b] Qa = quinaldinium; 4-*t*-BuQa = 4-*tert*-butyl-2-methylquinoline; *N*-MeOQa = *N*-methoxyquinaldinium. [c] By ^1H NMR with an internal standard after basic aqueous $Na_2S_2O_3$ workup and CH_2Cl_2 extraction. [d] Workup with $NaBH_4$/MeOH formed 4-*tert*-butyl-1,2,3,4-tetrahydro-2-methylquinoline in 56% yield.[3]

Thus, *N*-methoxypyridinium iodide forms 2- and 4-*tert*-butylpyridines with a ratio of 4-attack/2-attack greater than that observed for pyridine or pyridinium ion. Photolysis with 4 equiv of *t*-BuHgCl for 2 h produces 4-*tert*-butylpyridine (71%) and 2-*tert*-butylpyridine (23%) with a trace of 2,4-di-*tert*-butylpyridine. With 4 equiv of KI added, similar yields are observed (4-attack/2-attack = 3.5) in 30 min of sunlamp photolysis. The ratio observed with pyridinium ion itself depends somewhat upon the reaction conditions but is usually in the range of 1–2 while in the absence of a protonating agent pyridine initially gives a ratio of 4-attack/2-attack of ~0.5.[3] The higher selectivity observed for *N*-methoxypyridinium ion suggests that the reaction involves *t*-Bu• attack on the *N*-methoxypyridinium ion. The most reasonable route to the observed products involves reduction to the dihydropyridine derivatives followed by loss of MeOH.

With 2- or 4-substituted *N*-methoxyquinolinium perchlorates the reductive alkylation products could be **8** or **9**. Photolysis of *N*-methoxy-4-methylquinolinium perchlorate with *t*-BuHgCl with or without added KI rapidly forms 2-*tert*-butyl-4-methylquinoline. With 4 equiv of *t*-BuHgCl and 4–8 equiv of KI a yield of 90–93% was observed in 15–30 min. The reaction is faster than with lepidinium ion itself suggesting that the reaction initially formed **9b** followed by the loss of MeOH.



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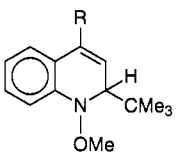
a: R = H
b: R = Me



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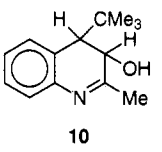
a: R = H
b: R = Me



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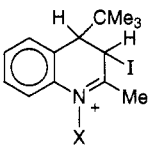
In the absence of added KI, photolysis of *N*-methoxy-2-methylquinolinium perchlorate forms quinaldine and its 4-*tert*-butyl derivatives, Table 2. Possibly the elimination of CH_2=O from the *N*-methoxy salt occurred prior to *tert*-butylation. The presence of both iodide and perchlorate ions had a dramatic effect on the reaction product since the hydrate **10** now becomes the dominant product. Although **10** is not produced in the reaction of quinaldinium tosylate with *t*-BuHgCl/KI in Me_2SO, even in the presence of 1 equiv of H_2O,[3] the hydrate becomes the major product in the reaction of quinaldinium perchlorate with *t*-BuHgCl/KI (Table 2). Apparently, the perchlorate yields a species which can trap the radical cation **2** (R = Me, X = OMe or H). Molecular iodine is a likely possibility. Hydrolysis of **11a** or hydrolysis and

Table 3. Photostimulated *tert*-Butylation of *N*-Methoxyquinolinium Perchlorate with 4 Equiv of *t*-BuHgCl in Me_2SO[a]

molar equiv			products[b,c] (%)	
KI	PTSA	workup	**12**	2-*t*-BuQ
8	0	$Na_2S_2O_3$	70	20
8	0	NaOMe, 85 °C		72[d]
8	0	$NaBH_4$/MeOH	55[e]	20
8	4	$Na_2S_2O_3$	*f*	45[g]
8	0	PTSA, 85 °C		64[h]

[a] 0.1 mmol in 2 mL of Me_2SO. Photolysis with a 275 W sunlamp for 10 min. [b] By ^1H NMR with toluene as an internal standard. [c] 2-*t*-BuQ = 2-*tert*-butylquinoline. [d] Also formed, 4-*tert*-butylquinoline (~3%), **4a** (~7%). [e] By GCMS there was ~10% of a *N*-methoxy-*tert*-butyltetrahydroquinoline, possibly the 4-*tert*-butyl isomer.[f] 9% of **12** or possibly its 4-*tert*-butyl isomer. [g] 20% of 2,4-di-*tert*-butylquinoline and 9% of **4a** also observed. [h] 26% of 2,4-di-*tert*-butylquinoline.



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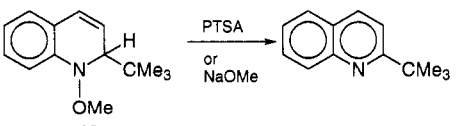
a: X = H
b: X = OMe

elimination of CH_2=O from **11b** could lead to **10**. Qualitatively, the products formed from quinaldinium and *N*-methoxyquinaldinium perchlorates are similar, although quantitative differences exist. As shown in Table 2 the reactions of the *N*-methoxy derivative are much faster than quinalidinium ion itself, suggesting that alkylation precedes demethoxylation.

From steric considerations we expected *t*-Bu• attack on *N*-methoxyquinolium ion to occur mainly at C-4 as was observed for the *N*-methylquinolinium cation. However, the observed products require >70% attack at C-2 to yield **1c** (R = H). Moreover, **1c** (R = H) did not readily lose the proton from C-2 and in the presence of I^- underwent reduction to form the 1,2-dihydroquinoline derivative **12**. Compound **12** proved difficult to isolate by chromatography, but treatment of the crude reaction product with either PTSA or NaOMe at 85 °C gave good yields of 2-*tert*-butylquinoline, reaction 3 and Table 3. This result clearly



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demonstrates that with quinolinium ion itself the formation of the substitutive (oxidative) alkylation product from C-2 attack and the additive (reductive) alkylation product from C-4 attack cannot be reasonably explained by postulating that electron transfer from I^- or *t*-$BuHgI_2^-$ to **1a** (R = H) does not occur readily because with **1c** (R = H) reduction is the dominant reaction.

From Table 3 it is clear that 70–90% of the products formed result from *t*-Bu• addition to C-2 of *N*-methoxyquinolium cation. The observation of a *N*-methoxy-*tert*-butyltetrahydroquinoline (~10%) upon $NaBH_4$ workup possibly indicates attack at C-4 with the formation of *N*-methoxy-4-*tert*-butyl-1,4-dihydroquinoline, a possible

Table 4. Reaction of 4 Equiv of *t*-BuHgCl with 0.05 M Quinoline *N*-Oxide in Me_2SO[a]

		% yield[b]				
KI (equiv)	time, h	Q	2-*t*-BuQ	2,4-di-*t*-BuQ	**4a**	**3**
0	9	tr	4	8	0	0
4	4	10	28	6	0	4
8	1	9	34	5	1	tr[c]
8	4	10	48	7	3	3
8[d]	4	0	28	35	5	5
8[e]	18	0	18	6	17	31
8[e,f]	18	0	20	5	15	32

[a] Photolysis with a 275 W fluorescent sunlamp at 35–40 °C. [b] By ^1H NMR and GC after aqueous $Na_2S_2O_3$ workup and extraction by CH_2Cl_2: Q = quinoline. [c] 7% of 2-*tert*-butylquinoline *N*-oxide detected by GCMS. [d] 4 equiv of PTSA added. [e] 1 or 10 vol % H_2O added. [f] With air passing through the reaction mixture.

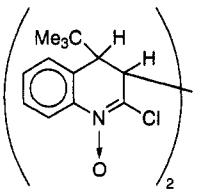
precursor to the **4a** observed in the reaction performed in the presence of PTSA (Table 3). Alternatively, in the presence of PTSA the formation **4a** (9%) could indicate that some of the reaction proceeded by demethoxylation to form quinolinium ion since **4a** is a major product of the *tert*-butylation of quinolinium ion but not of 2-*tert*-butylquinoline.[3]

Quinoline *N*-Oxides. Photolysis of pyridine *N*-oxide with *t*-BuHgCl/KI does not lead to significant reaction even in the presence of PTSA. No significant reaction was observed upon the photolysis of *t*-BuHgCl with quinoline *N*-oxide, whereas in the presence of KI the *N*-oxide reacts slowly to give mainly quinoline and the products previously observed in the *tert*-butylation of quinoline,[2] namely 2-*tert*-butylquinoline, 2,4-di-*tert*-butylquinoline, *trans*-2,4-di-*tert*-butyl-1,2,3,4-tetrahydroquinoline (**4a**), and the hydrate **3**, Table 4. The yield of the hydrate was increased by the addition of H_2O to the Me_2SO solvent. Initially formed quinoline is apparently converted to 2-*tert*-butylquinoline and 4-*tert*-butyl-1,4-dihydroquinoline via **1a** and **2a**. Further reaction of the dihydroquinoline forms **4a** while 2-*tert*-butylquinoline is slowly converted into **3**. Addition of PTSA had no significant effects upon the reaction of quinoline *N*-oxide although it increased the rate of reaction of the initially formed quinoline and led to the dehydration of **3**. At short reaction times (1 h) up to 7% of 2-*tert*-butylquinoline *N*-oxide could be detected (Table 4). However, at longer reaction times (>4 h) the substituted quinoline *N*-oxide was not observed, apparently because it was deoxygenated to give 2-*tert*-butylquinoline.

With quinaldine *N*-oxide in the presence of 4 equiv of KI in Me_2SO in the dark no reaction was observed in 20 h at 40 °C. However, with sunlamp irradiation a 76% yield of quinaldine was observed. Photolysis with 4 equiv of *t*-BuHgCl and 8 equiv of KI for 2 h produced 8–9% of quinaldine, 6–7% of 4-*tert*-butyl-2-methylquinoline, and 15–18% of 4-*tert*-butyl-2-methyl-1,4-dihydroquinoline (**5b**). After 8 h of photolysis the yields were 46–53%, 12–14%, and 8–13%, respectively. Iodide ion promoted deoxygenation of the *N*-oxide is apparently the first step in the reaction sequence. Similar reactions with lepidine *N*-oxide slowly produced traces of 2-*tert*-butyl-4-methylquinoline *N*-oxide (by GCMS), with the major products being 2-*tert*-butyl-4-methylquinoline and 2,6-di-*tert*-butyl-4-methylquinoline. With 4 equiv of *t*-BuHgCl and 8 equiv of KI the yields increased from 30 and 7% at 2 h to 59 and 20% at 9 h. Again, deoxygenation of the *N*-oxide appears to be the major initial step in the reaction.

Photolysis of *t*-BuHgCl with 2-chloroquinoline *N*-oxide produces the dimer **13**.

With 4 equiv of *t*-BuHgCl the yield of **13** isolated after



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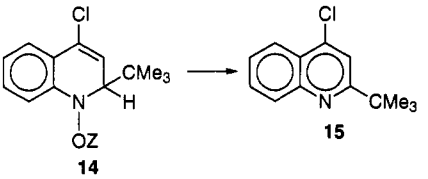
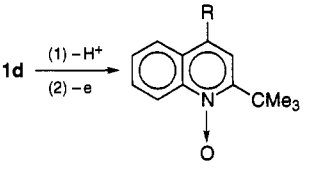
2 h of photolysis increased from 8 to 46 to 56% in the presence of 0, 4, and 8 equiv of KI, respectively. Deoxygenation of the *N*-oxide no longer occurred. The adduct radical **2d** with R = Cl, a resonance-stabilized nitroxide radical, was not reduced by the *t*-BuHgCl/KI reagent. However, with 4-chloroquinoline *N*-oxide the deoxygenated product 2-*tert*-butyl-4-chloroquinoline was formed. With 4 equiv of *t*-BuHgCl the yield after 9 h of photolysis increased from 65 to 86% upon the addition of 8 equiv of KI. It seems probable that the adduct radical **1d** with R = Cl is initially formed. Since dimerization of **1d** is impossible, the nitroxide may be converted to some intermediate of the general structure **14** (Z = H, Me_3C, HgI) which can undergo elimination, reaction 4.



14 **15**

Reactions in the Presence of DABCO. For the radical cations **1a-c** and **2a-c** oxidative alkylation in Me_2SO in the absence of added bases was only observed for **1a**, presumably because of the ease of deprotonation at the C-2 position. With **1b-c** loss of this proton followed by oxidation of the resulting pyridinyl radical would generate a cation. In the absence of adduct base such products were not important on the basis of observed material balances (Tables 1–3).

For quinoline *N*-oxides the loss of a proton from the adduct radicals **1d** followed by oxidation (reaction 5) yields the substituted *N*-oxides **16**. Although **16** was not



16
a: R = H
b: R = Me
c: R = Cl

an important product from 4-substituted quinoline *N*-oxides in the absence of added proton acceptors, it became an important and in some cases the dominant product in the presence of DABCO. Results for 2- and 4-chloroquinoline *N*-oxide are summarized in Table 5. With 2-chloroquinoline *N*-oxide the dimer **13** was the predominant product in the presence or absence of DABCO although in the presence of DABCO the 4-*tert*-butyl-2-chloroquinoline *N*-oxide could be detected at short reaction periods. At longer reaction periods the *N*-oxide appeared to undergo deoxygenation to yield 4-*tert*-butyl-2-chloroquinoline, a product not observed in the absence of DABCO. With 4-chloroquinoline *N*-oxide the presence of DABCO resulted in the major initial reaction product being **16c** instead of **15**. Again, at longer reaction times

Table 5. Products of the Reaction of 4 Equiv of *t*-BuHgCl with 2- and 4-Chloroquinoline *N*-Oxides in Me_2SO[a]

	molar equiv			products[b] (%)		
	KI	DABCO	time (h)	**13**	**15**	**16c**
2-Cl	0	0	2	8		
2-Cl	8	0	2	56		
2-Cl	8	4	2	22		*c*
2-Cl	8	4	5	20		*d*
4-Cl	0	0	9		65	
4-Cl	4	0	2		35	22
4-Cl	4	0	9		86	
4-Cl	8	0	2		68	20
4-Cl	8	0	9		84	
4-Cl	8	4	2		7	39
4-Cl	8	4	5		39	29

[a,b] See Table 4. [c] ~4% of 4-*tert*-butyl-2-chloroquinoline *N*-oxide and 3% of 4-*tert*-butyl-2-chloroquinoline detected. [d] 5% of 4-*tert*-butyl-2-chloroquinoline formed.

16c underwent deoxygenation to form **15** (Table 5). In a similar fashion, the formation of **16b** from 4-methylquinoline *N*-oxide increased from a trace (detectable by GCMS) in the absence of DABCO to 30% after photolysis for 1 h in the presence *t*-BuHgCl (4 equiv), KI (8 equiv), and DABCO (4 equiv). With quinoline *N*-oxide itself the yield of **16a** increased from 7% in the absence of DABCO to 20% in the presence of 4 equiv of DABCO in a 1 h reaction. With 2-methylquinoline *N*-oxide in the presence of DABCO little reaction occurred in 1 h. The only product detected was 4-*tert*-butyl-2-methylquinoline. If the *N*-oxide had been formed, deoxygenation must have occurred readily.

Conclusions

It does not appear that a presumed difference in the rates of electron transfer to the radical cations **1a** and **2a** provides a convincing explanation of the different reaction pathways followed by these intermediates in Me_2SO, i.e., proton loss from **1a** but reduction of **2a**. Thus, electron transfer to the intermediate **1** actually occurs in preference to deprotonation with R = Me or Cl and X = Me (**1b**) or for R = H or Me and X = OMe (**1c**). Here a decreased rate of proton loss is apparently dictated by an increase in vicinal strain upon deprotonation. However, the rate of electron transfer can control product formation since for **2a** with R = Me, X = H the 1,4-dihydroquinoline is formed while with R = *t*-Bu, X = H the hydrate **3** results. The difference in the reaction pathways observed for **1a** and **2a** extends to the adduct nitroxyl radicals **1d** and **2d**. The adduct radicals formed from quinoline *N*-oxides behave similar to **1a** and **2a** in that in the presence of DABCO proton loss occurs more readily from C-2 of **1d** than from C-4 of **2d**.

The regioselective addition of *t*-Bu• at the 2-position of *N*-methoxyquinolinium cation is puzzling. However, the addition of *t*-Bu• may be reversible and the yield of products arising from 2-attack may not be a fair measure of kinetic regioselectivity. With quinolinium ion itself in the absence of a reagent that can reduce the 4-adduct (**2a**, R = H), nearly exclusive substitution at C-2 is observed while in the presence of I^- about equal amounts of substitutive alkylation at C-2 and additive alkylation at C-4 are observed.[3] With *N*-methylquinolinium cation in the presence of I^- at least 85% of the alkylation products result from *t*-Bu• addition at C-4 followed by electron transfer to the adduct radical cation **2b** (R = H). In this case it seems reasonable that C-4 attack occurs in preference to C-2 attack for steric reasons. Reduction of the 4-adduct (**2b**) might also occur more readily than for the 2-adduct (**1b**) because of steric reasons. The steric effect is probably less for *N*-methoxyquinolinium cation but the dramatic reversal in regioselectivity between the *N*-methyl and *N*-methoxy derivatives seems to require some other explanation. However, reversability in *t*-Bu• addition with preferential electron transfer to the adduct radical cation **1c** (R = H) remains a possibility. Since **1c** is more localized than **2c**, its reduction by I^- or *t*-$BuHgI_2^-$ might occur more readily.

Experimental Section

General. Analyses were performed by GC using appropriate internal standards or by ^1H NMR using $PhCH_3$ or CH_2I_2 as the internal standard. NMR spectra were recorded at 300 MHz for ^1H and 75 MHz for ^{13}C. GCMS and HRMS were measured in the EI mode with an ionization potential of 70 eV. Elemental analyses were performed by Galbraith Laboratories, Inc.

Materials. 1-Methylquinolinium iodide, mp 143–144 °C (lit.[6] mp 142–144 °C), 2-chloro-1-methylquinolinium iodide, mp 220–221 °C, and 4-chloro-1-methylquinolinium iodide, mp 208–210 °C (lit.[7] mp 208–210 °C) were prepared in refluxing acetone.[6] 1,4-Dimethylquinolinium iodide was prepared by the reaction of lepidine with excess MeI at room temperature for 24 h, mp 173–174 °C (lit.[8] mp 174 °C). 1-Methoxypyridinium iodide was prepared by refluxing pyridine *N*-oxide with excess MeI,[9] mp 88–90 °C dec (lit.[9] 90 °C). The *N*-methoxyquinolinium perchlorates were prepared by reaction of the quinoline *N*-oxides with Me_2SO_4 with the perchlorate salts precipitated from ethanol by the addition of ethyl acetate[10] and had mp in agreement with literature values.[10,11] Quinoline 1-oxide was prepared from the hydrate by storage in a vacuum desiccator for 2 days.[12] 2-Chloroquinoline 1-oxide was prepared by a literature procedure[13] and had mp 104–105 °C (lit.[12] mp 105 °C). 4-Chloroquinoline 1-oxide was prepared by the reaction of acetyl chloride with 4-nitroquinoline 1-oxide[14] and had mp 134–135 °C (lit.[14] mp 133–133.5 °C). 2-Methyl- and 4-methylquinoline 1-oxides were prepared by oxidation of the quinolines[15] and had mp 76–77 °C (lit.[15] mp 75–77 °C) and 116–117 °C (lit.[13] mp 116–117 °C), respectively.

General Procedure. The quinoline derivatives (0.2–1.0 mmol), *t*-BuHgCl (1–5 mmol), and KI (2–10 mmol) were placed in a Pyrex tube, and 2–10 mL of deoxygenated Me_2SO was added. The solutions were stirred by a stream of N_2 bubbles and irradiated by a 275 W fluorescent sunlamp ca. 25 cm from the reaction tube at a temperature of 35–40 °C. Workup involved treatment of the reaction mixtures with saturated aq $Na_2S_2O_3$, neutralization if required, and extraction with CH_2Cl_2. The CH_2Cl_2 extracts were washed with aq $Na_2S_2O_3$ and saturated brine solutions, dried over $MgSO_4$ and concentrated under vacuum. Products were isolated by flash column chromatography using 230–240 mesh grade 60 Merck silica gel or for the quinoline *N*-oxides by thin layer chromatography using 5–17 μM grade 60A Merck silica gel plates (Aldrich Chemical Co.). Elution in both cases involved hexane/ethyl acetate.

Characterization of Products. The characterization of 2- and 4-*tert*-butylpyridine, 2-*tert*-butylquinoline, 2-*tert*-butyl-4-methylquinoline, 4-*tert*-butyl-2-methylquinoline, *cis*- and *trans*-2,4-di-*tert*-butyl-1,2,3,4-tetrahydroquinoline (**4a**), 4-*tert*-

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butyl-1,2,3,4-tetrahydro-2-methylquinoline, **3**, **5b**, and **15** have been previously reported.[3]

***trans*-2,4-Bis(1,1-dimethylethyl)-1,2,3,4-tetrahydro-1-methylquinoline (4b).** The compound was isolated as a solid: mp 32–33 °C; ^{1}H NMR ($CDCl_3$) δ 7.08 (ddd, J = 7.8, 7.2, 1.5 Hz, 1 H), 6.85 (dd, J = 7.2, 1.5 Hz, 1 H), 6.64–6.57 (m, 2 H), 3.02 (s, 3 H), 2.91 (dd, J = 11.1, 7.8 Hz, 1 H), 2.37 (dd, J = 6.0, 2.4 Hz, 1 H), 2.27 (ddd, J = 14.4, 7.8, 2.4 Hz, 1 H), 1.80 (ddd, J = 14.4, 11.1, 6.0 Hz, 1 H), 0.89 (s, 9 H), 0.88 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 149.63 (s), 129.35 (d), 128.99 (s), 127.11 (d), 116.18 (d), 115.79 (d), 66.68 (d), 46.91 (d), 44.49 (q), 38.56 (s), 34.00 (s), 30.18 (t), 28.99 (q), 27.68 (q); GC and HRMS *m/z* (relative intensity) calcd for M^+ 259.2300, obsd 259.2292 (24), 202 (100), 174 (20), 144 (58). Anal. Calcd for $C_{18}H_{29}N$: C, 83.33; H, 11.27; N, 5.40. Found: C, 83.39; H, 11.55; N, 5.70.

4-(1,1-Dimethylethyl)-1,4-dihydro-1-methylquinoline (5a). The compound was isolated as an oil: ^{1}H NMR ($CDCl_3$) δ 7.18–7.12 (m, 1 H), 7.00 (dd, J = 7.5, 1.5 Hz, 1 H), 6.86 (td, J = 7.5, 1.2 Hz, 1 H), 6.70 (dd, J = 7.2, 0.9 Hz, 1 H), 6.13 (d, J = 7.8, 1 H), 4.65 (dd, J = 7.8, 8.5 Hz, 1H), 3.10 (d, J = 5.7 Hz, 1 H), 3.04 (s, 3 H), 0.795 (s, 9 H); GC and HRMS *m/z* (relative intensity) calcd for $C_{14}H_{19}N$ (M^+) 201.1517, obsd 201.1519 (5), 202 (1), 186 (2), 144 (100).

2-(1,1-Dimethylethyl)-1,2-dihydro-1,4-dimethylquinoline (6b). The compound was isolated as an oil: ^{1}H NMR ($CDCl_3$) δ 7.12–7.05 (m, 2 H), 6.59 (td, J = 7.5, 0.9 Hz, 1 H), 6.48 (d, J = 7.8 Hz, 1 H), 5.47 (dd, J = 6.0, 0.9 Hz, 1 H), 3.59 (d, J = 6.3 Hz, 1 H), 3.09 (s, 3 H), 2.05 (s, 3 H), 0.82 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 146.28 (s), 130.61 (s), 128.35 (d), 123.52 (s), 123.17 (d), 119.70 (d), 115.24 (d), 111.04 (d), 70.25 (d), 43.42 (q), 41.77 (s), 26.21 (q), 18.98 (q); HRMS calcd for $C_{15}H_{21}N$ (M^+) 215.1674, obsd 215.1670.

4-Chloro-2-(1,1-dimethylethyl)-1,2-dihydro-1-methylquinoline (6c). The compound was isolated as an oil: ^{1}H NMR ($CDCl_3$) δ 7.38 (dd, J = 7.8, 1.5 Hz, 1 H), 7.14 (td, J = 8.4, 1.5 Hz, 1 H), 6.63 (td, J = 8.1, 0.6 Hz, 1 H), 6.49 (d, J = 8.4 Hz, 1 H), 5.78 (d, J = 6.3 Hz, 1 H), 3.72 (d, J = 6.6 Hz, 1 H), 3.10 (s, 3 H), 0.85 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 146.56(s), 129.87(d), 128.97(s), 124.49(d), 120.03(s), 119.44(d), 115.77(d), 111.47(d), 71.51(d), 43.33(q), 41.98(s), 25.98(q); GC and HRMS *m/z* (relative intensity) calcd for $C_{14}H_{18}NCl$ (M^+) 235.1128, obsd 237 (0.3), 235.1133 (0.9), 180 (30), 178 (100).

4-(1,1-Dimethylethyl)-3,4-dihydro-1-methyl-2(1*H*)-quinolinone (7). The compound was isolated as an oil: ^{1}H NMR ($CDCl_3$) δ 7.27 (t, J = 7.8 Hz, 1 H), 7.14 (d, J = 7.5 Hz, 1 H), 7.01 (t, J = 7.5, 2 H), 3.31 (s, 1 H), 2.92 (d, J = 15.6 Hz, 1 H), 2.70–2.58 (m, 2 H), 0.90 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 170.31 (s), 140.72 (s), 130.74 (d), 127.51 (d), 126.73 (s), 122.00 (d), 114.85 (d), 46.22 (d), 34.63 (s), 33.56 (t), 29.14 (q), 27.49 (q); FTIR (film, cm^{-1}) 2963, 1673; GC and HRMS *m/z* (relative intensity) calcd for $C_{14}H_{19}NO$ (M^+) 217.1467, obsd 217.1473 (16), 160 (100), 132 (15), 77 (10), 57 (13).

4-(1,1-Dimethyl)-3,4-dihydro-3-hydroxy-2-methylquinoline (10). The compound was isolated as a solid: mp 127 °C; ^{1}H NMR ($CDCl_3$) δ 7.32–7.10 (m, 4 H), 4.08 (s, 1 H), 2.90 (br s, 1 H), 2.62 (s, 1 H), 2.28 (s, 3 H), 0.84 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 169.47(s), 142.80(s), 132.09(d), 127.85(d), 126.34(d), 126.10(d), 124.78(s), 65.58(d), 53.42(d), 33.58(s), 28.05(q), 25.51(q); FTIR ($CDCl_3$, cm^{-1}) 3227, 1639; HRMS *m/z* (relative intensity) calcd for M^+ 217.1467, obsd 217.1470. Anal. Calcd for $C_{14}H_{19}NO$: C, 77.38; H, 8.88; N, 6.44. Found: C, 76.99; H, 8.94; N, 6.26.

2-(1,1-Dimethylethyl)-1,2-dihydro-1-methoxyquinoline (12). A pure sample of **12** could not be isolated by column chromatography because of decomposition to form 2-*tert*-butylquinoline. The ^{1}H NMR of crude **12** was consistent with the chemical shifts and coupling constants of **6b,c** while the absence of a significant amount of a tetrahydroquinoline upon $NaBH_4$ workup eliminated a 1,4-dihydroquinoline structure. The structure of **12** is based on its conversion to 2-*tert*-quinoline with either acid or base. After aqueous $Na_2S_2O_3$ workup and extraction by CH_2Cl_2 the crude **12** had: ^{1}H NMR ($CDCl_3$) δ 7.21 (td, J = 7.5, 1.2 Hz, 1 H), 7.13–7.08 (m, 2 H), 6.95 (td, J = 7.2, 1.2 Hz, 1 H), 6.63 (d, J = 8.1 Hz, 1 H), 4.83 (dd, J = 8.1, 5.7 Hz, 1 H), 3.84 (s, 3 H), 3.08 (d, J = 5.7 Hz, 1 H), 0.85 (s, 9 H); GCMS *m/z* (relative intensity) 217 (M^+, 11), 202 (10), 170 (11), 161 (14), 160 (79), 130 (100).

3,3′-Bi[2-chloro-4-(1,1-dimethylethyl)-3,4-dihydroquinoline 1-oxide] (13). The compound was isolated as a solid: mp 155–156 °C; ^{1}H NMR ($CDCl_3$) δ 8.25 (dd, J = 8.1, 0.9 Hz, 1 H), 7.44 (td, J = 7.8, 1.2 Hz, 1 H), 7.17 (td, J = 7.5, 1.2 Hz, 1 H), 6.43 (dd, J = 7.8, 0.9 Hz, 1 H), 3.56 (s, 1 H), 2.17 (s, 1 H), 0.78 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 139.83 (s), 134.31 (s), 130.48 (d), 129.51 (d), 128.54 (d), 127.31 (s), 120.05 (d), 48.26 (d), 45.78 (d), 35.10 (s), 27.26 (q); CIMS (NH_3) *m/z* (relative intensity) 490 ($M + NH_4^+$, 0.1), 473 (MH^+, 6), 236 ($M^+/2$, 4), 180 (100); HRMS *m/z* (M^+) calcd 472.1684, obsd 472.1675; FTIR ($CDCl_3$, cm^{-1}) 1587. Anal. Calcd for $C_{26}H_{30}Cl_2N_2O_2$: C, 65.96; H, 6.39; N, 5.92. Found: C, 65.43; H, 6.59; N, 5.73.

2-(1,1-Dimethylethyl)quinoline 1-Oxide (16a). The compound was isolated as a solid: mp 91–92 °C; ^{1}H NMR ($CDCl_3$) δ 8.80 (d, J = 8.7 Hz, 1 H), 7.81 (d, J = 8.1 Hz, 1 H), 7.73 (ddd, J = 8.7, 6.9, 1.5 Hz, 1 H), 7.65 (d, J = 8.7 Hz, 1 H), 7.58 (ddd, J = 8.1, 6.9, 0.9 Hz, 1 H), 7.46 (d, J = 8.7 Hz, 1 H), 1.63 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 150.45 (s), 136.09 (s), 130.24 (d), 129.49 (s), 127.86 (d), 127.72 (d), 124.90 (d), 120.07 (d), 119.94 (d), 36.72 (s), 26.98 (q); GC and HRMS *m/z* (relative intensity) calcd for M^+ 201.1154, obsd 201.1152 (82), 185 (10), 169 (17), 168 (23), 58(54), 56 (36), 51 (100). Anal. Calcd for $C_{13}H_{15}NO$: C, 77.58; H, 7.51; N, 6.96. Found: C, 77.50; H, 7.57; N, 6.91.

2-(1,1-Dimethylethyl)-4-methylquinoline 1-Oxide (16b). The compound was isolated as a solid: mp 83–84 °C; ^{1}H NMR ($CDCl_3$) δ 8.86 (d, J = 8.7 Hz, 1 H), 7.92 (dd, J = 8.1, 0.9 Hz, 1 H), 7.74 (ddd, J = 8.4, 6.9, 1.2 Hz, 1 H), 7.62 (ddd, J = 8.1, 6.9, 0.9 Hz, 1 H), 7.28 (s, 1 H), 2.65 (s, 3 H), 1.64 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 153.43 (s), 142.65 (s), 133.10 (s), 129.97 (d), 128.60 (s), 127.62 (d), 124.40 (d), 120.64 (d), 120.49 (d), 36.60 (s), 27.11 (q), 18.64 (q); GC and HRMS *m/z* (relative intensity) calcd for M^+ 215.1310, obsd 215.1308 (21), 198 (38), 173 (100). Anal. Calcd for $C_{14}H_{17}NO$; C, 78.10; H, 7.96; N, 6.51. Found: C, 77.92; H, 8.14; N, 6.42.

4-Chloro-2-(1,1-dimethylethyl)quinoline 1-Oxide (16c). The compound was isolated as a solid: mp 103–104 °C; ^{1}H NMR ($CDCl_3$) δ 8.81 (d, J = 8.7 Hz, 1 H), 8.14 (dd, J = 8.4, 1.2 Hz, 1 H), 7.79 (ddd, J = 8.4, 6.9, 1.2 Hz, 1 H), 7.68 (ddd, J = 8.4, 6.9, 1.2 Hz, 1 H), 7.53 (s, 1 H), 1.62 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 154.02 (s), 143.64 (s), 130.86 (d), 128.90 (s), 128.55 (d), 126.58 (s), 124.66 (d), 120.30 (d), 120.14 (d), 36.68 (s), 26.70 (q); GC and HRMS *m/z* (relative intensity) calcd for (M^+) 235.0764, obsd 237 (22), 236 (12), 235.0767 (66), 219 (13), 192 (9), 178 (4), 127 (3), 89 (10), 77 (10), 63 (80), 57 (17), 51 (100). Anal. Calcd for $C_{13}H_{14}ClNO$: C, 66.27; H, 5.99; N, 5.94. Found: C, 66.01; H, 5.99; N, 5.82.

2-Chloro-4-(1,1-dimethylethyl)quinoline 1-Oxide. This compound was detected by GCMS *m/z* (relative intensity) 237 (13), 236 (7), 235 (M^+, 39), 219 (3), 197 (6), 179 (16), 145 (5), 127 (7), 76 (16), 62 (73), 56 (100).

4-(1,1-Dimethylethyl)-1,2,3,4-tetrahydro-1-methoxyquinoline. Workup of the *tert*-butylation products from *N*-methoxyquinolinium perchlorate with $NaBH_4$/MeOH gave low yields of this compound which was isolated as an oil: ^{1}H NMR ($CDCl_3$) δ 7.19–7.11 (m, 2 H), 7.07 (d, J = 7.2 Hz, 1 H), 6.82 (ddd, J = 7.5, 6.6, 2.1 Hz, 1 H), 3.75 (s, 3 H), 3.54 (dt, J = 9.9, 6.3 Hz, 1 H), 3.01–2.93 (m, 1 H), 2.58 (dd, J = 8.7, 4.5 Hz, 1 H), 2.23–2.11 (m, 1 H), 1.99 (ddt, J = 14.4, 8.7, 6.0 Hz, 1 H), 0.91 (s, 9 H); ^{13}C NMR ($CDCl_3$) 150.00 (s), 130.84 (d), 126.65 (d), 126.21 (s), 119.50 (d), 112.50 (d), 60.79 (q), 51.48 (t), 45.40 (d), 35.73 (s), 28.42 (q), 23.94 (t); GC and HRMS *m/z* (relative intensity) calcd for $C_{14}H_{21}NO$ (M^+) 219.1623, obsd 219.1627 (14), 189 (12), 162 (36), 132 (100).

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