4-Fluoro-4'-(dimethylamino)biphenyl: mp 164 °C; ^{1}H NMR ($CDCl_3$) δ 2.9 (s, NMe_2, 6 H), 6.75–7.55 (m, Ar, 8 H). Anal. Calcd for $C_{14}H_{14}FN$: C, 78.11; H, 6.55; F, 8.82; N, 6.50. Found: C, 77.68; H, 6.53; F, 8.00; N, 6.31.

4-(Trifluoromethyl)-4'-(dimethylamino)biphenyl: mp 196 °C; ^{1}H NMR ($CDCl_3$) δ 2.5 (s, NMe_2, 6 H), 7.35 (d, J = 9 Hz, 4 H), 7.85 (d, J = 9 Hz, 4 H). Anal. Calcd for $C_{15}H_{14}F_3N$: C, 67.91; H, 5.32; F, 21.48; N, 5.28. Found: C, 69.07; H, 5.60; F, 20.15; N, 5.11.

4-Methoxy-4'-methylbiphenyl: mp 107 °C; IR (CCl_4) 3100–2820 (ArOMe) 1250 cm^{-1} (CO); ^{1}H NMR ($CDCl_3$) δ 2.35 (s, CH_3, 3 H), 3.8 (s, OCH_3, 3 H), 6.9 (d, J = 9 Hz, 2 H), 7.15 (d, J = 8 Hz, 2 H), 7.2–7.4 (m, 4 H). Anal. Calcd for $C_{14}H_{14}O$: C, 84.81; H, 7.11. Found: C, 84.78; H, 7.20.

4-(Trifluoromethyl)-4'-(methylthio)biphenyl: mp 165 °C; ^{1}H NMR ($CDCl_3$) δ 2.5 (s, SMe, 3 H), 7.2–7.65 (m, Ar, 8 H). Anal. Calcd for $C_{14}H_{11}F_3S$: C, 62.67; H, 4.13; S, 11.95; F, 21.24. Found: C, 64.94; H, 3.93; S, 10.42; F, 18.53.

Acknowledgment. We are grateful to the Centre National de la Recherche Scientifique for financial support. We thank the referees for help and comments.

Activation of Reducing Agents. Sodium Hydride Containing Complex Reducing Agents. 33. NiCRA's and NiCRAL's as New Efficient Desulfurizing Reagents

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Received March 2, 1989

It is shown that nickel-containing complex reducing agents alone or in the presence of 2,2'-bipyridine (NiCRA and NiCRA-bpy, respectively) are very efficient in the desulfurization of sulfur-containing organic compounds. A number of functional groups are resistant. Advantages of the inexpensive and nonpyrophoric CRA's are their easy preparation and handling. The mechanisms of these desulfurizations are discussed and compared to those with Ni(0) complexes.

Introduction

The desulfurization of organic compounds is an important reaction in organic chemistry. Indeed, it is a key process in the production of nonpolluting fuels.[1] On the other hand, the synthesis of organic compounds using sulfur chemistry as an auxiliary tool would not be possible without removal of the carbon–sulfur bond in the last step. A desulfurization procedure ought to be mild and chemoselective to be of use in synthesis. Considering the high diversity of the sulfurated functions to be removed and of the functional groups to be resistant, it is soon realized why many reagents have been proposed. Examination of the voluminous literature dealing with desulfurizations shows that in spite of the abundance of the procedures, numerous synthetic problems remain unsolved and that room exists for new reagents.

Among the more useful reagents, Raney nickel[2,3] and in situ generated nickel boride[4] are widely used heterogeneous reagents. Drawbacks of the former are their tedious preparation, hazardous handling,[3a] the difficulty of accurately determining the weight of Ni,[3] and the lack of chemo- and stereoselectivity. Nickel boride is more convenient. It is not pyrophoric and the amount of Ni used is easily known.[4] However, in spite of a lower reactivity, which limits its use,[4b,c] nickel boride lacks chemo- and stereoselectivity.

The desulfurization properties of Raney nickel and nickel boride have been mainly attributed to the large amount of hydrogen adsorbed on the surface of the finely divided catalyst.[2b,3a,5]

On the other hand, it is well-known that single electron transfer (SET) plays an important role in a large number of desulfurizations.[1,6] Thus, nickel reagents possessing a high SET ability might be good desulfurizing reagents in the absence of hydrogen.

The easily prepared, nonpyrophoric nickel-containing complex reducing agents (NiCRA's and NiCRAL's)[7] de-

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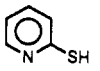
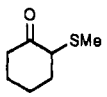
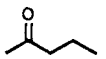
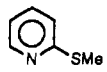
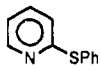
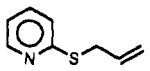
(7) Caubere, P. *Angew. Chem. Int. Ed. Engl.* **1983**, *22*, 599. In this paper we have adopted the following convention: a NiCRA prepared from NaH, *t*-AmONa, and nickel acetate will be abbreviated NiCRA ($x/y/z$), where the molar ratio NaH/*t*-AmONa/Ni(OAc)$_2$ (in that order) is equal to $x/y/z$. In the same way, a NiCRAL prepared from NaH, *t*-AmONa, nickel acetate, and 2,2'-bipyridine or triphenylphosphine will be abbreviated NiCRAL ($x/y/z/t$), where the molar ratio NaH/*t*-AmONa/Ni(OAc)$_2$/2,2'-bipyridine or triphenylphosphine (in that order) is equal to $x/y/z/t$.

0022-3263/89/1954-4848$01.50/0

Table I. Desulfurization of Thiols, Thioethers, and Dithioethers

run	substrate	procedure[a]	Ni/S[b]	t, h	product	yield,[c] %
1	$C_{12}H_{25}SH$	A	10	1	$C_{12}H_{26}$	94
2	PhSH	A	10	2	PhH	>90
3		A	10	17.5		>97
4	$C_{12}H_{25}SC_{12}H_{25}$	A	20	18	$C_{12}H_{26}$	72
5	$C_{12}H_{26}SPh$	A	10	2.5	$C_{12}H_{26}$	67
6	$C_{12}H_{26}SPh$	B	10	2.5	$C_{12}H_{26}$	70
8	$(C_6H_{13})(Me)CHSEt$	A	10	66	C_8H_{18}	85
9	$(C_6H_{13})(Me)CHSPr$	A	10	66	C_8H_{18}	80[d]
10	$(C_6H_{13})(Me)CHSPh$	A	20	17	C_8H_{18}	65
11	$(C_6H_{13})(Me)CHSPh$	B	20	2	C_8H_{18}	99
12	$Ph_2CHSCHPh_2$	A	10	19	Ph_2CH_2	98
13	Ph_2CHSPh	A	10	4	Ph_2CH_2	81
14	Ph_2CHSPh	B	10	18	Ph_2CH_2	99
15		A	20	2		90
16	$CH_3CO(CH_2)_3SEt$	A	20	2		76[e]
17	PhSMe	A	10	18	PhH	>98
18	PhSMe	B	10	2	PhH	98
19		A	10	1		98
20		A	10	15.5		95
21		A	10	1		95
22	$C_{12}H_{25}SSC_{12}H_{25}$	A	5	2	$C_{12}H_{26}$	96
23	$Ph_2CHSSCHPh_2$	A	10	0.5	Ph_2CH_2	83

[a] Procedure A: NiCRA (5/2/1); THF; 63 °C. Procedure B: NiCRA–bpy (4/2/1/2); DME; 65 °C. [b] Atom Ni/atom S. [c] Yields determined by GC analysis with comparison with authentic samples. [d] Conversion 80%. [e] Conversion 82%.

veloped in our laboratory [7-10] are powerful reducing[8] and coupling reagents.[9] Their properties have been attributed to the presence of sodium alkoxides, which could increase the SET ability of the hydride and Ni(0) species in the polymeric reagent.[7] Moreover, they were found to be stereo- and chemoselective in a number of reductions.[8c-f]

Thus, NiCRA's are new interesting desulfurizing reagents. A brief study reported in a short preliminary communication[10] verified this belief.

In this paper we report the behavior of NiCRA and NiCRA-bpy during the desulfurization of a number of thiols, thioethers, disulfides, and sulfur-containing heterocycles.

Results and Discussion

The results from the desulfurization of thiols, thioethers, and disulfides by NiCRA and/or NiCRA-bpy are given in Table I.

Comparison with literature data shows that NiCRA's are at least as efficient as Raney nickel[3] and more efficient than nickel boride.[4] Particularly, the presence of a nitrogen-containing heterocycle did not lower the reactivity of CRA, contrary to that observed with nickel boride.

Interestingly, CRA did not attack ketones (runs 15 and 16), while under other conditions it is known as a reducing agent for carbonyl groups.[8a,f] With these results in hand we turned toward the desulfurization of thiophenes and thiopyran derivatives (Table II).

These heterocycles were easily desulfurized with the appropriate reagent (run 3, for example). Again, ketones and esters were not attacked (runs 1–3).

Isolation of olefins containing substrates in run 7 was not very surprising since CRA's are known as weak reducing agents of hindered unsaturated double bonds.[8d,e] More interesting is the isolation of 1-phenylpropene (run 5), indicating that under appropriate conditions it ought to be possible to preserve a number of olefins during desulfurizations by CRA's. This possibility is presently under investigation.

Note that the formation of 2-phenylindane (run 10) indicates the possible intervention of a radical mechanism.[1,6]

Finally, we examined the behavior of NiCRA's against dibenzosulfur-containing heterocycles. The substrates are of particular interest. Indeed among them is the dibenzothiophene recognized as one of the most resistant to desulfurization.[1a,6] Moreover, their homogeneous desulfurization by Ni(0) complexes has been carefully studied by Eisch and co-workers, who gave some clues on the mechanism of these reactions.[1a]

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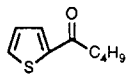
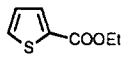
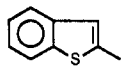
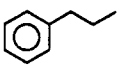
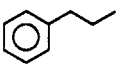
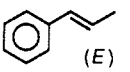
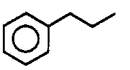
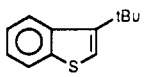
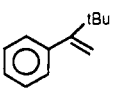
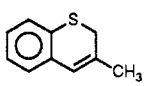
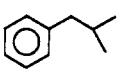
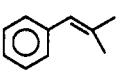
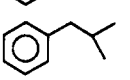
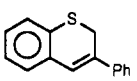
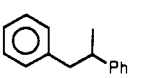
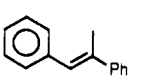
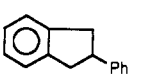
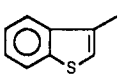
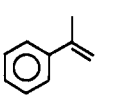
Table II. Desulfurization of Thiophene and Thiopyran Derivatives

run	substrate	procedure[a]	Ni/S[b]	t, h	product	yield,[c] %
1		B	10	2	$C_4H_9C(O)C_4H_9$	96
2		A	10	1	$C_4H_9CO_2Et$	99
3		B	3	3	$C_4H_9CO_2Et$	99
4		A	20	1		(99)
5		B	5	23[d]		(21)
					 (E)	(27)
6		B	10	15		(99)
7		B	10	18		83
8		B	5	19		(52)
						(47)
9		B	20	1.5		75 (80)
10		B	5	16		(40)
						(43) (Z:E = 1/3)
						(16)
11		B	5	18		81 (82)

[a] Procedure A: NiCRA (5/2/1); THF; 63 °C. Procedure B: NiCRA-bpy (4/2/1/2); DME; 65 °C. [b] Atom Ni/atom S. [c] Isolated yields by flash chromatography; in parentheses, yields determined by GC analysis with comparison with authentic samples. [d] Conversion 50%.

We performed these desulfurizations with NiCRA, NiCRA-bpy, or NiCRA-Ph_3P, with the results given in Table III.

With few exceptions, yields of desulfulization were excellent. Qualitatively we obtain the same results as Eisch and co-workers, that is to say, formation of open and cyclized products. However it is noteworthy that the simple addition of a ligand (compare runs 1, 2, and 3) or variation in its structure (compare runs 2 and 3 or 10 and 11) completely changes the ratios of the products formed. These results underline, once more, the versatility of CRA's. Of particular interest is the comparison of the results obtained with dibenzothiophene and its dimethyl derivatives (runs 14–16).

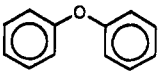
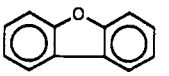
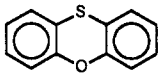
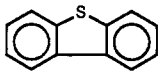
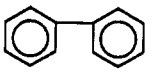
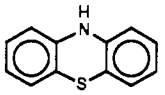
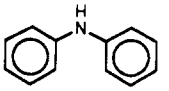
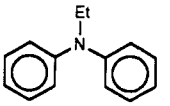
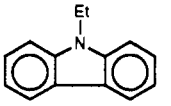
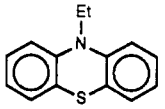
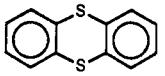
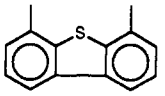
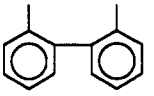
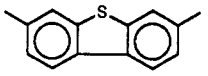
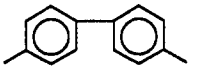
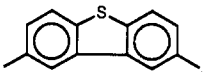
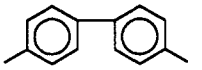
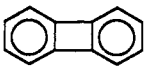
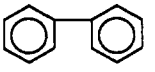
The reactivity of these substrates decreases following the sequence unsubstituted > 2,8-dimethyl > 3.7-dimethyl ≫ 4.6-dimethyl. This result is in agreement with the results of Eisch and co-workers,[1a] who studied the first three substrates. Taking into account the polymeric nature of CRA's, the very low reactivity of 4,6-dimethylbenzothiophene is mainly attributable to steric hindrance.

However, as far as the nature of the products formed are concerned, our results are completely different from those of Eisch. Indeed, these authors found that each dimethylbenzothiophene led to the corresponding biphenyl *with conservation of the orginial phenyl–phenyl bond.* This result eliminated the intermediate formation of dimethylbiphenylenes followed by ring opening of the four-membered ring.[1a]

In the present work the reverse was observed. Moreover, we verified that under conditions of runs 14–16 CRA's quantitatively transformed biphenylene into biphenyl (run 17). This ring opening is a well-known property of Ni(0) species.[1a,6] On the other hand the relative reactivity of benzothiophenes was well explained by Eisch and coworkers[1a] as due to the electronic effects of the methyl group on an intermediate radical anion. Finally, it was also shown that, like aryl halides, diaryl sulfides were also prone to oxidative addition on reaction with Ni(0) species.[1a] Taking into account all these observations of the properties of CRA's and the mechanism proposed for the coupling of aryl halides (to be published), the mechanism in Scheme I could explain the reactions observed in the present work (ligands of Ni were omitted for the sake of simplicity).

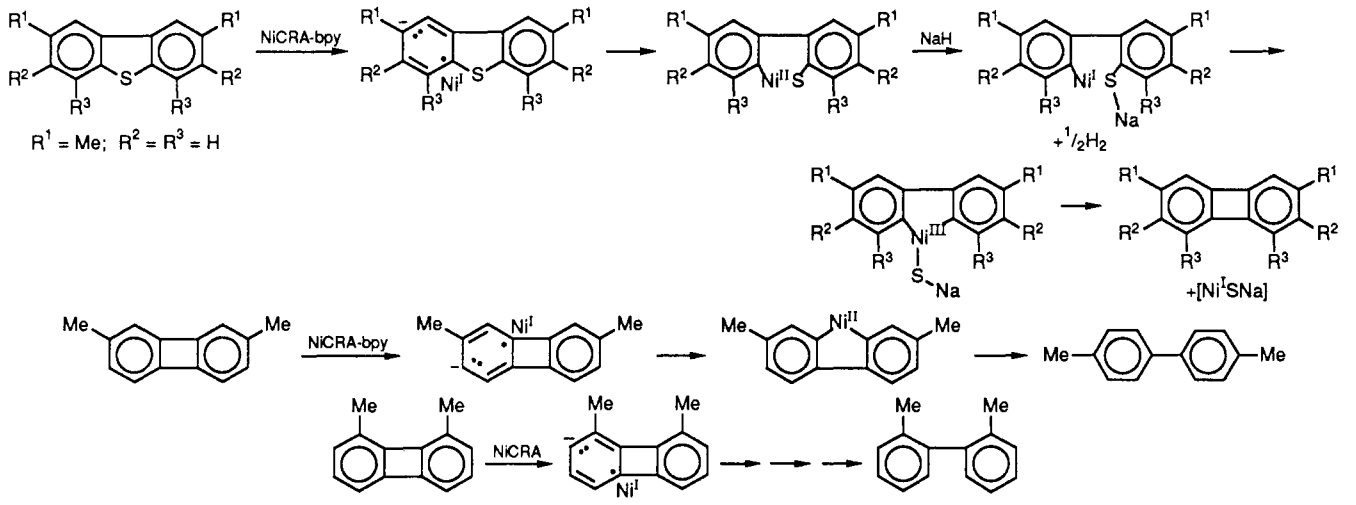
According to the Eisch hypothesis,[1a] the opening of 2,4-dimethylbiphenylene must be directed by the elec-

Table III. Desulfurization of Dibenzophene Derivatives

run	substrate	procedure[a]	Ni/S[b]	t, h	product (%)[c]		
							
1		A	10	27	(92)		(3)
2		B	2.5	42[d]	(40)		(48)
3		C	2.5	4	(42.7)		(57.3)
4		A	10	10			(99)
5		B	10	2			(99)
6		C	10	3			(94)
7		A	10	42			(99)
8		B	10	32			(99)
9		C	10	18			(99)
							
10		B	10	18[e]	(39)		(13)
11		C	10	18	(98)		(1)
					PhSPh	PhPh	PhH
12		B	2.5	89	(3)	(8)	(82)
13		B	2.5	3	(1)	(43)	(55)
14		B	10	70			(15)
15		B	10	46			(40)
16		B	10	4			(97)
17		B	10	0.5			(98)

[a] Procedure A: NiCRA (5/2/1); THF; 63 °C. Procedure B: NiCRA-bpy (4/2/1/2); DME; 65 °C. Procedure C: NiCRA-PPh_3 (4/2/1/4); DME; 65 °C. [b] Atom Ni/atom S. [c] Yields determined by GC analysis with comparison with authentic samples. [d] Conversion 88%. [e] Conversion 53%.

Scheme I



tron-donating effects of the methyl groups in such a way that in the radical anion the electronic density of the methylated carbon was as low as possible.

With 1,8-dimethylbiphenylene, electronic effects of the methyl group influence the rate of the SET, but not the way the ring opens, which is directed by the steric effect of the substituents.

Conclusion

CRA's were found to be very good reagents in desul-

furizations. This paper shows that they do not attack ketones or esters, as well as a number of olefinic bonds. As a consequence, their chemo- and stereoselectivity are actively being investigated in our laboratory and will be the topic of future publications.

Experimental Section

Instrumentation. All melting points were determined with a Tottoli capillary melting point apparatus. Infrared spectra (IR) were recorded on a Perkin-Elmer Model 580B spectrophotometer. NMR spectra were taken on a Bruker AW80 or a Bruker AM400 instrument. GC analyses were achieved with a Girdel 300 chromatograph equipped with a 6 ft × 0.25 in. column of 10% OV 101 on Chromasorb WAW or with a Spectra Physics 7100 chromatograph equipped with a 45-ft SE 30 capillary column. All reactions were conducted under a nitrogen atmosphere (quality R, L'Air Liquide). Flash chromatography was carried out on Merck silica gel 60 (230–400 mesh).

Starting Materials. Solvents. THF was distilled from a benzophenone–sodium adduct and stored over sodium wires. DME (Fluka) was distilled from sodium and stored over sodium wires. The absence of peroxides was checked before each run.[11]

Reagents. *tert*-Amyl alcohol (Aldrich) was distilled from sodium. Nickel acetate (Aldrich) was dried in vacuo for 12 h at 120–130 °C. 2,2′-Bipyridine (Fluka) was recrystallized before use from hexane. Sodium hydride (55–60% in oil, Fluka) was used after three washings with the reaction solvent under nitrogen. Each batch of sodium hydride was titrated by standard techniques[12] before use.

Substrates. 1-Dodecanethiol, thiophenol, 2-pyridinethiol, thioanisole, 3-methylbenzo[*b*]thiophene, dibenzothiophene, phenothiazine, and thianthrene were available from commercial sources (Aldrich, Lancaster Synthesis) and were used without further purifications. Dodecyl sulfide, mp 40 °C (from hexane), was prepared from bromododecane and sodium sulfide.[13] Dodecyl phenyl sulfide, mp 33–34 °C (from ethanol), 2-octylethyl sulfide, bp 70 °C (3 mm), 2-octyl propyl sulfide, bp 111 °C (15 mm), 2-octyl phenyl sulfide, bp 160 °C (15 mm), diphenylmethyl sulfide, mp 66 °C (from ethanol), diphenylmethyl phenyl sulfide, mp 80 °C (from ethanol), 5-(ethylthio)-2-pentanone, bp 108 °C (20 mm), 2-(methylthio)pyridine, bp 197 °C, 2-(phenylthio)pyridine, bp 130 °C (2 mm), and 2-(allylthio)pyridine, bp 85–87 °C, were prepared (yields varying from 90 to 98%) by the reaction of a sodium thiolate with an appropriate halide in hexane.[14] 2-(Methylthio)cyclohexanone bp 80 °C (4 mm), was prepared by the classical method.[15] Didodecyl disulfide, mp 30 °C (from ethanol), and diphenylmethyl disulfide, mp 151 °C (from ethanol), were prepared from the corresponding thiol and hydrogen peroxide (34% sol.) in aqueous NaOH (20%).[16] Butyl thiophene-2-yl ketone, bp 99 °C (3 mm), was prepared from thiophene, valeric acid, and P_2O_5.[17] Ethyl 2-thiophenecarboxylate, bp 94 °C 10 mm), was prepared by esterification of 2-thiophenecarboxylic acid (commercialy available) in ethanol in the presence of H_2SO_4 at reflux for 1 h.[18] 3-*tert*-Buylbenzo[*b*]thiophene, bp 149 °C (20 mmHg), was prepared from thianaphthene, phosphoric acid, and isobutylene at 125 °C.[19] 3-Methylbenzo[*b*]thiophene, mp 48–49 °C (from ethanol), 3-methyl-2*H*-1-benzothiopyran, bp 110–115 °C (5 mm), and 3-phenyl-2*H*-1-benzothiopyran, mp 64 °C (from ethanol), were prepared for 2-mercaptobenzoic acid (commercialy available) in three steps according the method of Arnoldi and Carughi.[20] Phenoxathiin, mp 56–57 °C (from methanol), was prepared from diphenyl ether.[21] *N*-Ethylphenothiazine, mp 108 °C (from ethanol), was prepared by alkylation of phenothiazine sodium salt. 4,6-Dimethyldibenzothiophene, mp 154–155 °C (from ethanol), was prepared by the action of *n*-butyllithium on dibenzothiophene in ethyl ether at 50 °C for 21 h followed by treatment with dimethyl sulfate.[22] 3,7-Dimethyldibenzothiophene, mp 147–148 °C (from ethanol), was prepared from biphenyl in four steps: (a) Bromination to yield 50% of 4,4′-dibromobiphenyl, mp 160–162 °C (from ethanol).[23] (b) Chlorosulfonation to form 3,7-dibromodibenzothiophene 5,5-dioxide, mp 308–309 °C (from ethanol).[24] (c) Reduction with $LiAlH_4$ in ethyl ether to provide 70% of 3,7-dibromodibenzothiophene.[22] (d) Bromine–lithium exchange with *n*-butyllithium below 0 °C in ethyl ether followed by treatment with dimethyl sulfate.[24] 2,8-Dimethyldibenzothiophene, mp 114–116 °C (from ethanol), was prepared in two steps from dibenzothiophene: (a) Bromination in glacial AcOH to yield 2,8-dibromodibenzothiophene, mp 221–223 °C (from ethanol).[25] (b) Bromine–lithium exchange with *n*-butyllithium in ethyl ether at 5 °C, followed by treatment with dimethyl sulfate.[24] Biphenylene, mp 110–112 °C (from ethanol), was prepared by thermolysis of benzenediazonium-2-carboxylate.[26]

Products. Dodecane, octane, diphenylmethane, cyclohexanone, 2-pentanone, 2-nonanone, ethyl valerate, 1-phenylpropane, (*E*)-β-methylstyrene, isobutylbenzene, 2-methyl-1-phenylpropene, α-methylstilbene, α-methylstyrene, diphenyl ether, dibenzofuran, biphenyl, diphenylamine, carbazole, phenyl sulfide, and 4,4′-bitolyl were available from commercial sources (Aldrich, Fluka, Merck, Lancaster Synthesis). α-*tert*-Butylstyrene, bp 75 °C (10 mm), was prepared from 2-phenyl-3,3-dimethyl-2-butanol in two steps: (a) reaction of pinacolone with phenyllithium (yield 78%); (b) dehydration over activated alumina.[19] 1,2-Diphenylpropane, bp 113–115 °C (2 mm), was prepared in two steps (70%) by treating benzenesulfonyl chloride with allyl alcohol (2-propen-1-ol) in the presence of 15% NaOH to give allyl benzenesulfonate, which was treated by $AlCl_3$ in C_6H_6.[27] 2-Phenylindan, bp 165 °C (11 mm), was prepared Clemmensen reduction of 2-phenyl-1-indanone according to the method of Galton et al.[28] 2,2′-Bitolyl was prepared by coupling of *o*-bromotoluene by NiCRA-bpy.[8b] *N*-Ethyldiphenylamine, bp 207 °C (70 mm), was prepared by alkylation of diphenylamine sodium salt.

General Procedures. Procedure A [NiCRA (5/2/1); THF; 63 °C]. *t*-AmOH (20 mmol) in 10 mL of THF was added dropwise to a suspension of NaH (70 mmol), and $Ni(OAc)_2$ (10 mmol) in refluxing THF (30 mL). After 2 h of stirring, the reagent was ready for use and the substrate could be added in THF (10 mL).

Procedure B [NiCRA-bpy (4/2/1/2); DME; 65 °C]. *t*-AmOH (20 mmol) in 10 mL of DME was added dropwise to a suspension of NaH (60 mmol), $Ni(OAc)_2$ (10 mmol), and 2,2′-bipyridine (20 mmol) in DME (30 mL) at 65 °C. After 2 h of stirring, the reagent was ready for use and the substrate could be added in DME (10 mL).

Procedure C [NiCRA-PPh_3 (4/2/1/4); DME; 65 °C]. Procedure B was employed, using triphenylphosphine (40 mmol) in place of 2,2′-bipyridine. The reactions were monitored by GC analysis of small aliquots. The internal standard was hydrocarbon (C_8–C_{16}). After completion of the reaction, the excess of hydride was carefully destroyed by dropwise addition of EtOH at 25 °C until hydrogen evolution ceased. The mixture was then acidified, and the organic phase was extracted into diethyl ether and dried over $MgSO_4$. After removal of the solvents, products were separated by flash chromatography using an appropriate EtOAc/hexane mixture as eluant. Note that volatile products must be

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isolated by distillation instead of chromatography. The yield of desulfurization reactions was determined by isolating and weighing the crude products and analyzing the mixture by GC (hydrocarbons C_8–C_{16} were employed as internal standards). Response factors were determined on pure samples of all components encountered in such analyses. Spectral data (^{1}H NMR, IR) and melting and boiling points of the desulfurization products were the same as authentic samples.

Acknowledgment. We are grateful to the Centre Natural de la Recherche Scientifique for financial support. We thank the referees for help and comments.

Superoxide Anion Radical ($O_2^{\bullet-}$) Mediated Base-Catalyzed Autoxidation of Enones

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Received February 14, 1989

Seventeen variously substituted cyclohex-2-en-1-ones were prepared and reacted with superoxide anion radical ($O_2^{\bullet-}$, generated from KO_2/18-crown-6) in inert nonpolar aprotic media at room temperature. The 4,4,6,6-tetrasubstituted cyclohexenones (**1b**, **1c**, and **1d**) proved to be totally inert, while those cyclohexenones possessing available acidic α'- or γ-hydrogens underwent $O_2^{\bullet-}$-mediated base-catalyzed autoxidation (BCA) generating various products depending on the nature and location of the substituents. Thus, 4,4- and 5,5-disubstituted substrates (**2b**, **2c**, **2e**, **2f** and **3b**, **3d**, **3f**–**3i**, respectively) gave 2-hydroxycyclohexa-2,5-dien-1-ones (**7**) as the major product (>80% yield) upon aqueous acid workup, while the corresponding 2-methoxy analogues **8** are obtained when the reaction is quenched with CH_3I. 2,3-Epoxycyclohexanones **13** and oxidative cleavage products **11** and **12** are formed in the case of the 6,6-disubstituted systems (**4a**–**4c**); these oxidation products are accompanied by dimers **14** when the substituent on **4** is CH_3 or H. Epoxide **23** is the primary isolable product in the 3,4,4-trialkyl system (**5d**). As expected for BCA processes, similar results were observed when these reactions were mediated by KOH (at room temperature) or $KOC(CH_3)_3$ (at −40 °C). In the case of 6,6-diphenylcyclohex-2-en-1-one (**4c**), however, *tert*-butoxide-mediated BCA at −40 °C yielded cyclopentene hydroxy acid **15** in addition to epoxide **13**. The saturated analogue of **4c**, **18**, yielded primarily the corresponding saturated hydroxy acid **19**, as well as several other oxidation products (**20**–**22**) depending on the reaction conditions. The mechanism of these transformations is rationalized in terms of base-induced reactions and rearrangements of the initially formed keto hydroperoxides.

Introduction

Despite the pivotal role of free-radical processes in nature, free-radical damage presents a serious and constant threat to living organisms.[1-3] One of the clearest sources of radicals in the body is superoxide anion radical, $O_2^{\bullet-}$, which is formed in a large number of reactions of biological importance in both enzymic and nonenzymic processes.[4] Fluxes of $O_2^{\bullet-}$, generated enzymatically or photochemically, have been shown to inactivate viruses, induce lipid peroxidation (a suspected source of senescence and carcinogenesis[3,5]), damage membranes, and kill cells.[4]

Given the importance of superoxide in biological processes, it is clearly of value to understand its organic chemistry and thereby its mechanism of action.[6,7] The introduction in 1972 of the KO_2–crown ether reagent[8] as a convenient source of $O_2^{\bullet-}$ in aprotic media allowed the organic chemist to carry out extensive studies on the reactions of $O_2^{\bullet-}$ with various functional groups.[9]

Our own research in this field began in 1975 with an exploration of the enone moiety. We reported that $O_2^{\bullet-}$ reacts with chalcones and tetracyclone via what is presumably an electron transfer to the extended π-system. The resulting substrate anion radical is oxygenated, ultimately producing oxidative cleavage products of these enones.[6,10,11] Dibenzal acetone reacts in a similar fashion.[12]

We next turned our attention to more simple enone systems in which electron transfer is not expected. The complete details[13] of these studies are reported below and,

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