The adduct **20a** is obtained in only 74% yield on dehydrosulfurating tetramethylenethiourea solutions (CH_2Cl_2) with HgO (yellow) in presence of equimolar quantities of *N,N'*-diphenylcarbodiimide; small amounts of unidentified sulfur-containing byproduct were also formed in this reaction. Analytical data of recrystallized samples (hexane or methanol) are given in Table II.

Reactions of Carbodiimides 1c,d with Hexafluoroacetone. (1) Introduction of gaseous hexafluoroacetone into a solution of 1.38 g (0.01 mol) of 1,3-diazacyclodeca-1,2-diene (**1d**) in 30 mL of chloroform leads to slow formation of cycloadduct **24b** (n = 7). Progress of the reaction can be followed by IR spectroscopy by monitoring disappearance of the carbodiimide band at 2120 cm^{-1} and the appearance of a new C=N band at 1740 cm^{-1}. The resulting reaction solution is concentrated in vacuo, leaving a colorless liquid (contaminated by trace amounts of heptamethyleneurea): bp 46–47 °C (0.1 mm); 3.90 g (83%). Anal. Calcd for $C_{14}H_{14}N_2O_2F_{12}$: C, 35.76; H, 3.00; N, 5.95. Found: C, 35.71; N, 2.96; N, 5.84.

(2) A reaction similar to the one described above is carried out with 1,3-diazacyclonona-1,2-diene (**1c**) and hexafluoroacetone. After approximately a 1-h reaction duration, IR spectra of the reaction mixture show a strong band at 1790 cm^{-1} and a small band at 1740 cm^{-1} aside from those of unchanged **1c**. Continued hexafluoroacetone introduction leads slowly to a nearly complete disappearance of the carbodiimide band at 2120 cm^{-1} and a significant decrease in the band at 1790 cm^{-1}. During distillation of the crude product in vacuo, a pressure drop is noticed as the bath temperature reaches 40–50 °C. A liquid, distilling at 53–55 °C (0.1 mm) at a bath temperature of 75–80 °C, is collected which consists according to its IR spectrum of a mixture of **1c** and **24a** (C=N at 1740 cm^{-1}); small amounts of a semisolid, consisting of oligomeric **1c**, are left behind.

Registry No. 1b, 85237-12-3; **1c**, 6248-74-4; **1d**, 6543-91-5; **1e**, 79568-35-7; **1f**, 72995-04-1; **1g**, 85237-13-4; **3b**, 19214-08-5; **3c**, 55040-59-0; **3d**, 55040-57-8; **3e**, 83594-28-9; **3f**, 55040-58-9; **4a**, 85237-14-5; **4b**, 65252-84-8; **4c**, 85237-15-6; **4d**, 85237-16-7; **4e**, 83594-29-0; **4f**, 83594-27-8; **4g**, 85237-17-8; **7**, 85237-18-9; **8**, 85237-19-0; **10**, 22246-75-9; **11**, 85237-20-3; **12**, 85237-21-4; **16**, 85237-22-5; **17**, 85237-23-6; **18** (n = 11), 85237-24-7; **18** (n = 6), 85237-25-8; **19** (n = 11), 85237-11-2; **19** (n = 6), 85237-10-1; **20a**, 20991-09-7; **20b**, 85237-26-9; **20c**, 85237-27-0; **20d**, 85237-28-1; **20e**, 85237-29-2; **20f**, 85237-30-5; **20g**, 85237-31-6; (*Z*)-**20h**, 85237-32-7; (*E*)-**20h**, 85237-33-8; **20i**, 85237-34-9; **21**, 85237-35-0; **23** (n = 6), 85237-36-1; **24a**, 85237-37-2; **24b**, 85237-38-3; 1-aza-2-methoxycyclohex-1-ene, 5693-62-9; 1-aza-2-methoxycyclohept-1-ene, 2525-16-8; 1-aza-2-methoxycyclooct-1-ene, 1889-06-1; 1-aza-2-methoxycyclododec-1-ene, 41471-03-8; 1-aza-2-methoxycyclotridec-1-ene, 29376-34-9; 2-azacyclododecanone, 1202-71-7; cycloundecanone, 878-13-7; benzosuberone, 826-73-3; hydroxylamine hydrochloride, 5470-11-1; pentamethylenethiourea, 5269-85-2; tetramethylenethiourea, 5700-04-9; phosgene, 75-44-5; thionyl chloride, 7719-09-7; *N,N'*-diphenylcarbodiimide, 622-16-2; hexafluoroacetone, 684-16-2; phenyl isocyanate, 103-71-9; *p*-chlorophenyl isocyanate, 104-12-1.

Reaction of (Arylmethyl)amines with Superoxide Anion Radical in Aprotic Media. Insights into Cytokinin Senescence Inhibition

Aryeh A. Frimer,* Gladis Aljadeff, and Joseph Ziv

The Department of Chemistry, Bar-Ilan University, Ramat Gan 52100, Israel

Received October 4, 1982

The cytokinins are a group of plant senescence retarding phytohormones, usually *N*-arylmethyl derivatives of adenine. Purine, adenine, and the cytokinins kinetin [6-(furfurylamino)purine] and 6-(benzylamino)purine were reacted with $O_2^{-}\cdot$ generated from KO_2 solubilized in diethylamine by 18-crown-6 polyether. The only reaction observed was simple deprotonation of the N-7 hydrogen, yielding an air-stable salt. In order to uncover other modes that might be available in the absence of this simple acid–base reaction, we reacted various (arylmethyl)amines (i.e., furfurylamine and benzylamine) and (arylmethyl)anilines (**2a–c**) with $O_2^{-}\cdot$ in benzene. The products in the case of (arylmethyl)amines were the corresponding aroylamines isolated in greater than 60% yield. Compounds **2a–c** yielded the corresponding amides (**3**), benzoic acids (**4**), nitrobenzenes (**5**), and arenes. Similar results were obtained when *tert*-butoxide or hydroxide replaced superoxide, with the rate of reaction decreasing in the order t-$BuO^- > O_2^{-}\cdot > HO^-$, the apparent order of decreasing basicity. The results suggest that the process observed involves a base-catalyzed autoxidation of the benzylic carbon of the benzylamines. The resulting hydroperoxide rearranges and/or undergoes oxidative cleavage, ultimately yielding the observed products. Aniline itself reacts with $O_2^{-}\cdot$, yielding azobenzene, nitrobenzene, and (4-nitrophenyl)phenylamine. The latter presumably results from the nitrobenzene trapping of the anilinyl radical.

The cytokinins are a group of plant senescence retarding phytohormones which are generally derivatives of the nucleic purine base adenine (**1b**), examples of which are kinetin [6-(furfurylamino)purine, **1c**] and N^6-benzyladenine [6-(benzylamino)purine, **1d**].[1] Various cytokinins have also displayed antiviral action,[2] while kinetin ribofuranoside has been shown to be an anticancer agent.[3]

Recently, Leshem et al. reported[4] in vivo experiments with intact pea plants which indicated that enzymatically generated (using xanthine–xanthine oxidase) superoxide anion radical ($O_2^{-}\cdot$) induced senescence in plant tissue which was inhibited by kinetin (**1c**). These experiments

(1) (a) Leshem, Y. "The Molecular and Hormonal Basis of Plant Growth Regulation"; Pergamon Press: New York, 1973; p 121 ff. (b) Kende, H. *Int. Rev. Cytol.* **1971**, *31*, 301. (c) Skoog, F.; Armstrong, D. J. *Annu. Rev. Plant Physiol.* **1970**, *21*, 359. (d) Hall, R. H. *Ibid.* **1973**, *24*, 415.

(2) Milo, G. E., Jr.; Sabai, B. I. *Virology* **1969**, *38*, 26.

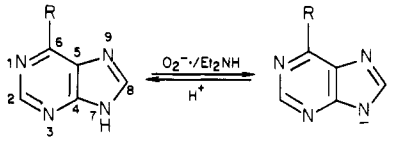
(3) Orr, M. F.; McSwain, B. *Cancer Res.* **1960**, *20*, 1362.

(4) (a) Leshem, Y. Y.; Grossman, S.; Frimer, A. A.; Ziv, J. In "Biochemistry and Physiology of Plant Lipids"; Appelqvist, L. A., Liljenberg, C., Eds.; Elsevier: The Netherlands, 1979; pp 193–198. (b) Leshem, Y. Y.; Wurzburger, J.; Grossman, S.; Frimer, A. A. *Physiol. Plant.* **1981**, *53*, 9. (c) Leshem, Y. Y.; Liftman, Y.; Grossman, S.; Frimer, A. A. In "Oxygen and Oxy-Radicals in Chemistry and Biology"; Rodgers, M. A. J., Powers, E. L., Eds.; Academic Press: New York, 1981; pp 676–678.

0022-3263/83/1948-1700$01.50/0

suggested that free radicals (such as $O_2^{-}\cdot$ or its derivatives) generated in the natural course of biological processes are a source of plant senescence and that cytokinin compounds inhibit this aging by scavenging these radicals.

In an attempt to glean information that might shed light on the mechanistic details of this senescence inhibition, we undertook a study of the reaction of cytokinins with $O_2^{-}\cdot$ in aprotic media. Although kinetin (**1c**) and benzyl-



1

a, R = H; b, R = NH_2; c, R =  ; d, R = $NHCH_2Ph$

adenine (**1d**) are generally insoluble in aprotic media, they do dissolve in nitrogen base solvents (e.g., triethylamine, diethylamine, and pyridine). When purine, adenine, kinetin, and benzyladenine (compounds **1a–d**) were reacted with KO_2/18-crown-6 in diethylamine, the only reaction observed was the deprotonation of the acidic N-7 hydrogen. The resulting salt precipitates out of solution and regenerates the starting purine quantitatively upon acid workup.

The results suggest that free cytokinins may react in the hydrophobic areas of the cell by protonation of $O_2^{-}\cdot$. However, it should be noted that for the anticancer agent kinetin ribofuranoside,[3] no such simple acid–base reaction is possible. Furthermore, the aqueous areas of the cell are buffered, and thus other modes are expected to come into play.

Results and Discussion

In order to discover some of the other modes available, we prepared a variety of cytokinin analogues (**2a–c**; see Table I) by heating the appropriate benzyl chlorides and anilines in the presence of aqueous sodium carbonate at 95–100 °C.[5] Analogues **2a–c** and components **7a** and **7b** were reacted with $O_2^{-}\cdot$ in benzene, and the results are listed in Table I.

While the mechanistic details are far from simple, the isolation of benzamides **3** and **8** and benzoic acids **4** as the major products clearly require steps leading to the oxidation of the benzylic carbon as the major reaction pathway. It should be noted, however, that simple benzylic and allylic hydrogens are generally inert to the reaction of $O_2^{-}\cdot$. Thus toluene, 9,10-dihydrophenanthrene, tetralin, acenaphthlene, cyclohexene, trimethyl- and tetramethylethylene, 2-methyl-2-pentene, and cholesterol are unaffected by $O_2^{-}\cdot$.[6] Nevertheless, benzylic hydrogens activated either by electron-withdrawing groups on the ring or by additional aryl groups do react. For example, Sagae and co-workers[7] report that *o*- and *p*- (but not *m*-) nitrotoluenes are oxidized by electrogenerated $O_2^{-}\cdot$ to the corresponding benzoic acids. Furthermore, various diarylmethanes have been oxidized by $O_2^{-}\cdot$ to the corresponding ketones, including anthrone, 9,10-dihydroanthracene, fluorene, xanthine, diphenylmethane, and distyrylmethane.[8] Since compounds **2a–c** and **7a,b** are monoarylmethanes and do not bear electron-withdrawing groups on the ring, the lability of the benzylic hydrogens must be attributed to the presence of an α-amino group.

Interestingly, in the case of nitrotoluenes[7] and diarylmethanes[8] benzylic hydrogen atom abstraction by $O_2^{-}\cdot$ has been proposed as the initial step (eq 1), which is followed

$$O_2^{-}\cdot + ArCH_2R \rightarrow HOO^{-} + Ar\dot{C}HR \quad (1)$$

$$Ar\dot{C}HR + O_2 \longrightarrow ArCHR(OO\cdot) \longrightarrow ArCR(=O) \quad (2)$$

by typical free radical autoxidative processes (eq 2). Considering that radicals are stabilized by α-nitrogen groups,[9] a radical process might possibly be involved in the $O_2^{-}\cdot$-mediated oxidation of (arylmethyl)amines **2a–c** and **7a,b**.

However, simple thermochemical calculations cast serious doubt on the suggestion that $O_2^{-}\cdot$ plays the role of a hydrogen atom abstractor except with particularly labile hydrogens or perchance under specific catalyzed conditions. Valentine[10] has evaluated the H–O bond-dissociation energy for HOO^{-} at around 63.4 kcal/mol. Thus, a hydrogen abstraction could be an exothermic process only if the R–H dissociation energy were less than 63.4 kcal/mole. A quick scan of any table of bond-dissociation energies[11] reveals that only a handful of substrates bear R–H bonds even remotely that weak. While the above calculations are strictly applicable only to the gas phase, these results do suggest that hydrogen abstraction is not expected to be a primary reaction pathway.

While $O_2^{-}\cdot$-induced free radical autoxidation seems to be a ruled out, based-catalyzed autoxidation[12] (BCA) has not. Indeed, Sawyer[13] has calculated that the effective basicity of $O_2^{-}\cdot$ is equivalent to that of a conjugate base of an acid with a pK_a of ~23. It should not be surprising, then, that even weakly acidic organic compounds (such as *n*-butanol[13d,14] which has a pK_a of 33 in DMF[15]) are efficiently deprotonated by $O_2^{-}\cdot$ and apparently cause the instantaneous disproportionation of O_2 (eq 3 and 4). The

$$RH + O_2^{-}\cdot \rightarrow R^{-} + HO_2\cdot \quad (3)$$

(5) (a) Willson, F. G.; Wheeler, T. S. "Organic Syntheses"; Wiley: New York, 1941; Collect. Vol. I, p 102. (b) Ogata, Y.; Nagura, K. *J. Chem. Soc., Perkin Trans. 2* **1974**, 1089. (c) The *p*-methylbenzyl chloride required for the preparation of **2c** was synthesized according to: Newman, M. S.; George, M. V. *J. Org. Chem.* **1961**, *26*, 4306.

(6) (a) Dietz, R.; Forno, A. E. J.; Larcombe, B. E.; Peover, M. E. *J. Chem. Soc. B* **1970**, 816. (b) Rosenthal, I.; Frimer, A. *Tetrahedron Lett.* **1975**, 3731. (c) Smith, L. L.; Kulig, M. J.; Teng, J. I. *Chem. Phys. Lipids* **1977**, *20*, 211.

(7) (a) Sagae, H.; Fujihira, M.; Lund, H.; Osa, T. *Bull. Chem. Soc. Jpn.* **1980**, *53*, 1537. (b) Sagae, H.; Fujihira, M.; Osa, T.; Lund, H. *Chem. Lett.* **1977**, 793.

(8) (a) Galiani, G.; Rindone, B. *Tetrahedron* **1981**, *37*, 8313. (b) Moro-oka, Y.; Chung, P. J.; Arakawa, H.; Ikawa, T. *Chem. Lett.* **1976**, 1293. (c) Tezuka, M.; Ohkatsu, Y.; Osa, T. *Bull. Chem. Soc. Jpn.* **1975**, *48*, 1471. (d) Lee-Ruff, E.; Timms, N. *Can. J. Chem.* **1980**, *58*, 2138. (e) Top, S.; Jaoven, G.; McGlinckey, M. *J. Chem. Soc., Chem. Commun.* **1980**, 643. (f) Dietz, E.; Peover, M. E.; Rothbaum, P. *Chem.-Ing.-Tech.* **1970**, *42*, 185.

(9) (a) Elad, D.; Sinnreich, J. *Chem. Commun.* **1965**, 471. (b) Elad, D.; Sinnreich, J. *Chem. Ind. (London)* **1965**, 768. (c) Elad, D.; Sinnreich, J. *Ibid.* **1966**, 1181.

(10) (a) Valentine, J. S., personal communication, 1981, regarding ref 10b. (b) Valentine, J. S. In "Biochemical and Clinical Aspects of Oxygen"; Caughey, W. S., Ed., Academic Press: New York 1979; pp 659–677.

(11) See for example: Weast, R. C., Ed. "Handbook of Chemistry and Physics", 61st ed.; Chemical Rubber Co.: Boca Raton, FL, 1980; p F-233.

(12) (a) Russel, G. A.; Janzen, E. G.; Bemis, A. G.; Geels, E. J.; Moye, A. J.; Mak, S.; Strom, E. T. *Adv. Chem. Ser* **1965**, *No. 51*, 112. (b) Russel, G. A. *Pure Appl. Chem.* **1967**, *15*, 185. (c) Russel, G. A.; Bemis, A. G.; Geels, E. J.; Janzen, E. G.; Moye, A. J. *Adv. Chem. Ser.* **1968**, *No. 75*, 174.

(13) (a) Sawyer, D. T.; Gibian, M. J. *Tetrahedron* **1979**, *35*, 1471. (b) Gibian, M. J.; Sawyer, D. T.; Ungermann, T.; Tangpoonpholvivat, R.; Morrison, M. M. *J. Am. Chem. Soc.* **1979**, *101*, 640. (c) Sawyer, D. T.; Gibian, M. J.; Morrison, M. M.; Seo, E. T. *Ibid.* **1978**, *100*, 627, footnote 20. (d) Sawyer, D. T.; Nanni, E. J. In "Oxygen and Oxy-Radicals in Chemistry and Biology"; Rodgers, M. A. J., Powers, E. L., Eds.; Academic Press: New York, 1981; pp 15–44.

(14) Stanley, J. P. *J. Org. Chem.* **1980**, *45*, 1413.

(15) Nanni, E. J.; Stallings, M. D.; Sawyer, D. T. *J. Am. Chem. Soc.* **1980**, *102*, 4481.

Table I. Reaction of Selected Benzylamines with Superoxide and *tert*-Butoxide in Aprotic Media

substrate			product yield[b]							
$RC_6H_4CH_2NHC_6H_4R'$ (2)	RCH_2NH_2 (7)	Rxn conditions[a]	RC_6H_4CONH-C_6H_4R' (3)	RC_6H_4-COOH (4)	$R'C_6H_4$-NO_2[c] (5)	$R'C_6H_4N$=NC_6H_4R' (6)	RC_6H_5[d]	$R'C_6H_5$[d]	$RCONH_2$ (8)	RH[d]
a (R = R' = H)		KO_2/55%/72 h	0.41	0.17	0.23	ND	0.35			
		$KO_2(O_2)$/35%/72 h	0.71	0.27	ND	ND				
		t-BuOK/72%/24 h	0.50	0.12	ND	0.20				
		t-BuOK (O_2)/52%/24 h	0.62	0.10	ND	0.19				
b (R = H; R' = *p*-CH_3)		KO_2/52%/72 h[e]	0.36	0.37	0.19	ND	0.02	0.11		
		KO_2 (argon)/42%/72 h	0.40	0.19	0.15	ND				
		t-BuOK/66%/24 h	0.49	0.20	0.18	0.04				
		t-BuOK (argon)/0%/72 h	no reaction							
c (R = *p*-CH_3; R' = H)		KO_2/52%/72 h	0.22	0.48	ND	ND	0.002	0.017		
		t-BuOK/78%/24 h	0.10	0.52	ND	ND				
	a (R = phenyl)	KO_2/100%/48 h							0.64	0.0
	b (R = furyl)	KO_2/100%/48 h							0.60	0.0

[a] Reagent/percent conversion of substrate/reaction time. Reactions were carried out at ambient temperature under dry air unless otherwise indicated. The mole ratio of KX (X = O_2 or *tert*-butoxide)/18-crown-6/substrate was 4:2:1. Generally, 100 mL of solvent (dry benzene, unless indicated otherwise[d,e]) was used per gram of substrate. [b] Moles of product isolated per mole of reacted substrated. ND indicates that the particular product was not detected in the product mixture, while a blank indicates that the particular analysis (GLC; see footnote *d*) was not performed. [c] Control studies indicate that up to 35% of nitrobenzene (5, R = H) present in the reaction product may be lost during the workup; hence, the yields listed for this product represent lower limits. In the case of 5b the product actually isolated is *p*-nitrobenzoic acid, since *p*-nitrotoluene is rapidly (0.5 h) and quantitatively oxidized to the latter under the reaction conditions. [d] Determined by GLC analysis of selected reactions run in ethylbenzene (see Experimental Section). [e] This reaction was repeated with toluene and ethylbenzene as solvents with essentially no change in the product distribution.

$$HO_2\cdot + O_2^{-}\cdot \rightarrow HO_2^{-} + O_2 \quad (4)$$

$$R^{-} + O_2 \rightarrow R\cdot + O_2^{-}\cdot \quad (5)$$

$$R\cdot + O_2 \rightarrow RO_2\cdot \quad (6)$$

$$RO_2\cdot + O_2^{-}\cdot \rightarrow RO_2^{-} + O_2 \quad (7)$$

$$RO_2^{-} + RH \rightarrow RO_2H + R^{-} \quad (8)$$

resulting benzylic carbanion may then combine with molecular oxygen via a series of steps typical of BCA processes[12] (eq 5–8), generating the corresponding hydroperoxide or more commonly its fragmentation products. A reaction sequence such as eq 3–8 would readily explain the $O_2^{-}\cdot$-induced oxidation of diarylmethanes[8,16] and nitrotoluenes[7] for which bona fide BCA reactions have been reported with other bases.[8e,12,17]

One indication that $O_2^{-}\cdot$ is indeed acting as a base in the case of benzylic amines is that essentially the same product distribution is obtained when *tert*-butoxide replaces superoxide (see Table I). Furthermore, although the conversion was very low, TLC analysis indicates that hydroxide too gives similar results. In these reactions, the order of decreasing rates is *tert*-butoxide > superoxide > hydroxide. If our hypothesis is correct, this should correspond to the order of decreasing basicity. Interestingly, while water and primary alcohols apparently cause the instantaneous disproportionation of $O_2^{-}\cdot$, *tert*-butyl alcohol reacts at appreciable rates only at relatively high concentrations.[14]

Relevant to the question of mechanism is the observation that the $O_2^{-}\cdot$ reaction proceeds essentially unchanged even when carried out under argon (after carefully degassing the solvent via five freeze–thaw cycles). This might lead some to suggest that $O_2^{-}\cdot$ first abstracts a hydrogen atom (eq 9) and then couples directly with the resulting

$$RH + O_2^{-}\cdot \rightarrow R\cdot + HO_2^{-}\cdot \quad (9)$$

$$R\cdot + O_2^{-}\cdot \not\rightarrow RO_2^{-} \quad (10)$$

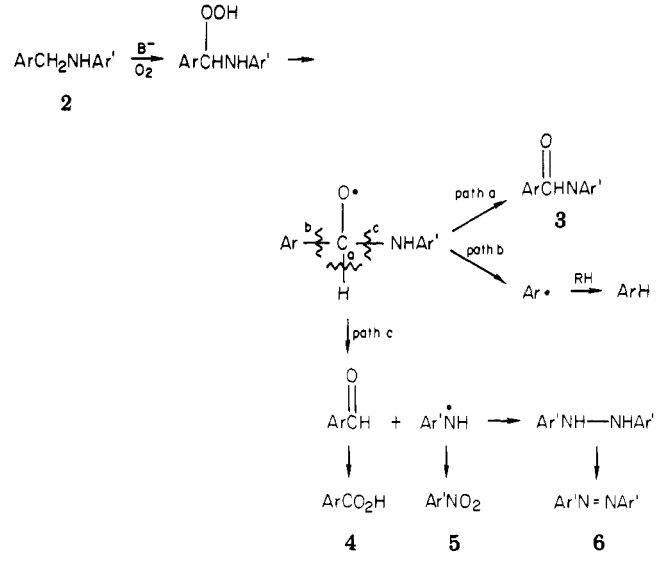
$$R\cdot + O_2^{-}\cdot \rightarrow R^{-} + O_2 \quad (11)$$

radical (eq 10). However, the scientific literature[18] clearly demonstrates that $O_2^{-}\cdot$ does not react with radicals by coupling (eq 10) but rather by electron transfer (eq 11).

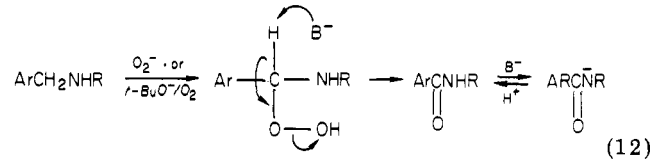
These argon atmosphere reactions would, therefore, seem to require that oxygen be generated during the course of the reaction. This is most conveniently accommodated by assuming that $O_2^{-}\cdot$ acts as a base, with the acidic substrate inducing disproportionation of $O_2^{-}\cdot$ to molecular oxygen (eq 3 and 4). Note, however, that oxygen generation per se does not rule out a hydrogen-abstraction process (eq 9) since a facile electron transfer from $O_2^{-}\cdot$ to the resulting radical would also generate O_2 (eq 11).

Overall, then, the results point toward a base-catalyzed autoxidation as the mode of action of $O_2^{-}\cdot$. However, irrespective of the exact mechanism, the primary product in these oxidations of benzylamines is expected to be the corresponding hydroperoxide which may undergo a

Scheme I. Suggested Mechanism for the Formation of Products



Kornblum–DeLaMare base-catalyzed dehydration[19] to the amide (eq 12). However, the latter is unlikely to be the



(12)

source of the various other products formed since amides are presumably essentially inert to $O_2^{-}\cdot$.[20] Thus, we have found that while benzanilide is deprotonated by superoxide it resists further oxidation. The stability of the benzanilide anion seems comparable to that of anions of 1,3-diketones which also resist oxidation by molecular oxygen[21a] or superoxide.[21b]

On the other hand, homolytic cleavage (catalyzed perhaps by trace metals) of the labile oxygen–oxygen hydroperoxide bond is not unexpected. The resulting alkoxy radical can undergo β cleavage in three directions (see Scheme I). Path a involves loss of a hydrogen atom which generates amide. Path b, on the other hand, entails the explusion of an aryl radical and would seem to be a minor pathway in view of the low yield of arene from the methylene end of the molecule (see Table I). In path c, scission occurs along the carbon–nitrogen bond, generating both an aryl aldehyde and an arylaminyl (anilinyl) radical. While the former is readily oxidizable to the corresponding benzoic acid **4**, the latter can either react with oxygen, generating nitroarene **5**, or couple, yielding azoarene **6**. We are not as yet able to explain, however, why an oxygen atmosphere increases the yield of amide (Table I, compound **2a**)[22] nor why nitroarenes **5** are formed with superoxide while azoarenes **6** are observed with *tert*-butoxide.

(16) (a) A Hammett $\sigma\rho$ plot for the reaction of substituted diarylmethanes with $O_2^{-}\cdot$ ($\rho > 4$) corroborates this suggestion.[16b] (b) Frimer, A. A.; Farkash, T., unpublished results, 1982.

(17) (a) Hawthorne, J. O.; Schowalter, K. A.; Simon, A. W.; Wilt, M. H.; Morgan, M. S. *Adv. Chem. Ser.* **1968**, *No. 75*, 203. (b) DiBiase, S. A.; Gokel, G. W. *J. Org. Chem.* **1978**, *43*, 447.

(18) (a) Frimer, A. A. In "The Chemistry of Functional Groups: Peroxides"; Patai, S., Ed.; Wiley: New York, 1983, p 429. (b) Frimer, A. A. In "Superoxide Dismutase"; Oberley, L. W., Ed.; Chemical Rubber Co.: Boca Raton, Florida, 1982; Vol. 2, p 83.

(19) (a) Kornblum, N.; DeLaMare, H. E. *J. Am. Chem. Soc.* **1951**, *73*, 880. (b) Hiatt, R. In "Organic Peroxides"; Swern, D., Ed.; Wiley-Interscience: New York, 1971; Vol. II, pp 79–80; 1972, Vol. III, p 23.

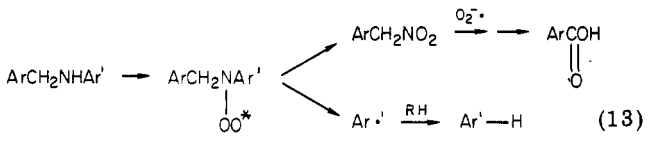
(20) (a) San Filippo, J., Jr.; Romano, L. J.; Chern, C.-I.; Valentine, J. S. *J. Org. Chem.* **1976**, *41*, 586. (b) Kornblum, N., Singaram, S. *J. Org. Chem.* **1979**, *44*, 4727.

(21) (a) Russel, G. A.; Moye, A. J.; Nagpal, K. L. *J. Am. Chem. Soc.* **1962**, 4154. (b) Frimer, A. A.; Gilinsky-Sharon, R.; Aljadeff, G. *Tetrahedron Lett.* **1982**, *23*, 130.

(22) A referee has suggested that oxygen saturation might suppress decomposition of the initially formed carbanion. However, when **2b** is deprotonated by *tert*-butoxide in an argon atmosphere, starting material is recovered quantitatively.

The intermediacy of the anilinyl radical has been invoked by various groups[23] to rationalize the conversion of aromatic amines by $O_2^{-}\cdot$ to symmetrical azobenzenes. As shown in Table II, we have also found that, upon reaction with KO_2/18-crown-6, aniline is converted to azobenzene in a 34% yield. However, we have also succeeded in isolating nitrobenzene (a minimum of 4% yield; see footnote *c* of Table I) and (4-nitrophenyl)phenylamine (**10**, 24% yield). Nitrobenzene is undoubtedly the product of autoxidation while the latter could well result from the trapping of the anilinyl radical by nitrobenzene. Indeed, when nitrobenzene is added to the reaction mixture from the start, the yield of azobenzene halves while that of (4-nitrophenyl)phenylamine (**10**) doubles. Here again a caveat is in order: the formation of an anilinyl radical in the case of aromatic amines does not require that $O_2^{-}\cdot$ serve as a hydrogen abstractor since a base-catalyzed autoxidative process would also ultimately lead to the generation of a radical via the electron-transfer process of eq 5. Indeed, azobenzene can also be obtained when potassium hydroxide[23d,24] or *tert*-butoxide (Table II) react with aniline in aprotic media. Interestingly, however, we have found that *tert*-butoxide, normally a more vigorous base in BCA processes than $O_2^{-}\cdot$ (see discussion above and ref 22 and 25), reacts with aniline more sluggishly than $O_2^{-}\cdot$ (see Table II). Furthermore, **10** is only formed in the *tert*-butoxide case when nitrobenzene (a good electron acceptor) is present from the beginning. In addition, in contradistinction to the $O_2^{-}\cdot$ case, the addition of nitrobenzene increases the yield of all the products. All this data suggests perhaps that, though both *tert*-butoxide and superoxide induce similar reactions in aniline, the mechanisms of initiation differ. Further research is clearly called for.[16b]

Noteworthy is the absence of benzene as one of the reaction products of aniline and $O_2^{-}\cdot$. This indicates that the anilinyl radical or its derivatives are not the source of the arene isolated in the reaction of $O_2^{-}\cdot$ with benzylanilines **2a–c**. We speculate that oxidation at nitrogen may lead to such results as outlined in eq 13. The hydrogen source



(13)

(RH) required for the conversion of aryl radical (Ar·) to arene may be one of a variety of compounds including crown ether and substrate.

A few final comments are in order. Chern and San Filippo[26] have reported that benzylhydrazine reacts with $O_2^{-}\cdot$ to yield benzoic acid (15%), benzaldehyde (6%), benzyl alcohol (8%), and toluene (54%). The first three products undoubtedly result from oxidation of the benzylic carbon as has been reported here. However, we see little if any toluene or analogous arene in the $O_2^{-}\cdot$ reactions of benzylamines **2a–c** and **7a,b**. This strengthens Chern and San Filippo's suggestion that in the case of the benzylhydrazines the corresponding azene is the initial intermediate formed which generates the benzyl radical (eq 14). No such mechanism is available in our system.

$$ArCH_2NHNH_2 \xrightarrow{O_2^{-}\cdot} ArCH_2N{=}NH \rightarrow ArCH_2N{=}N\cdot \rightarrow ArCH_2\cdot \quad (14)$$

Also of interest is the fact that the nature of the substitution on the nitrogen of benzylamine (**11**) seems to play a crucial role in controlling its reactivity toward $O_2^{-}\cdot$ (Scheme II). As described in this paper when R = H or aryl the reaction leads to amide and oxidative cleavage products, while when R = SO_2Ph or C(O)NHPh only starting material is recovered.[8a] The inertness of the latter two, like that of purines **1a–d** and amides **3** discussed above, may well result from the stability of the resulting resonance-stabilized anion at nitrogen. Quite surprisingly, ring hydroxylation products are observed when R = C(O)Ar. The mechanism of this latter process is discussed by Galiani and Rindone.[8a]

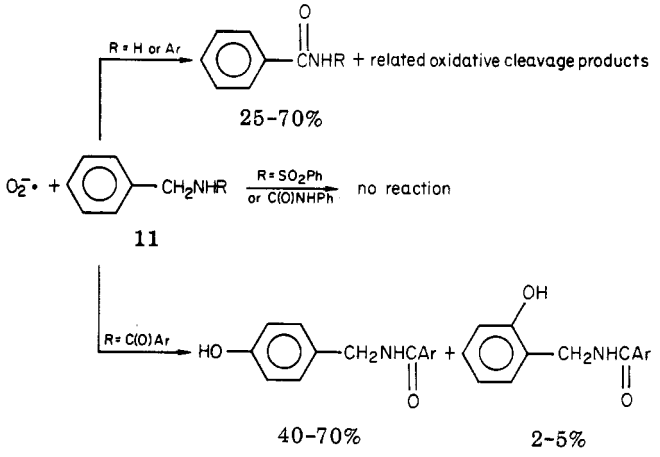
In conclusion, the results described above suggest that, in the hydrophobic areas of the cell, free cytokinin readily undergoes deprotonation of the acidic hydrogen on the nitrogen at the 7-position of the purine ring. Such a facile process would catalyze the disproportionation of the basic $O_2^{-}\cdot$. When such a mode is unavailable, $O_2^{-}\cdot$ induces what is probably a base-catalyzed autoxidation of the benzylic carbon, generating the corresponding amide and related oxidative cleavage products.

Table II. Product Distribution from the Reaction of Aniline with Superoxide and *tert*-Butoxide in Benzene

reaction conditions[a]	products[b] $C_6H_5NO_2$[c] (**5a**)	$C_6H_5N{=}NC_6H_5$ (**6a**)	C_6H_5NH-$C_6H_4NO_2$ (**10**)
KO_2/70%/3 h	0.04	0.17	0.12
KO_2 + $C_6H_5NO_2$/100%/3 h	0.39	0.075	0.26
t-BuOK/55%/3 h	0.04	0.045	ND
t-BuOK + $C_6H_5NO_2$/85%/3 h	0.13	0.064	0.20

[a] See footnote *a* of Table I. In these experiments 25 mL of solvent was used per gram of substrate. Where indicated, nitrobenzene (0.75 molar equiv vs. starting aniline) was also present in the starting reaction mixture. [b] Moles of product isolated per mole of reacted substrate. GLC analysis of the KO_2 reaction run in ethylbenzene failed to reveal any benzene. [c] See footnote *c* of Table I.

Scheme II



Experimental Section

^1H NMR spectra were obtained on Varian T-60 and HA-100 spectrometers. In reporting the data, the values obtained by using

(23) (a) Crank, G.; Makin, M. I. H. *Tetrahedron Lett.* **1979**, 2169. (b) Hussey, C. L.; Laker, T. M.; Achord, J. M. *J. Electrochem. Soc.* **1980**, *127*, 1865. (c) Poupko, R.; Rosenthal, I. *J. Phys. Chem.* **1973**, *77*, 1722. (d) Balogh-Hergovich, E.; Speier, S.; Winkelman, E. *Tetrahedron Lett.* **1979**, 3541.

(24) (a) Gokel, G. W.; Dupont-Durst, S. *Synthesis* **1976**, *168*, 181. (b) Gokel, G. W., Personal Communication, April 20, 1981.

(25) Frimer, A. A., Gilinsky-Sharon, P.; Hameiri, J.; Aljadeff, G. *J. Org. Chem.* **1982**, *47*, 2818.

(26) Chern, C. I.; San Filippo, J. *J. Org. Chem.* **1977**, *42*, 178.

the HA-100 spectrometer are asterisked. IR spectra were taken with a Perkin-Elmer Model 257 spectrometer. Mass spectra were run on a single-focusing Hitachi Perkin-Elmer RMV-6 spectrometer. Preparative thin-layer chromatography (PTLC) was carried out on Merck silica gel 60 F_{254} precoated plates. Gas chromatograms were obtained by using a Varian Aerograph Model 920 preparative GLC with peak areas determined by triangulation. Compounds **1a–d**, **2a**, **3a**, **4a–c**, **5a,b**, **6a**, **7a,b**, **8a**, **9**, and **10** are all commercially available from Aldrich. The ^{1}H NMR and IR spectra of these compounds are found in the Aldrich libraries of NMR[27] and IR[28] spectra. An authentic sample of **6b** was graciously supplied by Professor Henry J. Shine of Texas Tech University. The spectral data of the remaining compounds (**2b,c**, **3b**, **4b**, and **8b**) are given below.

Preparation of *N*-Benzylanilines 2b,c. Compounds **2b,c** were synthesized according to literature methods[5] and characterized by their spectral data which follows.

2b: ^{1}H NMR* ($CDCl_3$) δ 2.23 (3 H, s), 3.69 (1 H, br s, NH), 4.27 (2 H, s), 6.53 (2 H, d, J = 9 Hz), 6.98 (2 H, d, J = 9 Hz), 7.32 (5 H, s); IR (neat) 3390 (s) 3010 (s), 2890 (s), 2840 (s), 1940 (w), 1850 (w), 1600 (s), 1570 (m), 1500 (s), 1480 (s), 1455 (s), 1440 (s), 1390 (m), 1345 (m), 1310 (s), 1285 (s), 1250 (s), 1235 (s), 1170 (s), 1110 (s), 1050 (m), 1015 (m), 980 (w), 900 (w), 795 (s), 730 (s), 685 (s) cm^{-1}; mass spectrum (70 eV), m/e 197 (M^+), 120 ($M^+ - C_6H_5$), 106 ($M^+ - C_6H_5CH_2$), 91 ($CH_3C_6H_4^+$), 77 ($C_6H_5^+$).

2c: ^{1}H NMR* ($CDCl_3$) δ 2.33 (3 H, s) 3.80 (1 H, br s, NH) 4.24 (2 H, s) 6.67 (3 H, m) 7.2 (7 H, m); IR ($CHCl_3$) 3400 (m), 3030 (s), 2990 (s), 2910 (m), 1900 (m), 1590 (s), 1490 (s), 1460 (m), 1415 (s), 1370 (w), 1345 (w), 1310 (s), 1235 (s), 1165 (s), 1140 (m), 1095 (m), 1080 (m), 1055 (m), 1010 (m), 980 (m), 915 (w), 860 (m), 79 (s); mass spectrum (70eV), m/e 197 (M^+), 105 ($M^+ - NHC_6H_5$), 77 ($C_6H_5^+$).

General Oxidation Procedure. The experimental procedures employed in this paper are typified by the following description of the reaction of potassium superoxide with *N*-benzyl-*p*-toluidine (**2b**). Powdered potassium superoxide (710 mg, 10 mmol) was added at 25 °C to a dry benzene solution (70 mL) containing **2b** (500 mg, 2.5 mmol) and 18-crown-6 polyether (1.36 g, 5.1 mmol) contained in a 250-mL flask equipped with Teflon-coated stirring bar and topped with a drying tube. The resulting mixture was stirred for 72 h, during which time the course of the reaction was followed by TLC. The reaction mixture was then acidified with 10% HCl and extracted three times with 10% $NaHCO_3$ solution to remove inorganic salts, crown ether, and acidic products. The organic layer containing the nonacidic products was dried over $MgSO_4$ and concentrated. The resulting mixture was separated into product components by preparative TLC on silica with 3:1 hexane–acetone solution as the eluent. The combined $NaHCO_3$ extracts were acidified and extracted three times with ether. The combined ether extracts were dried and concentrated, and the product components were likewise separated by preparative TLC as above. The identity of the various fractions was readily determined by comparison of their spectral data (NMR, IR, and MS) and physical properties (melting point and TLC retention time) with those of authentic samples. In addition to the various products listed in Table I, 242 mg (1.2 mmol, 52% conversion) of unreacted substrate was recovered. Several minor unidentified fractions were also present. Each reaction was repeated at least once, and the results were found to be generally reproducible. The runs with the highest product yield were incorporated into Tables I and II.

The yields of benzene and toluene in these reactions were determined by repeating the reaction on a smaller scale in ethylbenzene as the solvent containing an internal standard. Samples from the reaction mixture prior to workup were injected on a 33 ft × 0.25 in. copper column at 115 °C packed with 10% SE-30 on Chromosorb W AW DMCS.

3b: ^{1}H NMR ($CDCl_3$) δ 2.35 (3 H, s) 7.2, 7.5, and 7.8 (overlapping m, 9 H); mass spectrum (70 eV), m/e (relative intensity) 211 (M^+, 46), 120 ($M^+ - C_6H_4CH_3$, 14), 105 ($C_6H_5CO^+$, 100), 92 ($CH_3C_6H_5$, 14), 91 ($CH_3C_6H_4^+$, 12), 77 ($C_6H_5^+$, 57).

4b: ^{1}H NMR ($CDCl_3$) δ 2.43 (3 H,S) 7.23 and 7.7 (overlapping m, 9 H); mass spectrum (70 eV), m/e (relative intensity) 211 (M^+, 15), 119 ($CH_3C_6H_4CO^+$, 100), 91 ($CH_3C_6H_4^+$, 46).

8b: ^{1}H NMR ($CDCl_3$) δ 6.2 (1 H, br s, NH), 6.5 (1 H, m, H-4), 7.16 (1 H, d, J = 3 Hz, H-3), 7.47 (1 H, br s, H-5) (this spectrum is nearly identical with that of 2-furoic acid hydrazide[27]); mass spectrum (70 eV), m/e (relative intensity) 111 (M^+, 99.3), 95 ($M^+ - NH_2$, 100).

Acknowledgment. We acknowledge the kind and generous support of the United States–Israel Binational Science Foundation.

Registry No. **1a**, 120-73-0; **1b**, 73-24-5; **1c**, 525-79-1; **1d**, 1214-39-7; **2a**, 103-32-2; **2b**, 5405-15-2; **2c**, 15818-64-1; **7a**, 100-46-9; **7b**, 617-89-0.

(27) Pouchert, C. J.; Campbell, J. R. "The Aldrich Library of NMR Spectra"; Aldrich Chemical Co.: Milwaukee, 1974.
(28) Pouchert, C. J. "The Aldrich Library of Infrared Spectra", 3rd ed.; The Aldrich Chemical Co.: Milwaukee, 1981.

Ferrous Ion Catalyzed Oxidations of 2-Propanol with Peroxyacetic Acid

Earl S. Huyser* and George W. Hawkins[1]

Department of Chemistry, University of Kansas, Lawrence, Kansas 66044

Received May 21, 1982

The ferrous ion catalyzed oxidations of 2-propanol by peroxyacetic acid are compared with the oxidations of 2-propanol with the Fenton reagent (ferrous ion and hydrogen peroxide). The peroxyacetic acid reactions are considerably faster than the hydrogen peroxide oxidations at similar concentrations of ferrous ion. Further, the peroxyacetic acid oxidations at low ferrous ion concentrations do not yield any detectable amounts of 2,5-hexanediol, a significant byproduct formed in the hydrogen peroxide oxidations when performed with sufficient ferrous ion present to achieve reaction rates comparable to those of the peroxyacetic acid oxidations at the low ferrous ion concentrations. These observations are discussed in terms of the hydrogen atom abstracting species encountered in these oxidation reactions.

The oxidations of secondary alcohols to ketones by organic peroxides has proven fruitful over the past 30 years in terms of providing insight into the behavior of free radicals as reaction intermediates.[2] Such studies have provided information concerning the reduction of the peroxide linkage by an intermediate α-hydroxyalkyl radical by its interaction with the peroxide either by hydrogen

(1) Taken in part from the thesis submitted to the University of Kansas for the M.S. degree by G.W.H., 1979.

(2) P. D. Bartlett and K. Nozaki, *J. Am. Chem. Soc.*, **69**, 2299 (1947); M. S. Kharasch, J. R. Rowe, and W. H. Urry, *J. Org. Chem.*, **16**, 905 (1951).

0022-3263/83/1948-1705$01.50/0