The results presented here show that a range of fenestranes with fourfold bridgehead substitution has become synthetically accessible. The NMR data clearly reveal that the barrier to conformational interconversion, and thus the unfavorable steric and, probably, dipolar interactions, increase in the order F, OH  $\ll$  CH<sub>3</sub>  $\ll$  CN, N<sub>3</sub>, SCH<sub>3</sub>, Cl, Br, much different from substituent trends in substituted cyclohexanes.<sup>23</sup> We feel that 2 represents an interesting parent system to study both dynamic and static effects of bridgehead substituents on the fenestrane framework. Preliminary force-field calculations suggest that the "planoid" distortions at the central carbon atoms of fenestrindans 3–12 are considerably affected by the nature of the bridgehead substituents.<sup>24</sup> Detailed investigations

(23) March, J. Advanced Organic Chemistry, Reactions, Mechanisms, and Structure, 3rd ed.; John Wiley & Sons: New York, 1985; pp 125-126. are underway including X-ray crystal structure analysis of bridgehead-substituted fenestrindans.

Acknowledgment. We are grateful to Professor H.-F. Grützmacher for support of our research and to Mr. K.-P. Mester and to Dr. B. Paisdor for performing, and for help evaluating, the dynamic NMR measurements. We thank Professor J. M. Cook for a preprint (ref 5e). Financial support by the Deutsche Forschungsgemeinschaft (Ku 663/1-1) is greatfully acknowledged.

Supplementary Material Available: Full experimental and spectrometric data of compounds 4-12 (6 pages). Ordering information is given on any current masthead page.

Articles

# Homolytic Alkylation of Enamines by Electrophilic Radicals<sup>1</sup>

Glen A. Russell\* and Keyang Wang

Department of Chemistry, Iowa State University, Ames, Iowa 50011

Received November 6, 1990

The electrophilic radicals  $R^{\bullet} = p \cdot O_2 N C_6 H_4 C H_2^{\bullet}$  or  $Me_2 C (NO_2)^{\bullet}$  add readily to  $C H_2 = C (NMe_2)_2$  to yield  $R C H_2 C (NMe_2)_2^{\bullet}$ , which undergoes electron transfer with  $p \cdot O_2 N C_6 H_4 C H_2 C I$  or  $Me_2 C (NO_2)_2$  to regenerate  $R^{\bullet}$ . Hydrolysis yields  $p \cdot O_2 N C_6 H_4 C H_2 C O N Me_2$  and  $Me_2 C = C H C (NMe_2)_2^{+}$ , respectively.  $p \cdot N I trobenzyl$  radicals add readily to N-pyrrolidino- or N-morpholino-1-cycloalkenes to yield after hydrolysis the  $\alpha - (p \cdot n I trobenzyl) cyclo-$ alkanones. Photostimulated alkylation of N-pyrrolidino-1-cycloalkenes by  $Me_2 C (NO_2)_2$  is not observed although in competitive reactions between the enamine and  $Me_2 C = NO_2 L I$ , the product from attack of  $Me_2 C (NO_2)^{\bullet}$  upon the enamine double bond is formed. The N-pyrrolidino-1-cycloalkenes are more reactive toward  $p \cdot O_2 N C_6 H_5 C H_2^{\bullet}$  than their morpholino analogues.

### Introduction

The free-radical chain reaction between PhCOCH<sub>2</sub>HgCl and 1-morpholinocyclohexene has been reported to involve addition of the acceptor radical PhCOCH<sub>2</sub><sup>•</sup> to the electron-rich double bond of the enamine followed by the electron transfer of reaction  $1.^2$  Perfluoroalkyl halides are also recognized to react with enamines by a radical chain process presumably involving electron transfer.<sup>3,4</sup>



Attempts to utilize simple alkylmercury halides in photostimulated reactions with enamines failed to yield

Scheme I ( $\mathbf{R} = Me_2C(NO_2)$  or  $p - O_2NC_6H_4CH_2$ )



p-O2NC6H4CH2CH- p-O2NC6H4CH2+CI

Me2C(NO2)2. Me2C(NO2). + NO2

the alkylation products observed with PhCOCH<sub>2</sub>HgCl, presumably because facile addition to an electron-rich system requires an electrophilic radical. In a search for further examples of radical alkylations of enamines, we have examined reactions with  $p-O_2NC_6H_4CH_2Cl$  and  $Me_2C(NO_2)_2$ , substrates known to react with a variety of anions in a free-radical chain sequence.<sup>5,6</sup> Photostimulated alkylation reactions were indeed observed between these substrates and various enamines. With  $p-O_2NC_6H_4CH_2Cl$ 

<sup>(24)</sup> MMPMI and MM2(87) force-field calculation programs (QCPE, University of Indiana, Bloomington) both gave  $\alpha = 112.5^{\circ}$  for 2 (X = H, Scheme 1), considerably lower than the X-ray value  $\alpha = 116.5^{\circ}$  [7a], and a gradual increase of  $\alpha$  up to 117-118° for X = Cl and Br.

Electron Transfer Processes. Part 53. This work was supported by the National Science Foundation and by the donors of the Petroleum Research Fund, administered by the American Chemical Society.
 Russell, G. A.; Kulkarni, S. V.; Khanna, R. K. J. Org. Chem. 1989,

<sup>(2)</sup> Russell, G. A.; Kulkarni, S. V.; Khanna, R. K. J. Org. Chem. 1989, 55, 1080.

<sup>(3)</sup> Cantacuzene, D.; Dorme, R. Tetrahedron Lett. 1975, 2037.
(4) Rico, I.; Cantacuzene, D.; Wakselman, C. Tetrahedron Lett. 1981, 22, 3405.

<sup>(5)</sup> Russell, G. A.; Danen, W. C. J. Am. Chem. Soc. 1966, 88, 5663.
(6) Kornblum, N.; Michel, R. E.; Kerber, R. C. J. Am. Chem. Soc. 1966, 88, 5662.

the free-radical chain alkylation reaction occurred readily with several enamines that are usually considered to be unreactive toward alkyl chlorides. The observed chain reactions are consistent with the mechanism of Scheme I in which the electrophilic nitro-conjugated radicals add regioselectivity to the enamine to yield an easily oxidized aminoalkyl radical. The results provide further support for the proposal that the free radicals [ $p-O_2NC_6H_4CH_2^{\circ}$ ,  $Me_2C(NO_2)^{\circ}$ ] are involved in the photostimulated reactions of  $p-O_2NC_6H_4CH_2C$  or  $Me_2C(NO_2)_2$  with anions such as  $Me_2C=NO_2^{-}$  since the intermediate radicals can be competitively trapped by the anion and the enamine.

# **Results and Discussion**

Free-radical chain reactions were observed to occur between  $p-O_2NC_6H_4CH_2Cl$  and the enamines 1-4 upon photolysis in Me<sub>2</sub>SO, CH<sub>3</sub>CN, or DMF at 35–40 °C. With



 $Me_2C(NO_2)_2$  reaction was observed with 1 but no significant reactions occurred with 2 or 3 although in competition reactions with  $Me_2C=NO_2Li$  the enamine 2b proved to be about as reactive as  $Me_2C=NO_2Li$  toward  $Me_2C(NO_2)^*$  and yielded the expected ketone 5 upon hydrolysis.



**Reactions of** *p*-Nitrobenzyl Chloride. Photolysis of *p*-nitrobenzyl chloride by a fluorescent sunlamp in DMF solution at 35-40 °C in the presence of the enamines 1-4 yielded upon hydrolysis the products expected from the iminium salts formed by Scheme I, i.e. 6-8. Table I



presents typical yields and other data which confirm that the reaction involves a free-radical chain process. Figure 1 further illustrates the effects of photostimulation and inhibition in the reaction between p-O<sub>2</sub>NC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>Cl and **2a**. From the data of Figure 1 the initial kinetic chain length (kcl) is calculated to be ~34 with sunlamp irradiation (from the ratio of the initial reaction rate to the rate of radical formation). Under similar conditions the observed kcl's were 30 for **2b**, 5 for **2c**, 3 for **3b**, 4 for **3c**, and 34 for **4**. With **2b** under fluorescent room light a kcl of 150 was measured in CH<sub>3</sub>CN. The reaction of p-O<sub>2</sub>NC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>Cl with **1**, **2a**, or **2b** occurs slowly in the dark by a process inhibited by  $(t-Bu)_2NO^{\circ}$ , which suggests the formation of free radicals by electron transfer between the enamine and the *p*-nitrobenzyl system.

Reactions of m-O<sub>2</sub>NC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>Cl or PhCH<sub>2</sub>Cl with 2-3 failed to produce the  $\alpha$ -alkylated ketones under conditions

Table I. Reaction of p-O<sub>2</sub>NC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>Cl with Enamines at 35-40 °C°

	equivalents			
enamine		(t-		
(equiv)	Et <sub>3</sub> N	Bu) <sub>2</sub> NO*	conditions	product (%) <sup>c</sup>
1 (2)	2	0	Me <sub>2</sub> SO, D, 2 h	6 (53)
1 (2)	2	0.1	$Me_2SO$ , D, 2 h	6 not detected
1 (2)	2	0	Me <sub>2</sub> SO, R, 30 min	6 (40)
1 (2)	2	0.1	Me <sub>2</sub> SO, R, 30 min	6 (8)
1 (2)	2	0	DMF, R, 30 min	6 (65)
1 (2)	2	0	DMF, D, 1 h	6 (17)
1 (2)	2	0	DMF, D, 13 h	6 (47)
1 (2)	2	0.1	DMF, D, 20 h	6 not detected
<b>2a</b> (2)	1	0	DMF, S, 5 min	7a (40)
<b>2a</b> (2)	1	0	DMF, S, 1 h	<b>7a</b> (72)
<b>2a</b> (2)	1	0	DMF, S, 3 h	7a (90)
<b>2a</b> (2)	1	0.1	DMF, S, 15 min	7a not detected
<b>2a</b> (2)	1	0	D <b>MF,</b> D, 1 h	7a (39)
<b>2a</b> (2)	1	0.1	DMF, D, 1 h	7a not detected
<b>2b</b> (2)	1	0	DMF, S, 20 min	7b (59)
<b>2b</b> (2)	1	0.1	DMF, S, 20 min	7b not detected
<b>2b</b> (2)	1	0	CH <sub>3</sub> CN, S, 20 min	<b>7b</b> (72)
<b>2b</b> (2)	1	0	CH <sub>3</sub> CN, D, 40 min	<b>7b</b> (71)
<b>2b</b> (2)	1	0	CH <sub>3</sub> CN, F, 10 min	<b>7b</b> (76)
<b>2b</b> (2)	1	0.1	CH <sub>3</sub> CN, F, 2 h	7b not detected
<b>2c</b> (2)	1	0	DMF, S, 1 h	7c (78)
<b>2c</b> (2)	1	0	DMF, D, 1 h	7c not detected
<b>2c</b> (2)	1	0.1	DMF, S, 1 h	7c (20)
<b>3b</b> (2)	1	0	CH <sub>3</sub> CN, S, 1 h	7b (47)
<b>3b</b> (2)	1	0	CH <sub>3</sub> CN, D, 4 h	7b not detected
<b>3b</b> (2)	1	0.1	CH <sub>3</sub> CN, S, 20 min	7b not detected
<b>3b</b> (2)	1	0.1	$CH_3CN, S, 1 h$	7b (16)
<b>3c</b> (2)	1	0	$CH_3CN, S, 4 h$	7c (75)
<b>3c</b> (2)	1	0	CH <sub>3</sub> CN, D, 4 h	7c not detected
<b>3c</b> (2)	1	0.1	$CH_3CN$ , S, 20 min	7c not detected
4 (2)	1	0	DMF, S, 80 min	8 (42) <sup>d</sup>
4 (2)	1	0	DMF, D, 4 h	8 not detected
4 (2)	1	0.1	DMF, S, 40 min	8 not detected

°0.5 M p-O<sub>2</sub>NC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>Cl. <sup>b</sup>D = dark, R = 350-nm Rayonet Photoreactor, S = 275-W G.E. fluorescent sunlamp ca. 20 cm from reaction vessel, F = fluorescent laboratory lighting. °Products analyzed by GC with an internal standard after hydrolysis and extraction by CH<sub>2</sub>Cl<sub>2</sub>. <sup>d</sup> Isolated yield.



**Figure 1.** Reaction of p-O<sub>2</sub>NC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>Cl (0.05 M) with 2a (0.10 M) in DMF at 35-40 °C in the absence (O,  $\bullet$ ) and presence ( $\Box$ ,  $\blacksquare$ ) of (t-Bu)<sub>2</sub>NO<sup>•</sup> (0.005 M);  $h\nu$  = irradiation by a 275-W fluorescent sunlamp 34 cm. from the Pyrex reaction tube.

where p-O<sub>2</sub>NC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>Cl gave 7. The absence of a chain reaction with PhCH<sub>2</sub>Cl undoubtedly reflects the increased reduction potential of the alkyl halide. Although m-O<sub>2</sub>NC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>Cl can be easily reduced, the resulting radical anion does not readily undergo the fragmentation step required to continue the chain process of Scheme I. A similar difference in reactivity is observed for p- and m-O<sub>2</sub>NC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>Cl in the S<sub>RN</sub>1 reaction with anions such as Me<sub>2</sub>C=NO<sub>2</sub><sup>-</sup>. The only products observed upon reac-

 Table II. Relative Reactivities of Enamines toward

 p-O2NC6H4CH2\* in DMF at 35-40 °C

		product	s, % <sup>b</sup>	
reactants (mmol) <sup>a</sup>		p-O.NC.H.		
Α	В	ĊH <sub>2</sub> ĊMe <sub>2</sub> NO <sub>2</sub>	other	$k_{\rm A}/k_{\rm B}$
2a (0.20)	$Me_2C = NO_2Li (0.20)$	30	7a, 59	2.0
<b>2b</b> (0.20)	$Me_2C = NO_2Li (0.20)$	46	7b, 40	0.9
2c (0.20)	$Me_2C = NO_2Li (0.20)$	37	7c, 55	1.5
1 (0.06)	$Me_2C = NO_2Li (0.03)$	66	6, 34	0.3
<b>3b</b> (0.10)	$Me_2C = NO_2Li (0.10)$	82	7b not detected	<0.05
<b>3c</b> (0.20)	Me <sub>2</sub> C=NO <sub>2</sub> Li (0.10)	79	7c not detected	<0.05
4 (0.20)	Me <sub>2</sub> C=NO <sub>2</sub> Li (0.10)	90	8 not detected	<0.05

<sup>a</sup> In 2 mL of DMF for 2-4. With 2, 0.05 mmol of p-O<sub>2</sub>NC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>Cl was employed; with 3, 0.10 mmol; and with 1, 0.03 mmol in 0.3 mL of DMF. Reactions of 2-4 were irradiated with a 275-W fluorescent sunlamp for 20 min while the reaction with 1 was irradiated for 30 min in a 350-nm Rayonet Photoreactor. <sup>b</sup>By GC with an internal standard after hydrolysis and CH<sub>2</sub>Cl<sub>2</sub> extraction of the reaction products.

tion of PhCH<sub>2</sub>Cl with 2 and 3 were the N-benzylated derivatives, 9a and 10a. Compounds 9b and 10b were also



observed with p-O<sub>2</sub>NC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>Cl, particularly in the absence of irradiation or in the presence of (t-Bu)<sub>2</sub>NO<sup>•</sup>. As indicated in eqs 2 and 3, a fast photostimulated reaction of **2b** leading to **7b** competes with a slower ionic process leading to **9b**. In reaction 2 all of the p-O<sub>2</sub>NC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>Cl was consumed in the 20-min reaction period while in the presence of (t-Bu)<sub>2</sub>NO<sup>•</sup> (reaction 3), 19% of the p-O<sub>2</sub>NC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>Cl was recovered.



Another indication of the free-radical nature of the reactions is the effect of Me<sub>2</sub>C=NO<sub>2</sub>Li upon the products of the reaction of  $p-O_2NC_6H_4CH_2Cl$  with 1-3. The nitronate anion traps  $p - O_2 NC_6 H_4 CH_2^{\bullet}$  to form  $p - O_2 NC_6 H_4 CH_2 CMe_2 NO_2$  by the  $S_{RN}1$  process,<sup>5,6</sup> and at the expense of products 6 or 7. With 2a, the ratio of 7a/p-O2NC6H4CH2CMe2NO2 formed was directly proportional to the ratio of  $2a/Me_2C=NO_2Li$  employed. Table II summarizes the relative reactivities observed in such competition experiments. The data of Table II show that 2 is much more reactive than 3 or 4 toward p- $O_2NC_6H_4CH_2$  and that 2a and 2c are slightly more reactive than 2b. In the ionic reaction with simple alkyl halides it is recognized that 2b is more reactive than 3b while 2c or 3c are not reported to yield significant amounts of the C-alkylated products.<sup>7</sup> The enamine 4 is also reported to be unreactive in normal ionic alkylations.<sup>7</sup>

**Reactions of 2,2-Dinitropropane.** The 2-nitro-2propyl radical has not been previously reported to undergo chain reactions involving addition to electron-rich double

Table III. Photostimulated Reaction between  $Me_2C(NO_2)_2$ and  $CH_2=C(NMe_2)_2^a$ 

time, min	irradiation <sup>b</sup>		% Me <sub>2</sub> C(NO <sub>2</sub> ) <sub>2</sub> <sup>c</sup>
1	R	70	30
5	R	62	28
3	R, $(t-Bu)_2 NO^{-d}$	0	100
5	R, $(t-Bu)_2 NO^{*d}$	10	90
120	dark	0	90
9	S	38	55
39	S	57 (47) <sup>e</sup>	37
39	S, $(t-Bu)_2 NO^{*d}$	0 (9) <sup>e</sup>	92 (60) <sup>e</sup>
139	S	64	32
139	S, (t-Bu <sub>2</sub> )NO <sup>•d</sup>	20	65

<sup>a</sup>0.05 mmol of Me<sub>2</sub>C(NO<sub>2</sub>)<sub>2</sub> and 0.10 mmol of CH<sub>2</sub>==C(NMe<sub>2</sub>)<sub>2</sub> in 0.5 mL of Me<sub>2</sub>SO-d<sub>6</sub>. <sup>b</sup>R = 350-nm Rayonet Photoreactor S = 275-W G.E. fluorescent sunlamp 34 cm from the reaction tube. <sup>c</sup>By <sup>1</sup>H NMR with benzene as the internal standard. <sup>d</sup>0.005 mmol. <sup>e</sup> With 0.10 mmol of Me<sub>2</sub>C(NO<sub>2</sub>)<sub>2</sub> and 0.07 mmol of CH<sub>2</sub>==C-(NMe<sub>2</sub>)<sub>2</sub>.

bonds other than in resonance-stabilized anions (i.e., the  $S_{RN}1$  reaction). Some  $S_{RN}1$  processes are retarded by the presence of vinyl ethers but products of the trapping of  $Me_2C(NO_2)^*$  have not been isolated.<sup>9</sup>

The photostimulated reaction of 1 with  $Me_2C(NO_2)_2$ occurs readily in a radical process which appears to follow Scheme I. The reaction in  $Me_2SO$  forms the ionic product 11, which can be isolated as the  $ClO_4^-$  salt. Cation 11 can be easily rationalized as arising by loss of  $HNO_2$  from the initial electron-transfer product,  $Me_2C(NO_2)CH_2C-(NMe_2)_2^+$ .

$$\begin{array}{ccc} \text{Me}_2\text{C} = \text{CHC}(\text{NMe}_2)_2^+ \text{ClO}_4^- & \text{O}_2\text{NCMe}_2\text{CMe}_2\text{NO}_2\\ 11 & 12 \end{array}$$

Table III presents data from which the initial kinetic chain length of reaction 4 can be estimated to be about 50 in Me<sub>2</sub>SO- $d_6$  at 35 °C. With irradiation at 350 nm

$$\mathrm{Me}_{2}\mathrm{C}(\mathrm{NO}_{2})_{2} + 1 \xrightarrow{h_{\nu}} 11 + [\mathrm{HNO}_{2}] + \mathrm{NO}_{2}^{-} \quad (4)$$

the reaction was very fast and was complete in 1 min, although in the dark the reaction was not observed for up to 2 h. Significant inhibition in the presence of 10 mol % of  $(t-Bu)_2NO^{\bullet}$  was observed with either 350-nm or sunlamp irradiation (Table III).

Further evidence for the free-radical nature of the reaction leading to 11 is provided by the trapping of Me<sub>2</sub>C- $(NO_2)^{\circ}$  by Me<sub>2</sub>C= $NO_2^{-}$  to yield 12. Thus, reaction 5 was followed by <sup>1</sup>H NMR in Me<sub>2</sub>SO-d<sub>6</sub>. In the absence of

$$1 + Me_2C(NO_2)_2 + Me_2C = NO_2Li \xrightarrow{360 \text{ nm}} 11 + 12 \quad (5)$$

 $Me_2C=NO_2Li$  reaction of 0.22 mmol of 1 with 0.05 mmol of  $Me_2C(NO_2)_2$  in 0.5 mL of  $Me_2SO-d_6$  gave a 62% yield of 11 (0.031 mmol) in 30 min. With equal amounts of 1 and  $Me_2C(NO_2)_2$  (0.05 mmol) the ratio of 11/12 decreased with increasing  $[Me_2C=NO_2Li]$  from 19 (0.01 mmol of  $Me_2C=NO_2Li$ ) to 3.2 (0.05 mmol) to 1.8 (0.10 mmol). There appears to be a competition between the enamine 1 and  $Me_2C=NO_2^-$  for a common intermediate, i.e.  $Me_2C(NO_2)^*$ , leading to the alkylation products 11 and 12.

Photochemical reactions of  $Me_2C(NO_2)_2$  with 2b or 3b failed to produce the expected 5. However, in competitive reactions between 2b and  $Me_2C=NO_2Li$ ,  $(EtO_2C)_2CHK$ , or  $(EtO_2C)_2C(Et)K$ , the expected 5 was observed. The products of these reactions and the relative reactivities observed toward  $Me_2C(NO_2)^*$  are summarized in Table IV. Toward  $p-O_2NC_6H_4CH_2^*$  the relative reactivities of

<sup>(7)</sup> Dyke, S. F. The Chemistry of Enamines; Cambridge University Press: Cambridge, 1973; p 17-20. Cook, A. G., Ed. Enamines: Synthesis, Structure, and Reactions, 2nd ed.; M. Dekker, Inc.: New York, 1988.
(8) Kuehne, M. E. J. Am. Chem. Soc. 1962, 84, 837.

<sup>(9)</sup> Russell, G. A.; Baik, W. J. Chem. Soc., Chem. Commun. 1988, 196.

Table IV. Relative Reactivities of Enamines toward Me<sub>2</sub>C(NO<sub>2</sub>)<sup>•</sup> at 35-40 °C

reactants (mmol) <sup>a</sup>			
Α	В	products $(\%)^b$	$k_{\rm A}/k_{\rm B}$
1 (0.10)	Me <sub>2</sub> C=NO <sub>2</sub> Li (0.10)	11 (61), 12 (34)	1.8
1 (0.05)°	Me <sub>2</sub> C=NO <sub>2</sub> Li (0.05)	11 (58), 12 (37)	1.6
<b>2b</b> (0.20)	Me <sub>2</sub> C=NO <sub>2</sub> Li (0.20)	12 (46), 5 (40)	0.9
<b>2b</b> (0.20)	(EtO <sub>2</sub> C) <sub>2</sub> CHK (0.20)	$Me_2C \longrightarrow C(CO_2Et_2)$ (22), 5 (5)	0.23
<b>2b</b> (0.20)	$(EtO_2C)_2C(Et)K$ (0.20)	O <sub>2</sub> NCMe <sub>2</sub> C(Et)- (CO <sub>2</sub> Et) <sub>2</sub> (50), 5 (9)	0.18

<sup>e</sup>0.05 mmol of Me<sub>2</sub>C(NO<sub>2</sub>)<sub>2</sub> in 2 mL of Me<sub>2</sub>SO-d<sub>6</sub> for 1 and 2 mL of DMF for 2b. Reactions of 1 were photolyzed for 15 min at 350 mm, while 2b was photolyzed for 20 min with a 275-W G.E. fluorescent sunlamp. <sup>b</sup>By <sup>1</sup>H NMR with benzene as an internal standard for reactions of 1. With 2b reaction products were analyzed by GC with biphenyl as the internal standard. °0.01 mmol of Me<sub>2</sub>C- $(NO_2)_2$  in 0.5 mL of Me<sub>2</sub>SO- $d_6$ .

 $1:2b:Me_2C=NO_2Li$  in DMF ([Li<sup>+</sup>] = 0.1 M) are 0.3:0.9:1.0. Under similar conditions the reactivities toward Me<sub>2</sub>C- $(NO_2)^{\bullet}$  of  $2b:Me_2C=NO_2Li:(EtO_2C)_2CEt^{-}$  are 0.9:1.0:5. It has been previously demonstrated that the reactivities of  $(EtO_2C)_2CMe^-$  and  $Me_2C=NO_2^-$  toward  $Me_2C(NO_2)^{\bullet}$  are dependent upon the counterions and solvent; with [Li<sup>+</sup>] = 0.2 M in DMF the observed relative reactivities were 1.3 but increased for the free ions to 10 in Me<sub>2</sub>SO and 20 in THF.<sup>10</sup> The relative reactivities of  $1:Me_2C=NO_2Li$  toward  $Me_2C(NO_2)^*$  in  $Me_2SO-d_6$  ([Li<sup>+</sup>] = 0.05 or 0.1 M) of  $1.7 \pm 0.1$  is a reversal of the reactivity observed toward  $p-O_2NC_6H_4CH_2^*$  in DMF (0.3) and probably reflects different steric requirements for the attack of Me<sub>2</sub>C(NO<sub>2</sub>)<sup>•</sup> and  $p-O_2NC_6H_4CH_2$  upon  $Me_2C=NO_2Li$ .

Reactions of Other Nitroarenes. Attempts to extend the alkylation of 2b to  $p-O_2NC_6H_4CMe_2^{\bullet}$  by use of p- $O_2NC_6H_4CMe_2NO_2$  as the radical precursor failed. In competition experiments with Me<sub>2</sub>C=NO<sub>2</sub>Li, only p- $O_2NC_6H_4CMe_2CMe_2NO_2$  was observed (in 90% yield). The reaction of p-O<sub>2</sub>NC<sub>6</sub>H<sub>4</sub>CMe<sub>2</sub>NO<sub>2</sub> with 1 also failed to give the alkylation product even in a competition reaction with  $EtC(CO_2Et)_2^-$  where  $p-O_2NC_6H_4CMe_2C(Et)(CO_2Et)_2$ was formed in high yield. It appears that steric effects are more important in the addition of radicals to enamines than to resonance-stabilized anions such as  $Me_2C=NO_2^{-1}$ or  $RC(CO_2Et)_2$  since **2b** has a reactivity comparable with  $Me_2C = NO_2^{-}$  toward the unhindered *p*-nitrobenzyl radical (Table II). Differences in the electron affinities of the radicals may also be important since the more electrophilic  $Me_2C(NO_2)^*$  and  $p-O_2NC_6H_4CH_2^*$  attack 1 or 2b whereas  $p-O_2NC_6H_4CMe_2$  does not.

2,4-Dinitrochlorobenzene reacts readily with 2a,b (but not with 2c or 3a-c) to yield upon hydrolysis the  $\alpha$ -(2,4-dinitrophenyl)cycloalkanones.<sup>8</sup> We have repeated the reaction with 2b in the presence of  $(t-Bu)_2NO^{\bullet}$  and found no evidence for an electron-transfer chain reaction. The yield of the arylated ketone in  $CH_2Cl_2$  was 40% in 1 h in the absence of the nitroxide while in the presence of 10 mol % of the nitroxide (based on the 0.6 equiv of 2,4- $(NO_2)_2C_6H_3Cl$  employed) yields of 15% (10 min) and 40% (1 h) were observed.

#### **Experimental Section**

All reactions were conducted under a nitrogen atmosphere in solvents that had been deoxygenated for 10-15 min by nitrogen bubbling through a hypodermic needle. Photolyses utilized a 275-W General Electric fluorescent sunlamp or a Rayonet RPR-100 photochemical chamber reactor with 350-nm "blacklight phosphor" bulbs (16  $\sim$  24-W bulbs) which maintained a reaction temperature of  $\sim$ 45 °C. The purity of all title compounds was estimated to be >95% by NMR, GC, and/or elemental analysis.

Reagents. 2,2-Dinitropropane,<sup>11</sup> 1-(1-methyl-1-nitroethyl)-4nitrobenzene,<sup>12</sup> and the lithium salt of 2-nitropropane<sup>13</sup> were prepared according to literature procedures. N, N, N', N'-Tetramethyl-1,1-ethenediamine (1) was prepared by the literature procedure in 35% yield by reactions of CH<sub>3</sub>CONMe<sub>2</sub> with Me<sub>2</sub>NH in the presence of TiCl<sub>4</sub>:<sup>14</sup> bp 113-114 °C; <sup>1</sup>H NMR (Me<sub>2</sub>SO-d<sub>6</sub>) δ 3.09 (s, 2 H), 2.48 (s, 12 H) [lit.<sup>14</sup> bp 115 °C, <sup>1</sup>H NMR (C<sub>6</sub>H<sub>6</sub>)  $\delta$  3.40 (s, 2 H), 2.47 (s, 12 H)]. The enamines 2 and 3 were prepared by a standard method.<sup>15</sup> 1-(3,4-Dihydro-1-naphthalenyl)pyrrolidine (4) was prepared in 60% yield by condensation of  $\alpha$ -tetralone and pyrrolidine in the presence of TiCl<sub>4</sub>:<sup>16</sup> bp 134-137 °C (2 Torr); <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  7.42 (d, J = 7.8 Hz, 1 H), 7.23–7.12 (m, 3 H), 5.26 (t, J = 4.6 Hz, 1 H), 2.95 (m, 4 H), 2.65 (t, J = 7.5Hz, 2 H), 2.24–2.17 (td, J = 7.5, 4.6 Hz, 2 H), 1.90 (m, 4 H) [lit.<sup>16</sup> <sup>1</sup>H NMR  $\delta$  5.1 (J = 4.6 Hz)].

N,N,N',N'-Tetramethyl-1,1-diamino-3,3-dimethylallyl Perchlorate (11). To 2,2-dinitropropane (134 mg) in 5 mL of CH<sub>3</sub>CN was added Et<sub>3</sub>N (150  $\mu$ L) and 1 (300  $\mu$ L), and the mixture was irradiated for 1 h with a 275-W G.E. sunlamp in a Pyrex tube. The reaction mixture was poured into 20 mL of saturated aqueous NaClO<sub>4</sub> and extracted with two 20-mL volumes of CH<sub>3</sub>CHCl<sub>2</sub>. The extract was dried over Na<sub>2</sub>SO<sub>4</sub>, the solvent was evaporated, and the residue was recrystallized from EtOAc to give 48 mg (19%) of 11 as yellow crystals: mp 98 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 5.806 (s, 1 H), 3.285 (s, 12 H), 2.010 (d, J = 0.9 Hz, 3 H), 1.810 (d, J = 0.9Hz, 3 H); <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ 167.14, 155.22, 115.39, 42.55, 25.82, 20.57; IR 1095 (ClO<sub>4</sub><sup>-</sup>), 1612 (NC<sup>+</sup>N) cm<sup>-1</sup>; MS (FAB glycerol matrix) m/z 155 (100, C<sub>9</sub>H<sub>19</sub>N<sub>2</sub><sup>+</sup>). Anal. Calcd for C<sub>9</sub>H<sub>19</sub>ClN<sub>2</sub>O<sub>4</sub>: C, 42.44; H, 7.52; N, 11.00. Found: C, 42.44; H, 7.52; N, 10.90.

N,N-Dimethyl-p-nitrobenzenepropanamide (6). To pnitrobenzyl chloride (343 mg) in 10 mL of CH<sub>3</sub>CN was added 100  $\mu$ L of Et<sub>3</sub>N and 600  $\mu$ L of 1, and the mixture was irradiated with a 275-W sunlamp for 1 h. The reaction product was added to 2 mL of Et<sub>a</sub>N in 50 mL of water and after 1 h extracted with three 30-mL volumes of CH<sub>3</sub>CHCl<sub>2</sub>. The extract was washed and evaporated to give a residue, which was purified by flash column chromatography (EtOAc-hexane) to give 177 mg of 6 as white crystals: mp 87 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  8.050 (d, J = 8.7 Hz, 2 H), 7.309 (d, J = 8.7 Hz, 2 H), 3.000 (t, J = 7.5 Hz, 2 H), 2.572 (t, J = 7.5 Hz, 2 H), 2.884 (s, 3 H), 2.866 (s, 3 H); IR 1348, 1519,1639 cm<sup>-1</sup>; HRMS calcd for  $C_{11}H_{14}N_2O_3$  222.10045, obsd m/z 222.10058; GCMS m/z (relative intensity) 222 (M<sup>+</sup>, 91), 207 (2), 178 (3), 176 (2), 136 (6), 86 (20), 45 (100).

2-((4-Nitrophenyl)methyl)cyclohexanone (7b).<sup>17</sup> To pnitrobenzyl chloride (343 mg) in 10 mL of CH<sub>3</sub>CN was added 300  $\mu$ L of Et<sub>3</sub>N and 501 mg of **3b**. The Pyrex tube was irradiated for 10 h by a 275-W sunlamp. The reaction mixture was poured into 50 mL of H<sub>2</sub>O containing 6 mL of concd hydrochloric acid and stirred for 12 h before neutralization with NaHCO<sub>3</sub> and extraction with three 30-mL volumes of CH<sub>2</sub>Cl<sub>2</sub>. The extract was dried over Na<sub>2</sub>SO<sub>4</sub>, the solvent was evaporated, and the residue was purified by flash column chromatography (EtOAc-hexane) followed by recrystallization from cyclohexane to give 162 mg (35%) of 7b as white crystals: mp 70–71 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  8.074 (d, J = 8.7 Hz, 2 H), 7.297 (d, J = 8.7 Hz, 2 H), 3.244 (dd, J = 13.2, 4.8 Hz, 1 H), 2.628–2.242 (m, 4 H), 2.097–1.2849 (m, 6 H);  ${}^{13}C$  NMR (CDCl<sub>3</sub>)  $\delta$  211.34 (s), 148.50 (s), 146.36 (s), 129.90 (d), 123.45 (d), 52.04 (d), 42.16 (t), 35.48 (t), 33.81 (t), 27.93 (t),

<sup>(10)</sup> Russell, G. A.; Ros, F.; Mudryk, B. J. Am. Chem. Soc. 1980, 102, 7601.

<sup>(11)</sup> Garvey, L. C.; Grakauskas, V.; Baum, K. J. Org. Chem. 1985, 50, 1699

<sup>(12)</sup> Kornblum, N.; Cheng, L.; Kerber, R. C.; Kestner, M. M.; Newton, B. N.; Pinnick, H. W.; Smith, R. G.; Wade, P. A. J. Org. Chem. 1976, 41, 1560

<sup>(13)</sup> Kornblum, N.; Boyd, S. D.; Ono, N. J. Am. Chem. Soc. 1974, 96, 2580

<sup>(14)</sup> Wilson, J. D.; Hobbs, C. F.; Weingarten, H. J. Org. Chem. 1970, 35, 1542.

<sup>(15)</sup> Hünig, S.; Lücke, E.; Brenninger, W. Organic Syntheses; John Wiley and Sons, Inc.: New York, 1973; Collect. Vol. V, p 808.
(16) Van der Vlugt, F. A.; Verhoeven, J. W.; Pandet, U. K. Recl. Trav. Chim. Pays-Bas 1970, 89, 1258.
(17) Aoki, S.; Fujimura, T.; Nakamura, E.; Kuwajima, I. J. Am. Chem.

Soc. 1988, 110, 3296.

2-((4-Nitrophenyl)methyl)cyclopentanone (7a). Compound 7a was isolated as white crystals: mp 56 °C; <sup>1</sup>H NMR (CDCl<sub>2</sub>)  $\delta$  8.098 (d, J = 8.7 Hz, 2 H), 7.299 (d, J = 8.7 Hz, 2 H), 3.190 (dd, J = 13.8, 4.5 Hz, 1 H), 2.640 (dd, J = 13.8, 9.0 Hz, 1 H), 2.400-2.297 (m, 2 H), 2.138-1.909 (m, 3 H), 1.811-1.652 (m, 1 H), 1.490 (ddd, J = 23.1, 10.8, 3.3 Hz, 1 H); <sup>13</sup>C NMR  $\delta$  (CDCl<sub>3</sub>) 218.84 (s), 147.85 (s), 146.39 (s), 129.60 (d), 123.50 (d), 50.36 (d), 37.77 (t), 35.25 (t), 28.98 (t), 20.36 (t); IR 1342, 1518, 1731 cm<sup>-1</sup>; HRMS calcd for  $C_{12}H_{13}NO_3$  219.08954, obsd m/z 219.08927; GCMS m/z (relative intensity) 219 (M<sup>+</sup>, 79), 136 (15), 83 (56), 40 (100).

2-((4-Nitrophenyl)methyl)cycloheptanone (7c). Compound 7c was isolated as white needles: mp 130 °C; <sup>1</sup>H NMR (CDCl<sub>2</sub>)  $\delta$  8.053 (d, J = 8.4 Hz, 2 H), 7.252 (d, J = 8.4 Hz, 2 H), 3.147-3.080 (dd, J + 13.6, 6.6 Hz, 1 H), 2.85-2.95 (m, 1 H), 2.632-2.562 (dd, J)J = 13.5, 7.4 Hz, 1 H), 2.399–2.366 (m, 2 H), 1.783–1.183 (m, 8 H);  ${}^{13}C$  NMR (CDCl<sub>3</sub>)  $\delta$  214.15 (s), 148.11 (s), 146.43 (s), 129.88 (d), 123.51 (d), 53.04 (d), 43.32 (t), 37.63 (t), 30.85 (t), 29.10 (t), 29.06 (t), 23.88 (t); IR 1348, 1520, 1699 cm<sup>-1</sup>; HRMS calcd for  $C_{14}H_{17}NO_3$  247.12084, obsd m/z 247.12082.

3,4-Dihydro-2-((4-nitrophenyl)methyl)-1(2H)**naphthalenone** (8). To the enamine 4 (478 mg) and 170  $\mu$ L of Et<sub>3</sub>N dissolved in 25 mL of DMF was added p-nitrobenzyl chloride (206 mg). The reaction mixture was irradiated for 80 min with a 275-W sunlamp before being poured into 200 mL of water containing 3.6 mmol of HCl. After being stirred for 12 h the mixture was extracted with three 30-mL volumes of CH<sub>2</sub>Cl<sub>2</sub> and the extract dried over Na<sub>2</sub>SO<sub>4</sub>. The solvent was evaporated, and the residue was purified by flash column chromatography to yield after recrystallization from cyclohexane 141 mg of 8 (42%): mp 150 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  8.122 (d, J = 8.7 Hz, 2 H), 8.016 (d, J = 7.8 Hz, 1 H), 7.447 (t, J = 7.5 Hz, 1 H), 7.380 (d, J = 8.4 Hz, 2 H), 7.286 (t, J = 7.5 Hz, 1 H), 7.201 (d, J = 7.8 Hz, 1 H), 3.54-3.46 (m, 1 H), 2.97-2.93 (m, 2 H), 2.86-2.73 (m, 2 H), 2.12-2.01 (m, 1 H), 1.87-1.71 (m, 1 H); IR 1348, 1520, 1678 cm<sup>-1</sup>. Anal. Calcd for C<sub>17</sub>H<sub>15</sub>NO<sub>3</sub>: C, 72.58; H, 5.37; N, 4.98. Found: C, 72.24; H, 5.59; N, 4.99.

2-(1-Methyl-1-nitroethyl)cyclohexanone (5).<sup>18</sup> Compound 5 was obtained a solid: mp 52 °C; the <sup>1</sup>H NMR agreed with the literature values; <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ 208.07 (s), 88.55 (s), 57.19 (d), 42.68 (t), 29.67 (t), 27.58 (t), 25.26 (t), 24.89 (q), 22.61 (q); GCMS m/z (relative intensity) 139 (59), 98 (0.6), 95 (72), 69 (100); Cl-MS (NH<sub>3</sub>) 203 (M + NH<sub>4</sub><sup>+</sup>, 100).

4-((4-Nitrophenyl)methyl)morpholine (10b).<sup>19</sup> Isolated material had the following properties: <sup>1</sup>H NMR (CDCl<sub>2</sub>)  $\delta$  8.154 (d, J = 8.7 Hz, 2 H), 7.500 (d, J = 8.7 Hz, 2 H), 3.698 (t, J = 4.8 Hz)Hz, 4 H), 3.563 (s, 2 H), 2.433 (t, J = 4.8 Hz, 4 H); IR (CDCl<sub>3</sub>) 1346, 1522, 1115, 1265 cm<sup>-1</sup>; GCMS m/z (relative intensity) 222 (M<sup>+</sup>, 85), 136 (100), 100 (27), 86 (60).

1-((4-Nitrophenyl)methyl)pyrrolidine (9b).<sup>20</sup> Isolated material had the expected <sup>1</sup>H NMR: GCMS m/z (relative intensity) 206 (M<sup>+</sup>, 58), 205 (100), 136 (10), 84 (86).

Other Reaction Products. 1-Nitro-4-(1,1,2-trimethyl-2nitropropyl)benzene<sup>21</sup> and diethyl ethyl(1-methyl-1-nitroethyl)malonate<sup>22</sup> were prepared by literature procedures. Diethyl isopropylidenemalonate was isolated and compared with an authentic sample from Aldrich Chemical Co.: <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  4.21 (q, J = 7.2 Hz, 4 H), 2.04 (s, 6 H), 1.26 (t, J = 7.2 Hz, 6 H).

Supplementary Material Available: <sup>1</sup>H NMR spectrum for 6 and <sup>13</sup>C NMR spectra for 7a-c (5 pages). Ordering information is given on any current masthead page.

- (18) Russell, G. A.; Hershberger, J.; Owens, K. J. Am. Chem. Soc. 1979, 101, 1312.
- (19) Kirkpatrick, D. L.; Johnson, K. E.; Sarlorelli, A. C. J. Med. Chem. 1986, 29, 2048.
- (20) Matter, O. Swiss Patent no. 268,094, Aug. 1, 1950.
   (21) Kornblum, N.; Davies, T. M.; Earl, G. W.; Holy, N. L.; Kerber,
   R. C.; Musser, M. T.; Snow, D. H. J. Am. Chem. Soc. 1967, 89, 725.

(22) Russell, G. A.; Norris, R. K.; Panek, E. J. J. Am. Chem. Soc. 1971, 93, 5839.

# A New Route to 9,9a-Dihydro-3*H*-pyrrolo[1,2-*a*]indoles via Radical Cyclization

Frederick E. Ziegler\* and Lucio O. Jeroncic

Sterling Chemistry Laboratory, Yale University, New Haven, Connecticut 06511-8118

Received November 30, 1990

A new method for the preparation of 9,9a-dihydro-3H-pyrrolo[1,2-a]indoles, an important substructure for the synthesis of mitomycins, is presented. A number of representative indoles are allylated on nitrogen with 1,3-dihalopropenes followed by n-Bu<sub>3</sub>SnH-mediated radical cyclization. The effect of the substitution patterns of the indoles and reaction conditions is explored. In all reactions the products of cyclization predominate; however, uncyclized materials are produced along with isomers and oxidation products of the cyclized substances.

# Introduction

The development of methods for the synthesis of the 9,9a-dihydro-3H-pyrrolo[1,2-a]indole 3 nucleus has been a challenge in the chemistry of the mitomycins.<sup>1</sup> Danishefsky<sup>2</sup> and Naruta<sup>3</sup> have reported methods that form both C-N bonds of the pyrrolo ring. The cyclization of terminal vinyl radicals with isolated olefins to form cyclopentenes has been reported by Beckwith,<sup>4</sup> Parsons,<sup>5</sup> and



Hart.<sup>6</sup> Owing to the ready availability of the indole nucleus and the ease with which it can be N-allylated, we chose to explore the reaction sequence of Scheme I. During the course of these studies, Beckwith<sup>7</sup> reported the

<sup>(1)</sup> For reviews on earlier synthetic efforts directed toward the mitosanes, see: (a) Kametani, T.; Takahashi, K. Heterocycles 1978, 9, 293. (b) Takahashi, K.; Kametani, T. Heterocycles 1979, 13, 411. (c) Franck, R. W. Fortschr. Chem. Org. Naturst. 1979, 38, 1.

<sup>(2)</sup> Danishefsky, S.; Berman, E. M.; Ciufolini, M.; Etheredge, S. J.; Segmuller, B. E. J. Am. Chem. Soc. 1985, 107, 3891.

<sup>(3)</sup> Naruta, Y.; Nagai, N.; Maruyama, K. J. Chem. Soc., Perkin Trans. I 1988, 1143.

 <sup>(4)</sup> Beckwith, A. L. J.; O'Shea, D. M. Tetrahedron Lett. 1986, 27, 4525.
 (5) Neary, A. P.; Parsons, P. J. J. Chem. Soc., Chem. Commun. 1989, 1090.

<sup>(6)</sup> Ghosh, T.; Hart, H. J. Org. Chem. 1989, 54, 5073.