The presence of 3 and 4 is most easily explained by homolytic cleavage of the N-O bond of the ester. It has been pointed out previously that an alternative pathway for the production of any radical in the presence of PBN is nucleophilic attack by an anion on the nitrone followed by oxidation of the resulting adduct.¹³ This is not a very likely pathway in this case since heterolytic cleavage of the N-O bond would lead to a nitrenium ion, not an amidyl anion.

Benzovl tert-butvl nitroxide (2) is generally formed under conditions in which an oxidizing reagent is present.^{12,13} There is considerable evidence that nitrenium ions can oxidize such species as I⁻ and other soft bases.¹⁸ It may be that the presence of 2 indicates that heterolytic N-O bond cleavage is competing with the homolytic process. The relative yield of 2 changes with the substituent X in a manner that is consistent with this hypothesis.

We have not yet characterized the products of the decomposition of la-c in benzene. However in aqueous solution they decompose predominantly to give O-pivaloxyacetanilides 6. N-(benzoyloxy)benzanilide decomposes



when heated in decalin, nitrobenzene, and DMF to yield the analogous O-(benzoyloxy)benzanilide and other products such as benzanilide and N-benzoyl-4-aminobiphenyl, which are best explained by radical reaction processes.¹⁹

Our results provide support for a mechanism involving homolytic N-O bond cleavage for the recently reported cross-linking of DNA and protein mediated by N-acetoxy-N-acetyl-2-aminofluorene, a reaction that is sensitive to the presence of radical traps.²⁰ Other reactions of the carcinogenic esters, including attack at C-8 of guanosine, may proceed via radical pathways also.

We are expanding our studies of the radical reactions of these esters with an emphasis on exploring the viability of such reactions in more polar solvents.

Acknowledgment. We are grateful for the assistance of Bruce Huberman, Lee Pollack, and John Dionis who aided in the syntheses of compounds 1a-c. We are also thankful to Dr. Fred Greenaway of this department who provided us with the simulation program and many helpful suggestions. B.A.B. would like to thank the General Electric Foundation for a Summer Research Fellowship. This work was supported by grants from the Petroleum Research Fund, administered by the American Chemical Society, and the American Cancer Society (BC-348).

Registry No. 1a, 88867-64-5; 1b, 88867-65-6; 1c, 88887-33-6; 2, 35822-90-3; 3 (X = Me), 88887-34-7; 3 (X = H), 88867-66-7; 3 (X = NO₂), 88867-67-8; 4 (X = Me), 88887-35-8; 4 (X = H), 88867-68-9; 4 (X = NO₂), 88867-69-0; N-phenylhydroxylamine, 100-65-2; N-hydroxyacetanilide, 1795-83-1; pivaloyl chloride, 3282-30-2; N-(p-tolyl)hydroxylamine, 623-10-9; N-hydroxy-pacetotoluide, 27451-21-4; O-pivaloyl-N-(p-nitrophenyl)-

hydroxylamine, 88867-70-3; N-(p-nitrophenyl)hydroxylamine, 16169-16-7.

Supplementary Material Available: Details of the syntheses and characterization of la-c (4 pages). Ordering information is given on any current masthead page.

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Metal-Halogen Exchange-Initiated Intramolecular **Conjugate Addition Reactions of Unsaturated Esters**

Summary: Intramolecular conjugate addition reactions of internal unstabilized nucleophilic centers formed through rapid lithium-halogen exchange reactions have been used to generate carbocycles from ω -iodo- α,β -unsaturated esters.

Sir: There has been much recent interest in carbocycle synthesis via both intramolecular radical cyclizations¹ and intramolecular Michael addition reactions of stabilized carbanionic centers.² We now describe cyclization reactions of ω -iodo- α , β -unsaturated esters 1, which presumably proceed through highly unstabilized nucleophilic intermediates 2 formed by rapid lithium-halogen exchange. While there are several examples of extremely rapid exchange reactions with cyclopropyl³ and aryl halides,⁴ little is known about the relative rates of such reactions at saturated centers.⁵ We have found that such exchange reactions are in some cases rapid enough to permit the formation of unstabilized nucleophilic centers in the presence of Michael acceptors with which they may subsequently undergo direct intramolecular addition reactions.⁶ Results of cyclizations of the type depicted in eq 1 are shown in Table I.



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 (3) Stein, C. A.; Morton, T. H. Tetrahedron Lett. 1973, 4934.

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1978, 43, 2325–2330. Parham, J. C.; Templeton, M. A. Cancer Res. 1980, 40, 1475–1481; J. Org. Chem. 1982, 47, 652–657. Novak, M.; Pelecanou, M.; Roy, A. K.; Andronico, A. F.; Plourde, F. M.; Olefirowicz, T. M. J. Am. Chem. Soc., submitted for publication.

⁽¹⁹⁾ Horner, L.; Steppan, H. Liebigs Ann. Chem. 1957, 606, 24-47. (20) Rayshell, M.; Ross, J.; Werbin, H. Carcinogen.-Compr. Surv. 1983, 4, 501-507.

^{(6) 2,2-}Dimethyl-6-iodohexanenitrile reportedly gives 2,2-dimethylcyclohexane in unspecified yield upon treatment with n-BuLi through a pathway thought to involve metal-halogen exchange followed by an intramolecular 1,2-addition reaction: Larcheueque, M.; Debal, A.; Cuvigny, T. J. Organometal. Chem. 1975, 87, 25. The recently reported cyclization of م, فأiodides with t-BuLi is likely an example of an exchange-initiated alkylation reaction: Bailey, W. F.; Gagnier, R. P. Tetrahedron Lett. 1982, 23. 5123.

Table I. Reaction of ω -Iodo- α , β -Unsaturated Esters with Alkyllithium Reagents

	substrate, 1				temp.	vield 4. ^b
entry		R,	n	RLi ^a	°C	%
1 2 3	1a	Н	4	n-BuLi	-100 -78 -8	82 52 14
4 5 7 8 9 10	1b 1c 1d 1e	Me H Me H	4 3 5	<i>sec</i> -BuLi <i>t-</i> BuLi ^c MeLi n-BuLi	-100	22 68 0 ^d 86 (83) ^e 78 (69) ^e 0 ^f 14

^a Reactions were conducted by the slow addition of a small excess of RLi to a vigorously stirred solution of 1 in THF. ^b Yields were determined by GLC. ^c 2 equiv. ^d 49% of 5 isolated, 68% recovery of 1a. ^e Isolated yield. ^f 7 is produced in 42% yield.

Treatment of *tert*-butyl ester 1a ($R_1 = H, n = 4$)⁷ with *n*-BuLi in THF at -100 °C⁸ gives, after protonation of the intermediate enolate 3 with EtOH, tert-butyl cyclopentylacetate (4a, $R_1 = H$, n = 4) in 82% yield.⁹ Lower yields (66%) are observed with the corresponding ethyl ester. Increasing amounts of as yet unidentified polar products are produced with more reactive sec-BuLi and t-BuLi as metalating agents. The use of less reactive MeLi gives, in addition to recovered 1a, only tertiary alcohol 5.



the product of 1,2-carbonyl addition. An increase in the reaction temperature also results in a decrease in the yield of 4a (52% at -78 °C, 14% at -8 °C) with the major product at -8 °C being 6, which results from a further Michael condensation of enolate 3a with unreacted 1a followed by an intramolecular alkylation of the newly generated enolate. The successful cyclization of $\beta_{,\beta}$ -disubstituted 1b ($R_1 = Me$, n = 4)¹⁰ is also noteworthy in that such a substitution pattern often has a deleterous effect on intermolecular conjugate addition reactions.¹¹

The formation of four-membered carbocycles also appears to be feasable by exchange-initiated cyclization reactions. Treatment of 1c ($R_1 = H$, n = 3) with *n*-BuLi in

THF at -100 °C gives, after quenching, tert-butyl cyclobutylacetate (4c) in 78% yield. Cyclobutane formation was not observed, however, when $\beta_1\beta_2$ -disubstituted 1d (R₁ = Me, n = 3, $E:Z \sim 3:1$) was subjected to similar treatment. Instead, a more favorable transition-state geometry for a γ -proton abstraction in 2d not present in previous cases apparently allows the cyclization to be subverted through dienolate formation in the major E isomer and 7 is produced in 42% yield after quenching.¹²



Cyclizations leading to cyclohexane derivatives have been less successful. tert-Butyl cyclohexylacetate (4e) is formed from 1e under comparable conditions in only 14% yield along with several unidentified polar products and 8. It appears that in this case the rate of ring closure from 2e is slow enough to allow utilization of equilibrium-supplied *n*-BuLi in other pathways, including the direct conjugate addition reaction leading to 8.13

We have also examined the suitability of other Michael acceptor moieties for use in metal-halogen exchange-initiated cyclization reactions (eq 2-4). Treatment of un-



saturated aryl ketone 9 with *n*-BuLi at -100 °C in THF gives, after quenching with EtOH, ketone 10 in 86% isolated yield. In this case direct 1,4-addition is apparently faster than lithium-halogen exchange. This result is especially surprising in light of the generally accepted claim that unsaturated ketones give predominantly products resulting from 1,2-carbonyl addition with unstabilized organolithium reagents.¹⁴ In the case of the corresponding

⁽⁷⁾ Cyclization substrates 1 were prepared by Emmons-Wadsworth-Horner condensations of tert-butyl diethylphosphonoacetate with the corresponding ω -chloro aldehyde or ketone followed by chloride exchange with NaI in acetone.

⁽⁸⁾ This temperature is assumed to result from the cooling of rapidly stirred solutions with a MeOH-nitrogen bath.

⁽⁹⁾ The structures of all new compounds are supported by spectral data and elemental analyses except in the cases of unstable tertary allylic alcohols 5 and 13 where satisfactory analytical results could not be obtained

⁽¹⁰⁾ The preparation of 4b illustrates a typical cyclization procedure: A solution containing 165 mg (0.5 mmol) of 1b in 6 mL of THF was vigorously stirred at -100 °C⁸ under an argon atmosphere. A precooled solution (-78 °C) of n-BuLi (0.43 mL, 1.37 N in hexane) was added dropwise over 3 min with continued stirring for 5 min followed by the addition of 125 μ L of EtOH. The mixture was concentrated under reduced pressure at room temperature and diluted with water, and the crude presente at room temperature and under with water, and the preparative TLC (silica gel, CH₂Cl₂). Bulb-to-bulb distillation (160 °C, 25 mm) gave 82 mg (83%) of 4b as an oil.⁹
(11) March, J. "Advanced Organic Chemistry: Reactions, Mechanisms and Structure", 2nd ed.; McGraw-Hill: New York, 1977; p 729.

⁽¹²⁾ The course of this reaction suggests the formation of a highly basic terminal carbon and lends support to the notion that our cyclizations proceed through an organolithium intermediate (2) rather than by an also plausable pathway involving a terminal radical generated in a SET

change reactions: Panek, E. J. J. Am. Chem. Soc. 1974, 96, 7959. (13) Contrary to the general finding that unsaturated ethyl esters give only the 1,2-addition product with alkyllithium reagents,¹¹ we find that tert-butyl 3-butylheptanoate, the product of 1,4-addition, is the major product (67%) when tert-butyl (E)-3-heptenoate is added to n-BuLi in THF at either -100 or -5 °C. Inverse addition at -5 °C results in 7-butyl-7-hydroxy-5-undecene, the product of 1,2-addition, being the major product. On the other hand, the conjugate addition of Grignard reagents to unsaturated sec-butyl esters is common: Munch-Peterson, J. Org. Chem. 1957, 22, 170.

⁽¹⁴⁾ Wakefield, B. J. "The Chemistry of Organolithium Compounds"; Pergamon Press: New York, 1974; p 133.

methyl ketone 11, trace amounts of cyclopentyl acetone (12) resulting from the exchange-initiated cyclization sequence are observed along with a small amount of 14, the product resulting from the direct conjugate addition of *n*-BuLi, but the major product 13 arises from direct 1,2carbonyl addition. Under similar conditions, unsaturated amide 15 also gives a small amount of cyclic amide 16 (15%) along with unidentified polar condensation products and 17, which apparently arises from direct conjugate addition to the olefinic link followed by intramolecular alkylation of the resulting enolate. Direct uncatalyzed conjugate additions of alkyllithium reagents to unsaturated amides have been reported.¹⁵

Our success in achieving cyclizations with unsaturated esters suggests the possibility of executing a variety of new cyclization reactions where the lithium-halogen exchange rate exceeds the rate of the direct reaction of the metalating agent with an internal electrophilic center. We are presently investigating such possibilities.

Acknowledgment. We are grateful to the National Science Foundation for support of this work.

Registry No. 1a, 88931-70-8; 1b, 88931-71-9; 1c, 88931-72-0; 1d, 88931-73-1; 1e, 88931-74-2; 4a, 88931-75-3; 4b, 88931-76-4; 4c, 79033-94-6; 4e, 16537-06-7; 7, 88931-77-5; 8, 88931-85-5; 9, 88945-39-5; 10, 88931-78-6; 11, 88931-79-7; 12, 1122-98-1; 13, 88931-80-0; 14, 88931-81-1; 15, 88931-82-2; 16, 88931-83-3; 17, 88931-84-4; tert-butyl (E)-3-heptenoate, 88931-86-6; 7-butyl-7hydroxy-5-undecene, 88931-87-7; tert-butyl 3-butylheptanoate, 88931-88-8.

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On the Stability of the Phenalenyl Cation Incorporated into a Bicyclo[3.2.2]nona-2,6,8-trienyl **Framework**¹

Summary: In order to evaluate the thermodynamic stability of the elusive bicyclo[3.2.2]nona-2,6,8-trienyl cation (1), the phenalenyl cation incorporated into a bicyclo-[3.2.2]nona-2,6,8-trienyl framework such as 3a has been synthesized; from the examination of ¹H and ¹³C NMR spectra and the reduction potential of 3a, it is suggested that 3a is stabilized to some extent by a positive charge delocalization from the phenalenyl part into the etheno bridges.

Sir: The concept of bicycloaromaticity proposed by Goldstein and Hoffmann² in 1971 has stimulated development of the longicyclic carbocations and anions. In contrast to the vast amount of literature concerning the highly stabilized 7-norbornadienyl cation,³ very little has

been revealed about its higher vinylogue, the bicyclo-[3.2.2]nona-2,6,8-trienyl cation 1.⁴ Many attempts to



generate 1 even under conditions of long life have failed owing to its facile rearrangement into energetically favored 9-barbaralyl cation 2.5 The well-known stable phenalenyl cation $3c^6$ consists of an antisymmetric nonbonding molecular orbital (NBMO) (A) similar to that of the allyl cation (B). In this regard the chemical and physical behaviors of the phenalenyl cation incorporated into a bicyclo[3.2.2]nona-2,6,8-trienyl framework, 3a, in which no energetically economical path to the corresponding barbaralyl cation is available, are of particular interest. We now report the synthesis of 3a together with the evidence that 3a is more stable than the progenitor cation 3c.

The etheno-bridged phenalenyl cation 3a⁷ was prepared by starting from the phenalenone $5a^8$ as shown in Scheme The ethano-bridged cation $3b^7$ as a reference com-I.9 pound is also prepared from 5a through diimide reduction $(KOOCN=NCOOK/HOAc in MeOH + CH_3CN, room)$ temperature) to 5b followed by the same manner as in the preparation of 3a.

The ¹H and ¹³C NMR chemical shifts¹⁰ of $3a-c^{11}$ are





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(6) For reviews, see: Reid, D. H. Q. Rev. Chem. Soc. 1965, 19, 274. Murata, I. In "Topics in Nonbenzenoid Aromatic Chemistry"; Nozoe, T., Breslow, R., Hafner, K., Ito, S., Murata, I., Eds.; Hirokawa: Tokyo, 1976; Vol. 1, p 159.

(7) **3a**: a red solid, mp 190 °C (dec in a sealed tube); UV (CH₃CN) λ_{max} (1) 3a: a red solid, mp 190 °C (acc in a sealed tube); UV (CH₃CN) λ_{max} nm (log ϵ) 248 (4.04), 275 (sh, 3.61), 356 (3.97), 420 (4.31), 500 (sh, 3.33), 539 (sh, 3.25). Anal. (C₁₉H₁₃BF₄) C, H. 3b: a yellow solid, mp 180 °C (dec in a sealed tube); UV λ_{max} nm (log ϵ) 228 (4.50), 379 (sh, 4.18), 415 (4.64), 457 (sh, 3.58). Anal. (C₁₉H₁₅BF₄) C, H. (8) Sugihara, Y.; Hashimoto, K.; Yoshikawa, M.; Murata, I. Tetrahe-dron Lett. 1982, 23, 1925.

(9) Due to their structures consisting of phenalene skeletons, 6a and 6b were highly contaminated with the corresponding double-bond isomers.

(10) ¹H NMR spectra were measured in CF₃COOD for 3a-c and in CDCl₃ for 4a, 5a, 6a, 4b, 5b, and 6b.

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 Story, P. R.; Saunders, M. Ibid. 1960, 82, 6199; 1962, 84, 4876. Lustgarten, R. K.; Brookhart, M.; Winstein, S. Ibid. 1967, 89, 6350. Brookhart, M.; Lustgarten, R. K.; Winstein, S. Ibid. 1967, 89, 6352, 6354. Lustgarten, R. K.; Brookhart, M.; Winstein, S. Ibid. 1968, 90, 7364.