Decarbonylation of 9,10-Dihydro-9,10-methanoanthracen-11-one (Dibenzonorbornadienone). Effects of Nitro Substituents and Solvents

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Several attempts to isolate norbornadien-7-one and benzonorbornadien-9-one have failed because of very facile decarbonylation.[1] 9,10-Dihydro-9,10-methanoanthracen-11-one (dibenzonorbornadienone) (1) was prepared,[2,3] but undergoes decarbonylation easily in the formation of anthracene. However, such decarbonylations with the corresponding monoenes, norbornen-7-one and related compounds, are not so easy and require various conditions.[1] The decarbonylations are special examples of a general type defined as cheletropic reactions.[4-7] It is obvious that the formation of aromatic compounds is a driving force for the above reactions. Importance of electronic factors was suggested.[1b,7] We were interested in the reactions leading to deactivated aromatic compounds, for example, nitroanthracene, and wanted to compare these with results from the parent aromatic compound. This note describes the effect of nitro substituents in the decarbonylation of 1, together with a study of solvent effects. The basic principle employed here is that introduction of substituents into the aromatic moiety can cause a variation of aromatic character while maintaining steric effects constant. Another important advantage in the present system is that it allows one to carry out kinetic studies by a UV technique.

Results and Discussion

Nitro groups were chosen as substituents because they are among the strongest electron-withdrawing substituents and thus might produce large kinetic effects. Whereas the nitration of 1 gave a complex mixture, that of 11-isopropylidenedibenzonorbornadiene (2), from which 1 was derived,[3] was successful. Thus, when 2 was treated with copper(II) nitrate at room temperature in a mixture of acetic anhydride and dichloromethane, the usual workup followed by silica gel chromatography afforded the β-mononitro compound 3. The unusually strong β orientation of this ring system on electrophilic aromatic substitutions is known.[8] Ozonolysis of 3 led to 2-nitro-9,10-dihydro-9,10-methanoanthracen-11-one (4). Introduction of the second nitro group into another benzene ring was carried out by treatment of 4 with a mixture of fuming nitric acid, sulfuric acid, and nitromethane at 0 °C. The resulting 5 is thought to be composed almost exclusively of a mixture of 2,6- and 2,7-dinitro derivatives.[8]

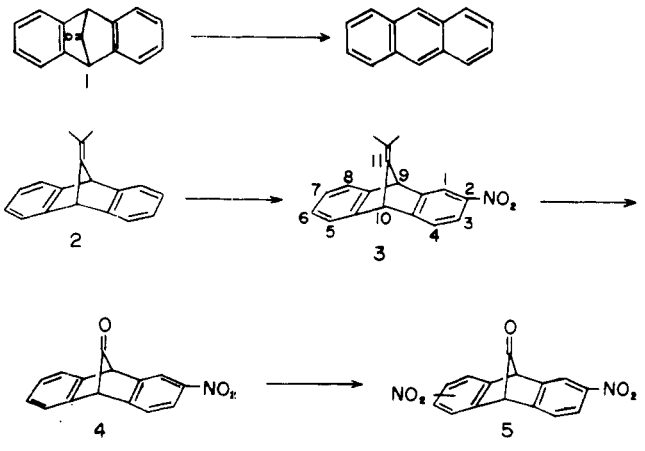
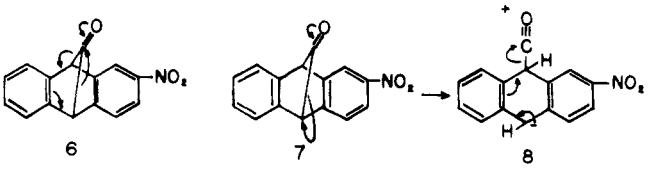


Table I. Decarbonylation Rates in Dioxane

compd	temp, °C	k_1, s^{-1}	$\Delta H^{\ddagger}$, kcal mol^{-1}	$\Delta S^{\ddagger}$, eu	rel k (25 °C)
1	25.2	$(2.52 \pm 0.02) \times 10^{-5}$	26.1	7.7	1
	39.0	$(1.69 \pm 0.01) \times 10^{-4}$			
	47.6	$(5.93 \pm 0.05) \times 10^{-4}$			
	25.0	2.39×10^{-5} [a]			
4	25.8	$(7.58 \pm 0.17) \times 10^{-5}$	25.9	9.1	2.8
	39.9	$(5.37 \pm 0.04) \times 10^{-4}$			
	47.2	$(1.51 \pm 0.02) \times 10^{-3}$			
	25.0	6.64 ± 10^{-5} [a]			
5	24.9	$(1.43 \pm 0.02) \times 10^{-4}$	23.0	1.2	6.1
	39.5	$(9.23 \pm 0.52) \times 10^{-4}$			
	25.0	1.45×10^{-4} [a]			

[a] Calculated from the observed rates.

Thermal decarbonylation of 1, 4, and 5 resulted in quantitative formation of anthracene and its nitro derivatives. The rates were determined by following UV maxima of the forming anthracenes. The first-order rate constants obtained in dioxane solvent are presented in Table I and compared at 25.0 °C. Introduction of nitro substituents causes rate enhancement by a factor of 3 for the mononitro and 6 for the dinitro. Although the rate-increasing tendency with the electron-withdrawing substituents is clear, the factors are not notable. This smallness in factors is not to be unexpected if we consider a widely suggested view that the cheletropic reaction undergoes, in concert, a cleavage of two σ bonds, which terminate at a single bond;[4-6] in the present case, concerted elimination of CO leads to anthracene in one step as pictured in 6. Further,



as the present decarbonylation proceeds with relief of strain existing in the [2.2.1] system, increasing π delocalization energy due to anthracene formation and elimination of the small stable molecule CO, it is probably an exothermic reaction. The transition state must appear early in the reaction coordinate and resemble the ground state, so that the main factor for rate differences may be only electrostatic effects of nitro substituents.

The solvent effect on the decarbonylation was checked at 27 °C with 4 in ethanol, dioxane, benzene, or heptane. As shown in Table II, the results indicate that as solvent polarity decreases, the rate increases. The compound 4 is perhaps more polar than the transition state leading to nitroanthracene (the reaction proceeds with polarity decrease). In addition, the decarbonylation is accompanied by a molecular volume increase.[9] The large positive entropy of activation in Table I is suggestive of a transition-state configuration in which both bonds to the carbon of the carbon monoxide unit have been broken. Therefore, a more polar solvent would have a higher internal pressure and resist this transformation, as supported by the data in Table II.

Table II. Solvent Effects on Decarbonylation at 27.0 °C

compd	solvent	k_1, s^{-1}
4	ethanol	$(0.88 \pm 0.05) \times 10^{-4}$
	dioxane	0.89×10^{-4} [a]
	benzene	$(1.28 \pm 0.01) \times 10^{-4}$
	heptane	$(2.19 \pm 0.09) \times 10^{-4}$

[a] Calculated by Arrhenius plots of the data in Table I.

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An alternative mechanism which might be considered is initial cleavage of the C(9)–CO bond, resulting in the dipolar ion (7 → 8) and subsequent elimination of CO to form anthracene. Formation of an intermediate such as 8 having an anionic charge at the carbon α to the aromatic ring may be faciliated by introduction of the nitro group, which may be in accord with the data in Table I. Such a mechanism would also be favored by polar solvents. Inconsistently, the data in Table II show a rate depression with an increase of solvent polarity.

Experimental Section

Melting points were taken using a capillary and are corrected. Infrared spectra were determined with a 215 Hitachi grating infrared spectrophotometer and ^1H NMR spectra with a Varian T-60A.

2-Nitro-11-isopropylidenedibenzonorbornadiene (3). 11-Isopropylidenedibenzonorbornadiene (2, 939 mg) was dissolved in a mixture of 10 mL of dichloromethane and 50 mL of acetic anhydride. To the solution was added 758 mg of copper(II) nitrate, and the mixture was allowed to stand overnight at room temperature with stirring. The reaction mixture was filtered to remove the precipitate and concentrated under reduced pressure. The residue was extracted with ether, and the ether layer was washed with water, dried, and evaporated, leaving 2.4 g of an oil. When the oil was chromatographed over silica gel, 50% benzene–50% hexene eluant gave the starting material 2, and then 100% benzene eluant gave 3: mp 197–197.5 °C; NMR ($CDCl_3$) δ 1.60 (s, 6 H, isopropylidene), 4.85 (s, 2 H, bridgehead), 6.85–7.40 (m, 4 H, aromatic), 7.35 (d, 1 H, aromatic H at C_4), 7.90 (d of d, 1 H, aromatic H at C_3), 8.05 (d, 1 H, aromatic H at C_1); IR ($CHCl_3$) 1350, 1530 cm^{-1} (NO_2). Anal. Calcd for $C_{18}H_{15}NO_2$: C, 77.96; H, 5.45; N, 5.05. Found: C, 78.26; H, 5.52; N, 5.01.

Dibenzonorbornadien-11-one (1). Ozone gas was absorbed by a solution of 210 mg of 2 in 10 mL of dichloromethane at −30 °C with stirring. When 2 disappeared, nitrogen gas was introduced to remove excess ozone and then dimethyl sulfide was added. After being stirred for 15 min, the mixture was washed with ice water, dried, and evaporated, leaving 195 mg of a crystalline ketone: IR ($CHCl_3$) 1800 cm^{-1} (C=O).

2-Nitrodibenzonorbornadien-11-one (4). A solution of 97 mg of 3 in 10 mL of dichloromethane was treated as above. A crystalline ketone (61 mg) was obtained: IR ($CHCl_3$) 1350 and 1520 (NO_2), 1805 (C=O) cm^{-1}.

Dinitrodibenzonorbornadien-11-one (5). To a solution of 251 mg of 4 in 10 mL of dichloromethane was added 1.31 g of a nitric acid–sulfuric acid mixture (prepared by mixing 5 g of fuming nitric acid, 90 g of sulfuric acid, and 8 g of water) at 0 °C with stirring. The mixture was stirred for 2 h, poured into ice water, and extracted with dichloromethane. The dichloromethane solution was washed with ice water, dried, and evaporated under reduced pressure, leaving 290 mg of crystal: IR ($CHCl_3$) 1810 and 1830 (C=O), 1350 and 1530 (NO_2) cm^{-1}.

Kinetic Measurements. Rates were determined by measuring intensities at UV maxima of the anthracene or nitroanthracenes produced using a Hitachi recording spectrometer. The UV maxima used were the following: 340, 358, and 378 nm for anthracene in dioxane; 346, 364, and 415 nm for 2-nitroanthracene in dioxane; and 345 nm for dinitroanthracene. The UV maxima of 2-mononitroanthracene in other solvents used for kinetics were as follows: 346, 363, and 415 nm in ethanol; 348, 365, 417, and 440 nm in benzene; and 344, 362, 383, 403, and 426 nm in heptane. First-order plots were linear.

Registry No.—1, 30131-11-4; 2, 30131-12-5; 3, 68928-10-9; 4, 68936-71-0; 5 (isomer 1), 68928-11-0; 5 (isomer 2), 68928-12-1.

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Synthesis and pH Effects on the Hydrolysis of 5′-Adenosyl Phenylalaninate

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Considerable research on the mechanism of protein synthesis has resulted in the current view that two ribosomal bound aminoacyl-tRNA's undergo an intermolecular reaction that culminates in the formation of a dipeptidyl-tRNA bound to the A (acceptor) site on the ribosome. Subsequent reactions leading to the coded protein sequence are a repetitive sequence of steps involving ribosomal movement of the peptidyl-tRNA to the P site, codon–anticodon binding of the next specific aminoacyl-tRNA at the A site, and peptide bond formation.

Chemical models of coded peptide bond formation have been described by both Li and Zemlicka[1] and Ringer, Chladek, and Ofengand[2] using 2′(3′)-aminoacyladenosine derivatives.

The genetic coding mechanism defines peptide bond formation as occurring through 3′-aminoacyladenylates on the tRNA terminus. Although this process appears to be the successful survivor of evolution, it does not preclude other primative recognition patterns as progressive steps in development of ribosomal protein synthesis. One such mechanism of amino acid–nucleic acid recognition process that has the necessary chemical features for peptide synthesis is that involving 5′-aminoacyl nucleosides. Selectivity can be gained by application of the stacking and hydrogen-bonding properties that order nucleic acid structures. An entropic advantage that favors peptide bond formation can be gained by the use of polynucleotides as templates to order the interacting aminoacylnucleosides in juxtaposition. This report describes the initial phases of this research, the synthesis and pH stability of the 5′-adenosine ester of phenylalanine.

Formation of the intermediate 5′-(2′,3′-*O*-isopropylidene)-adenosyl *N*-(carbobenzyloxy)-DL-phenylalaninate (3) was found to proceed in excellent yield (94%) by acylation of 2′,3′-*O*-isopropylideneadenosine with the symmetrical anhydride of *N*-(carbobenzyloxy)-DL-phenylalanine (2) in pyridine solvent (Scheme I). Facile removal of the isopropylidene protecting group was accomplished in aqueous methanolic hydrochloric acid to yield 5′-adenosyl *N*-(carbobenzyloxy)-DL-phenylalaninate (4, 70%). Subsequent hydrogenolysis of 4 using 5% palladium on barium sulfate in methanol containing 5% hydrochloric acid produced 5′-adenosyl DL-

Table I. Observed Rate Constants for the Hydrolysis of 5′-Adenosyl Phenylalaninate at 37 °C[a]

pH	$t_{1/2}$, min	$k_{obsd} \times 10^3$, min^{-1}	log k_{obsd}
5.2	1700	0.41	−3.39
5.9	740	0.94	−3.03
7.0	260	2.64	−2.58
8.0	95	7.33	−2.13
8.7	88	7.9	−2.10
9.0	91	7.6	−2.12
10.0	20	34	−1.47
10.4	7.6	91	−1.04
10.8	3.3	207	−0.68

[a] These values were extrapolated to zero buffer concentration from experimental results using 0.1 and 0.05 M phosphate buffer adjusted to 0.30 ionic strength with potassium chloride.

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