THE JOURNAL OF Organic Chemistry

VOLUME 46, NUMBER 11

MAY 22, 1981

Reactions of Benzenediazonium Ions with Adenine and Its Derivatives

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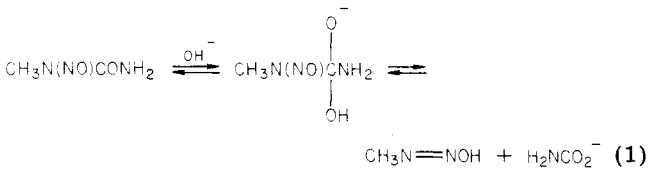
Received October 1, 1980

Adenine, adenosine, and 5′-adenylic acid react readily with benzenediazonium ion and its derivatives at pH 8–11 to yield derivatives of (*E*)-6-(3-phenyl-2-triazen-1-yl)purine. The structural assignments for these compounds, some of which are unstable, are based on their spectroscopic properties and their degradation reactions in acid solution and with sodium dithionite to yield 6-hydrazinopurine. The triazenes decompose in basic aqueous solution at 60–90 °C to produce 8-aryladenines. For adenosine and 5′-adenylic acid, the ribose residues are cleaved during this process. Several lines of evidence indicate that the triazenes are converted to 8-aryladenines in intermolecular processes. Both the benzenediazonium ion and the phenyl radical can be intercepted during the reaction. Consequently, the phenylation reaction may be confidently formulated as an intermolecular free-radical substitution reaction.

Recent work has shown that the decomposition reactions of *N*-methyl-*N*-nitrosourea and other nitrosoureas proceed in neutral and basic aqueous solution by the initial addition of hydroxide ion to the carbonyl group of the nitrosourea to form a tetrahedral intermediate.[1-3] (eq 1). This intermediate decomposes to form an alkyldiazo hydroxide and a carbamic acid derivative. The products are eventually formed from these substances in subsequent, relatively rapid, pH-dependent reactions. The reactions of carbamate anions in aqueous solution have been discussed.[4] Less is known about the behavior of the extremely reactive alkyldiazo hydroxides.[5] Although the reactions of these compounds with the nucleic acids have not been studied directly, it seems safe to conclude that they are intermediates in the alkylation reactions of genetic material.[6] Accordingly, we turned our attention to the reactions of diazo hydroxides with the purines. Because the alkyldiazo hydroxides are very unstable, we elected to investigate the reactions of the more stable benzenediazonium hydroxides to identify the key intermediates.



(1)

The reactions of the benzenediazonium ions with the purines have been studied previously. However, the various reports present conflicting commentary. Burian reported that 4-sulfobenzenediazonium ion reacted with hypoxanthine to form an adduct.[7] An attempt to repeat this work was unsuccessful.[8] Guanine, xanthine, and isoguanine, however, react readily with benzenediazonium ions to yield 8-azo coupling products. Reductive cleavage of these adducts provides the corresponding 8-amino derivatives.[9-11] Neither adenine nor hypoxanthine are reported to react in this way.[9] Kössel noted that 4-sulfobenzenediazonium ion reacted with 3′- and 2′-deoxy-5′-adenylic acid and with 3′- and 2′-deoxy-5′-guanylic acid.[12,13] He concluded, largely on the basis of the electronic spectra of the compounds, that the reaction products were triazenes rather than azo compounds. In view of the different results and interpretations, we studied the reactions of adenine and its derivatives with several benzenediazonium ions in basic solution to establish the structures of the reaction products with confidence. Certain of the initial reaction products are unstable. Consequently, we also examined the decomposition reactions which led to the formation of 8-aryladenine derivatives.

Results and Discussion

Preliminary experiments established that the reaction between adenine and the benzenediazonium ions pro-

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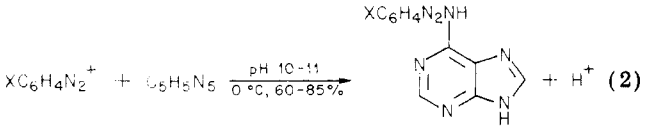
Table I. Spectroscopic Properties for 6-[3-(4-Substituted-phenyl)-2-triazen-1-yl]purines[d]

compd	NMR,[a] chemical shifts, ppm				IR,[b] cm^{-1}	UV,[c] nm
	C^2-H	C^8-H	phenyl	other		
1a	8.61 (s)	8.53 (s)	7.40 (t, 1 H), 7.53 (t, 2 H), 7.75 (d, 2 H)		3410 (m, br), 1620, 1580 (s) 870 (m)	374
1b	8.59 (s)	8.51 (s)	7.34 (d), 7.68 (d) [J = 8.2 Hz]	2.27 (s, CH_3)	3410 (m, br), 1620, 1575 (s), 872 (m)	372
1c	8.59 (s)	8.51 (s)	7.66 (d), 7.70 (d) [J = 8.7 Hz]		3420 (m, br), 1625, 1585, 1578 (s), 870 (w)	395
1d	8.60 (s)	8.52 (s)	7.67 (d), 7.73 (d) [J = 8.4 Hz]			397

[a] In dimethyl-d_6 sulfoxide. The assignments for C^2-H and C^8-H were secured by the examination of the spectra of 1a-*8-d* and 1c-*8-d*. [b] Potassium bromide pellet. [c] At pH 10.5; another weaker absorption was observed near 240 nm. [d] Satisfactory analyses were reported for compounds 1a–c.

ceeded readily in basic aqueous solution between pH 8 and 11 to form an adduct. In most experiments, the reagents were mixed at 0 °C, and the reaction was carried out between pH 10 and 11 at 25 °C. Neutralization of the solution led to the precipitation of a yellow solid. The reactions proceeded about equally well with the substituted and unsubstituted ions to provide the adducts in 60–85% yield. The 4-methylphenyl and the phenyl derivatives were somewhat unstable and decomposed slowly during chromatography and upon storage. The analytical data obtained for the adducts were compatible with the formulation of the product as a triazene, 1 (eq (eq 2). The spectroscopic properties are summarized in Table I.



1a, X = H
b, X = CH_3
c, X = Br
d, X = SO_3H

The NMR spectrum of 1c is representative. The resonances of the protons at the 2- and 8-positions of the adenine nucleus of 1c appear at 8.59 and 8.51 ppm, respectively. The resonances of the protons in the benzene nucleus appear at 7.70 and 7.66 ppm with J = 8.7 Hz. The chemical shifts of these aromatic protons are identical with the chemical shifts of the low-field resonances of the aromatic protons in 1,3-bis(4-bromophenyl)triazene (2) in the same solvent. Because the low-field resonances in 2 can be assigned to the protons of the azo fragment, 4-BrC_6H_4N=NN, this observation strongly suggests that the triazene has the same structural unit rather than the alternative 4-BrC_6H_4NHN=N structure. The infrared spectra of the adducts 1 and other representative derivatives of adenine contained several very characteristic frequencies which distinguished between reactions of the diazonium ion at a nitrogen atom of the ring and at the 6-amino group.[14] These frequencies include the stretching mode of the 6-amino group near 3300 cm^{-1} and the in-plane deformation mode near 1670 cm^{-1}. These frequencies are present in a variety of adenine derivatives, but they are absent in the spectra of the triazenes. The triazenes possess a less intense absorption near 3420 cm^{-1} and no absorption in the region of 1670 cm^{-1}. In addition, the characteristic N^9–H out-of-plane deformation near 870 cm^{-1} is present in the triazenes.[15] The spectroscopic results, therefore, suggest that the triazene should be formulated as 6-[3-(4-bromophenyl)-2-triazen-1-yl]purine.

Kössel had proposed that the adducts obtained from adenine derivatives in the reactions with 4-sulfobenzenediazonium ions were triazenes on the basis of the absorption maximum from 370 to 440 nm.[13,16] Similar absorptions were observed in this work. However, we also observed a second weaker absorption at 240 nm. This absorption is apparently characteristic of many 1,3-diaryltriazenes.[17]

The structural assignment for 1 is supported by the finding that N^6-methyladenine and N^6-acetyladenine do not form triazenes under the experimental conditions. The failure of the reaction with N^6-methyladenine was not unexpected. Dodin and his co-workers have demonstrated that there is a strong intramolecular hydrogen bond in this adenine.[18] This stabilization of the starting material coupled with a significant steric requirement for product formation presumably raises the energy requirements significantly.

The degradation reactions of the triazenes were also studied. We first found that the adducts 1 decompose rapidly at room temperature at pH 3 in the presence of 2-naphthol to give adenine and the azo coupling products of 2-naphthol quantitatively. Second, the reduction of triazene 1c with sodium dithionite provides a mixture of the starting material (41%), adenine (5%), and 6-hydrazinopurine (47%). These results strongly support the assignment of the structure as 6-[3-(4-bromophenyl)-2-triazen-1-yl]purine.

The spectroscopic observations for the triazenes suggest that a single isomer is obtained in each case. These substances are assigned the E configuration on the basis of other work in which it has been established by X-ray crystallography that 1,3-bis(4-bromophenyl)triazene is the E isomer[19] and in which it has been proposed that diazonium ions react with amines selectively to form the E isomer.[20] Repulsive steric interactions are minimized in this isomer in which there is a strong intramolecular hydrogen bond between the proton of the 6-amino group and the N^7 nitrogen atom.

The benzenediazonium ions also react with adenosine and 5′-adenylic acid under the conditions used for the reactions of adenine. The products with phenyl, 4-

(14) The infrared spectra of the purines are discussed in: Lister, J. H. "Heterocyclic Compounds"; Wiley-Interscience: New York, 1971; Vol. 24.

(15) This assignment has been questioned by some workers in the field. The matter is discussed by: Jones, R. L., ref 14, p 507.

(16) Kössel, H. *Z. Anal. Chem.* **1964**, *205*, 445.

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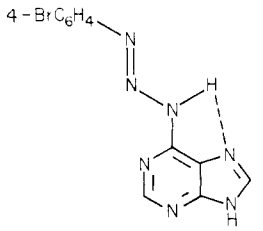
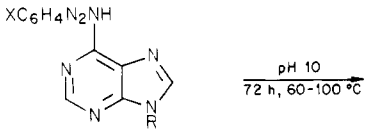


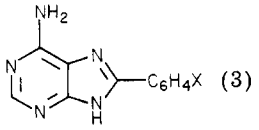
methylphenyl, 4-bromophenyl, and 4-sulfophenyl substituents were obtained in 18–42% yield. The spectroscopic properties of these compounds are summarized in Table II.

The spectroscopic observations recorded for these compounds are quite similar to the spectra of the corresponding products obtained with adenine. The resonances of the protons of the ribose and ribose-5-phosphate units were very well resolved at 270 MHz, providing secure evidence for the integrity of that portion of the structure. The short- and long-wavelength absorptions near 240 and 380 nm also appear in the spectra of these compounds.[13,16,17] Moreover, the triazenes prepared from adenosine and 5′-adenylic acid decompose in acid solution in the same way as the triazenes prepared from adenine. All these observations indicate that the adducts are also (*E*)-6-(3-phenyl-2-triazen-1-yl)purine derivatives.

All the triazenes prepared in this study decompose slowly in dilute basic solution at ambient temperature. For convenience, we studied this decomposition at 60–100 °C. The triazenes of adenine, **1**, decompose under these conditions to yield adenine and 8-aryladenine derivatives as the only purine containing products (eq 3). The triazenes



1, R = H
3, R = ribose,
4, R = ribose-5-phosphate



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a, X = H; b, X = CH_3; c, X = Br; d, X = SO_3H

obtained from adenosine (**3**) and 5′-adenylic acid (**4**) also decompose under these conditions to yield 8-aryladenine derivatives in 10–20% yields. The structures of these products were established by their spectroscopic properties and by comparison with authentic samples.

The 8-aryladenines may form in several ways. On the one hand, the reaction may proceed by an intramolecular fragmentation reaction through a radical pair intermediate (Scheme I). On the other hand, the reaction may proceed via the dissociation of the triazene to adenine and benzenediazonium ion with the subsequent formation of phenyl radicals from the diazonium ion in the basic solution (Scheme II).[21]

Several lines of evidence support the conclusion that the reaction proceeds by an intermolecular free-radical reaction. First, the addition of excess adenine to a solution of the triazene results in a 50% increase in the quantity of the 8-aryladenine formed in the reaction. Second, the

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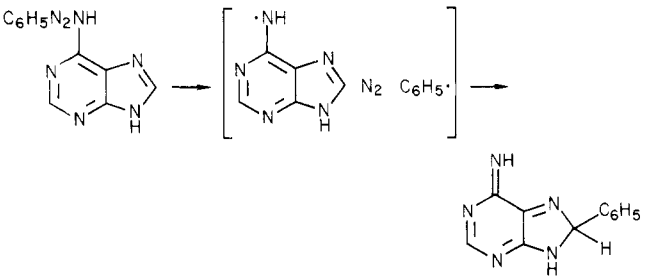
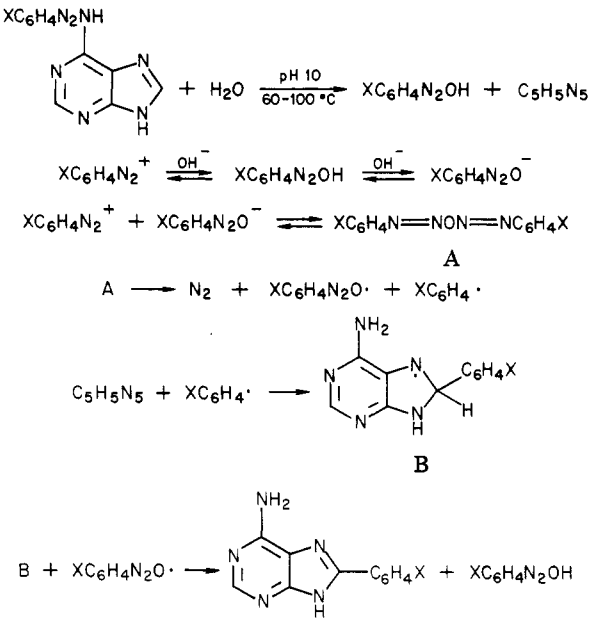
Scheme I



Scheme II



benzenediazonium ion can be intercepted quantitatively when the triazenes decompose in the presence of 2-naphthol. 8-Aryladenine derivatives could not be detected among the products of this reaction by sensitive chromatographic procedures. In a third approach, the triazene **1c** was decomposed in the presence of 2,6-diaminopurine. Quantitative analysis showed that the product was a mixture of 8-aryladenine and 8-aryl-2,6-diaminopurine. In this instance, adenine and 2,6-diaminopurine compete effectively for the 4-bromophenyl radical, and both 8-aryl derivatives are formed. The results indicate that the diaminopurine is 1.9-fold more reactive than adenine under these conditions. Fourth, the reaction of **1c** was carried out in the presence of *n*-butyl mercaptan. At low concentration of this hydrogen donor, the quantity of 8-(4-bromophenyl)adenine was clearly reduced. At higher concentration, the formation of the 8-(4-bromophenyl)-adenine was completely suppressed. The only purine-containing product formed under these conditions is adenine. Finally, we examined the reactivity of adenine toward the phenyl cation. Benzenediazonium ion decomposes slowly in trifluoroethanol to yield this cation. The phenyl cation reacts competitively with aromatic compounds and with the solvent in this solution. To gauge the reactivity of adenine toward the phenyl cation, we examined the reaction between the benzenediazonium ion and adenine in trifluoroethanol. Adenine was recovered unchanged from the reaction solution after 48 h. Apparently, the reaction of the phenyl cation with adenine is much slower than the reaction of the cation with the poorly nucleophilic solvent. This observation and other considerations suggest that the phenyl cation is not involved in

Table II. Spectroscopic Properties of the 6-[3-(4-Substituted-phenyl)-2-triazen-1-yl]purine Derivatives

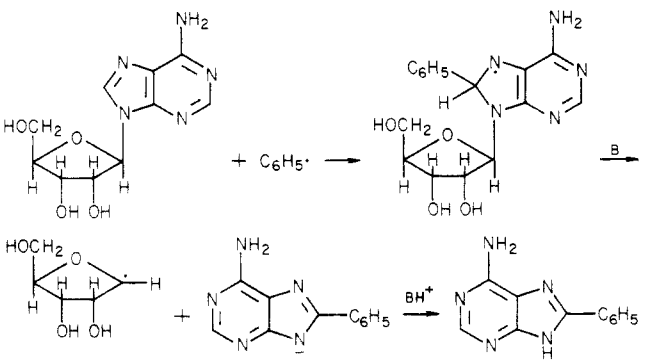
compd	NMR, chemical shifts, ppm				UV,[c] λ_{max}, nm
	C^2-H	C^8-H	phenyl	other	
			Adenosine Derivatives[a,d]		
3a (X = H)	8.65 (s)	8.80 (s)	7.40 (d, 1 H), 7.53 (t, 2 H), 7.77 (d, 2 H)		385
3b (X = CH_3)	8.59 (s)	8.75 (s)	7.37 (d), 7.69 (d), [J = 8.0 Hz]	2.37 (s, CH_3)	379
3c (X = Br)	8.61 (s)	8.75 (s)	7.67 (d), 7.72 (d), [J = 8.9 Hz]		396
3d (X = SO_3H)	8.66 (s)	8.80 (s)	7.72 (d), 7.77 (d), [J = 8.8 Hz]		380
			5′-Adenylic Acid Derivatives[b]		
4a (X = H)	8.24 (s)	8.31 (s)	7.40–7.71 (m)		382
4b (X = CH_3)	8.23 (s)	8.29 (s)	7.23 (d), 7.61 (d), [J = 8.5 Hz]	2.31 (s, CH_3)	374
4c (X = Br)	8.14 (s)	8.27 (s)	7.58 (d), 7.66 (d), [J = 8.3 Hz]		384
4d (X = SO_3H)	8.27 (s)	8.33 (s)	7.55 (d), 7.66 (d), [J = 7.8 Hz]		398

[a] In dimethyl-d_6 sulfoxide. The assignments for C^2-H and C^8-H were secured by the examination of the spectra of 3a-*8-d* and 3c-*8-d*. [b] In basic solution, pH 13.0. [c] In basic solution, pH 10.5. [d] Satisfactory analyses were reported for 3a and 3c.

the formation of 8-phenyladenine in basic aqueous solution. Thus, all the lines of evidence support the conclusion that the reaction proceeds via the dissociation of the triazene into adenine and a benzenediazonium ion. Further decomposition of the diazonium ion as outlined in Scheme II produces phenyl radical which reacts with adenine to form the 8-phenyl derivatives. No evidence has thus far been obtained which requires the serious consideration of a radical pair intermediate.

The observation that the phenylation of adenosine and 5′-adenylic acid occurs preferentially to yield 8-phenyladenine is striking. Sensitive chromatographic procedures indicate that neither 8-phenyladenosine nor 8-phenyladenylic acid are formed under the experimental conditions. In addition, when 6-[3-(4-bromophenyl)-2-triazen-1-yl]purine riboside was hydrolyzed in aqueous solution at pH 10.5, only traces of adenine were formed. Observations of this kind negate an interpretation based upon the hydrolysis of 6-[3-(4-bromophenyl)-2-triazen-1-yl]-purine riboside to yield adenine which subsequently undergoes phenylation. Rather, the results strongly suggest that the sugar fragment is lost from the intermediate in the course of the phenylation reaction (Scheme III).

Scheme III



Experimental Section

The chemicals and solvents used in this work were obtained from commercial sources. These compounds were purified as necessary prior to use. The electronic, infrared, and NMR spectra were recorded on Cary 219, Perkin-Elmer 283, and Bruker 270-MHz spectrometers.

(*E*)-6-(3-Phenyl-2-triazen-1-yl)purines. The triazenes derived from adenine and its derivatives were prepared by the same general method. 4-Bromobenzenamine (1.72 g, 10 mmol) was dissolved in hot water (5 mL). Concentrated hydrochloric acid (1.85 mL) was added to the warm solution. When the solution was cooled to 0 °C, a solid white cake formed, and water (10 mL) was added to dissolve the solid. Sodium nitrite (0.72 g, 5% excess) in water (3 mL) was slowly added; the mixture was kept at 0 °C during the addition process. The 4-bromobenzenediazonium salt solution was added dropwise to a solution of adenine (0.675 g, 5 mmol) in 0.62 N sodium hydroxide (40 mL) at 0 °C. The pH was adjusted to 10–11 by the dropwise addition of sodium hydroxide. After the addition, the solution was stirred for 15 min. The solution was neutralized to pH 7 with 0.5 N hydrochloric acid; the precipitate which formed was filtered, washed thoroughly with chloroform, water, and methanol, and air-dried to yield (*E*)-6-[3-(4-bromophenyl)-2-triazen-1-yl]purine (1.28 g, 80%) as a yellow solid. The spectroscopic properties are presented in Table I.

(*E*)-6-(3-Phenyl-2-triazen-1-yl)purine Ribosides. Very similar procedures were employed for the preparation of the triazenes of adenine, adenosine, and 5′-adenylic acid with several benzenediazonium ions. The preparation of (*E*)-6-(3-phenyl-2-triazen-1-yl)purine riboside (**3a**) is described. Aniline (0.93 g, 10 mmol) was dissolved in hot water (5 mL). Concentrated hydrochloric acid (1.85 mL) was added to the warm solution. Then the solution was cooled to 0 °C, and water (10 mL) was added to keep the solution clear. The benzenediazonium salt solution was added dropwise to a solution of adenosine (1.34 g, 5 mmol) in 0.62 N sodium hydroxide (40 mL) at 0 °C. The pH was adjusted to 10–11 by the dropwise addition of sodium hydroxide. After the addition, the solution was stirred for 10 min. The solution was neutralized to around pH 7 with 1.0 N hydrochloric acid, and the precipitate which formed was filtered, washed thoroughly with chloroform, water, and methanol, and air-dried to yield **3a**, (*E*)-6-(3-phenyl-2-triazen-1-yl)purine riboside hemihydrate (0.42 g, 22%), as a pale yellow solid. The characteristic strong infrared frequencies of the skeletal vibrations of the purine ring at 1620 and 1575 cm^{-1} were observed.

The other spectroscopic properties of this compound and the other triazenes of adenosine (**3**) and 5′-adenylic acid (**4**) are presented in Table II. No analytical data could be obtained for the 5′-adenylic acid derivatives **4** because these compounds invariably decomposed during the purification process presumably under the influence of intermolecular acid catalysis.

Degradation of (*E*)-6-[3-(4-Bromophenyl)-2-triazen-1-yl]purine. (A) In Acid Solution. The triazene (0.318 g, 1 mmol) was dissolved in dilute hydrochloric acid (15 mL) at pH 3. 2-Naphthol (0.144 g, 1 mmol) was added to the mixture. The reaction was allowed to proceed for 30 min at ambient temperature. The precipitate was collected and washed with 1.0 N

Table III. Product Distribution in the Decomposition of 6-[3-(4-Bromophenyl)-2-triazen-1-yl]purine in Basic Aqueous Solution in the Presence of 2,6-Diaminopurine

10^2[reagents], M		10^3[products], M	
6	1c	7	5c
5.00	5.00	6.10	2.77
3.33	6.67	5.54	7.20
4.00	6.00	9.54	7.20
6.00	4.00	6.86	2.44
6.67	3.33	6.85	1.99

sodium hydroxide to remove adenine. The residue was washed thoroughly with water and air-dried to yield 1-[(4-bromophenyl)azo]-2-naphthol (0.31 g, 95%) identical in all respects with an authentic sample.

(B) Sodium Dithionite. The triazene (0.318 g, 1 mmol) was dissolved in 0.38 N sodium hydroxide (30 mL). Sodium dithionite (8.70 g, 50 mmol) was added in small portions. The solution was stirred at room temperature for 2 h and at 50 °C for 14 h and then was heated at 100 °C for 15 min. During the process, the solution which eventually became pale yellow was maintained at about pH 9. The cooled mixture was neutralized, and the precipitate which formed was filtered, washed with water, and dried. The product distribution was determined by NMR spectroscopy in dimethyl-d_6 sulfoxide using the fully resolved resonances of the C^2 and C^8 protons. Pure compounds were used as analytical standards. An authentic sample of 6-hydrazinopurine was prepared by the method of Montgomery and Holum.[22] This analysis indicated that the product mixture contained 41% of the triazene 1c, 5% adenine, and 47% 6-hydrazinopurine.

Decomposition of (*E*)-6-(3-Phenyl-2-triazen-1-yl)purines. Similar results were obtained with all the triazenes. The typical results obtained with the 4-bromophenyl derivative are described. The triazene (0.636 g, 2 mmol) was dissolved in aqueous sodium hydroxide solution (40 mL) at pH 10.0. The solution was heated in stages from 60 to 100 °C for 48–72 h, and the solution slowly turned dark brown. The reaction mixture was cooled and neutralized to pH 7. The precipitate was collected, washed thoroughly with chloroform and water, and dried to give 8-(4-bromophenyl)adenine (0.093 g, 16%). The NMR spectrum was recorded in dimethyl-d_6 sulfoxide: δ 8.04 (s, 1 H), 7.08 (br, 2 H), 8.06 (d), 7.69 (d, J = 8.5 Hz). This compound was identical with an authentic sample prepared by the method of Fu and co-workers.[23]

The other reaction products are adenine and the familiar highly colored condensation products obtained in the decomposition of diazonium compounds in alkaline solution.

8-(4-Bromophenyl)adenine (5c). 4,5,6-Triaminopyrimidine sulfate (4.83 g, 20 mmol) was dissolved in 1.0 N sodium hydroxide (40 mL), and purified 4-bromobenzoyl chloride (4.83 g, 22 mmol) was added dropwise. After the addition, the mixture was stirred for 1 h. The solution was neutralized to pH 7 and cooled to 4 °C for a few hours, and the precipitate which formed was filtered, washed with ice–water and cold ether, and dried. The crude product was recrystallized from water (1 g of product in 500 mL) to yield 4,6-diamino-5-[(4-bromobenzoyl)amino]pyrimidine (4.6 g, 75%).

4,6-Diamino-5-(4-bromobenzoyl)aminopyrimidine (0.45 g, 1.2 mmol) was cooled to 0 °C, and phosphorus pentoxide (2 g, 14 mmol) was added and mixed with the solid. Then 85% phosphoric acid (2 mL) was added dropwise to the cold mixture. After 10 min, the mixture was refluxed 1.5 h at about 165 °C. The product was poured onto crushed ice with vigorous stirring and then cooled at 4 °C for 18 h. The precipitate which formed was collected and washed with ice–water and cold ether prior to recrystallization from 2.0 N hydrochloric acid to yield 8-(4-bromophenyl)adenine (70 mg, 20%). The NMR spectrum of **5c** was recorded in dimethyl-d_6 sulfoxide: δ 8.04 (s, 1 H), 7.08 (br, 2 H), 8.06 (d, 2 H), 7.69 (d, 2 H, J = 8.5 Hz). Anal. Calcd for $C_{11}H_8N_5Br$: C, 45.45; H, 2.78. Found: C, 45.32; H, 2.71.

8-(4-Methylphenyl)adenine (**5b**) and the known 8-phenyladenine (**5a**) were also prepared by this method. The NMR spectra of these compounds were recorded in dimethyl-d_6 sulfoxide. For **5b**: δ 8.14 (s, 1 H), 7.15 (br, 2 H), 8.04 (d, 2 H), 7.36 (d, 2 H, J = 8.2 Hz). For **5a**: δ 8.14 (s, 1 H), 7.18 (br, 2 H), 8.14 (d, 2 H), 7.53 (m, 3 H). Anal. Calcd for $C_{12}H_{11}N_5$·HCl (**5b**): C, 55.07; H, 4.62; N, 26.76. Found: C, 55.48; H, 4.57; N, 26.77.

Inhibition of Purine Phenylation by 2-Naphthol. The 4-bromophenyltriazene (0.318 g, 1 mmol) was decomposed at pH 10 in the presence of 2-naphthol (0.144 g, 1 mmol) in water at 90 °C. The solution quickly turned dark red. After 24 h, the reaction mixture was cooled, and the precipitate which formed was collected, washed with 1.0 N sodium hydroxide and with water, and air-dried to yield 1-[(4-bromophenyl)azo]-2-naphthol (0.32 g, 95%) which was identical with an authentic sample. No 8-phenyladenine was obtained.

Inhibition of Purine Phenylation by Butanethiol. The (bromophenyl)triazene **1c** (0.477 g, 1.5 mmol) was dissolved in aqueous sodium hydroxide (15 mL) at pH 10. Purified butanethiol (0.27 g, 3.0 mmol) was added. The reaction was carried out in the usual way, and the products were isolated as already described. The yield of 8-(4-bromophenyl)adenine decreased to 8.7%. When excess *n*-butyl mercaptan (15 mmol) was used, the formation of 8-(4-bromophenyl)adenine was completely inhibited.

Competitive Experiments. 2,6-Diaminoadenine and 6-[3-(4-Bromophenyl)-2-triazen-1-yl]purine. The triazene **1c** and 2,6-diaminopurine (**6**) were dissolved in aqueous sodium hydroxide at pH 10. The solution was heated at 90 °C for 72 h. The solution was worked up in the usual way. Thin-layer chromatography on silica gel with 80% chloroform–methanol indicated that only two products were formed. The relative yields of 8-(4-bromophenyl)adenine and 8-(4-bromophenyl)-2,6-diaminopurine (**7**) were determined by NMR spectroscopy in pyridine-d_5 by using authentic samples of the products for calibration. 8-(4-Bromophenyl)-2,6-diaminopurine (**7**) was prepared by the method of Elion and co-workers.[24] The results are summarized in Table III.

Decomposition of the (*E*)-6-[3-(4-Bromophenyl)-2-triazen-1-yl]purine Riboside (3c). Triazene **3c** (0.901 g, 2.0 mmol) was dissolved in water (40 mL), and 1.0 N sodium hydroxide was added to maintain the pH value about 10. The solution then was heated at 90 °C for 72 h. The cooled solution was neutralized to pH 7, and the precipitate which formed was filtered, washed thoroughly with chloroform and water, and air-dried to yield 8-(4-bromophenyl)adenine (70 mg, 12%). Adenosine was isolated from the aqueous solution. Only a very small amount of adenine is formed under the reaction conditions.

Decomposition of the (*E*)-6-[3-(4-Bromophenyl)-2-triazen-1-yl]purine Riboside 5′-Phosphate (4c). Triazene **4c** was prepared as described previously. When the addition of diazonium salt solution was complete, the mixture was stirred overnight and then heated at 90 °C for 72 h at pH 9–10. The products were isolated as described to yield 14% 8-(4-bromophenyl)adenine (**5c**) and 5′-adenylic acid.

Acknowledgment. This research was supported by Grant No. CA-20049, awarded by the National Cancer Institute, DHEW. The NMR work was assisted by Grant No. CA-14599, awarded by the National Cancer Institute of the Public Health Service.

Registry No. (*E*)-**1a**, 77070-95-2; (*E*)-**1b**, 77070-96-3; (*E*)-**1c**, 77070-97-4; (*E*)-**1d**, 77070-98-5; (*E*)-**3a**, 77070-99-6; (*E*)-**3b**, 77071-00-2; (*E*)-**3c**, 77071-01-3; (*E*)-**3d**, 77071-02-4; (*E*)-**4a**, 77079-59-5; (*E*)-**4b**, 77079-60-8; (*E*)-**4c**, 77079-61-9; (*E*)-**4d**, 77079-62-0; **5a**, 17720-22-8; **5b**, 77071-03-5; **5c**, 77071-04-6; **6**, 1904-98-9; **7**, 77071-05-7; 4-bromobenzenediazonium, 17333-82-3; benzenediazonium, 2684-02-8; 4-methylbenzenediazonium, 57573-52-1; 4-sulfobenzenediazonium, 2154-66-7; adenine, 73-24-5; adenosine, 58-61-7; 5′-adenylic acid, 61-19-8; 2-naphthol, 135-19-3; 1-[(4-bromophenyl)-azo]-2-naphthol, 7150-24-5; 6-hydrazinopurine, 5404-86-4; 4,5,6-triaminopyrimidine sulfate, 73384-15-3; 4-bromobenzoyl chloride, 586-75-4; 4,6-diamino-5-[(4-bromobenzoyl)amino]pyrimidine, 77071-06-8.

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