in much smaller yield.[2,5,9] The present results are remarkable in terms of the large F_2NO-SF_5 intensity ratio indicating therefore that F_3NO competes very favorably with SF_6 for electron capture, although SF_6 is itself known to be an extremely efficient electron scavenger.[19] The high F_2NO-F_3NO^- ratio is explained if the dissociative path is favored, as seems to be the case for SF_6.

Acknowledgment. We thank Professor Gleb Mamantov (University of Tennessee) and Dr. F. Q. Roberto (Edwards AFB, Calif.) for supplying us with samples of FNO and F_3NO. We are also grateful to Drs. A. Hasegawa and C. M. L. Kerr for helpful discussions. Correspondence about the F_2NO radical with Dr. W. B. Fox (Naval Research Laboratory, Washington, D.C.) and Dr. J. R. Morton (National Research Council, Ottawa) is also acknowledged.

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(10) Although the F_2NO spectrum obtained in the previous work[8a] was not published, the close agreement between the F_2NO parameters derived from powder and isotropic spectra is understandable on the basis of our own low-temperature studies. Thus, we find that although radicals do not tumble in the SF_6 matrix below the phase transition at −179°, the spectrum of F_2NO in SF_6 at −196° shows comparatively little anisotropic broadening, even to the extent that the second-order ^{19}F splittings are retained. However, at much lower temperatures (ca. −250°) the pattern becomes typical of a highly anisotropic powder spectrum from a stationary radical. These results suggest that intramolecular motion, probably inversion coupled with rotation, is responsible for the nearly isotropic appearance of the F_2NO spectrum in a randomly oriented sample at −196°. An inversion barrier of only 0.064 kcal mol^{-1} has been calculated theoretically for the H_2NO radical (Y. Ellinger, R. Subra, A. Rassat, J. Douady, and G. Berthier, *J. Am. Chem. Soc.*, **97**, 476 (1975)).

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(12) An unidentified spectrum derived from an irradiated solution of NO in SF_6 was previously analyzed[2] as a ^{19}F doublet ($a_F' = 187$ G) of ^{19}F triplets (a_F (2) = 143 G). The spectrum of F_2NO would fit this description exactly if the central components of the ^{14}N triplets were masked by the usually more intense lines of SF_5 (see Figure 1) thereby converting the ^{14}N triplet interaction to an apparent doublet ($2a_N = a_F'$). Accordingly, a previous tentative assignment[9] to $ONSF_4$ can probably be discounted.

(13) Despite the interference from other spectral lines, it can be deduced from several spectra of F_3NO^- recorded in different experiments that the second-order splitting for line 3 at low field must be less than that for line 10 at high field by about 5 G. Assuming, as expected, that the ^{14}N and ^{19}F coupling constants have the same sign, a calculation of these second-order splittings from the previously determined hyperfine parameters gave values of 14.8 G (line 3) and 19.8 G (line 10). For a comprehensive discussion of the closely related ethyl radical spectrum, see R. W. Fessenden, *J. Magn. Reson.*, **1**, 277 (1969).

(14) The spin densities in the 2s orbitals of nitrogen and fluorine were calculated from the isotropic coupling constants using the magnetic parameters A_0 (^{14}N) = 552 G and A_0 (^{19}F) = 17,200 G: P. W. Atkins and M. C. R. Symons, "The Structure of Inorganic Radicals", Elsevier, Amsterdam, 1967 p 21.

(15) F_3NO^- and the valence-isoelectronic species F_3SO (J. R. Morton and K. F. Preston, *J. Chem. Phys.*, **58**, 2657 (1973) and ref 2) possess the same spin density in the central-atom ns orbital and the sums of the fluorine couplings are 585 G (F_3NO^-) and 555 G (F_3SO).

(16) (a) A switching mechanism is readily visualized through a C_{3v} intermediate but other rearrangement pathways could also be considered. (b) Recently, ESR evidence was presented for the fluxional behavior of the analogous F_3POEt radical at −8°: I. H. Elson, M. J. Parrott, and B. P. Roberts, *J. Chem. Soc., Chem. Commun.*, 586 (1975).

(17) Calculations were carried out using the original INDO parameterization for first-row elements (J. A. Pople, D. L. Beveridge, and P. A. Dobosh, *J. Chem. Phys.*, **47**, 2026 (1967)) and with bond lengths close to those determined for the neutral F_3NO molecule (V. Plato, W. D. Hartford, and K. Hedberg, *J. Chem. Phys.*, **53**, 3488 (1970)).

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A Novel Photorearrangement of Cephalosporins

Sir:

An extreme lability of cephalosporin C to uv light was observed in early investigations on this important class of antibiotics.[1] Because photolysis resulted in destruction of cephalosporin C antibiotic activity,[1] the β-lactam dihydrothiazine nucleus was suggested as the site of photoreactivity.

In view of previous observations, we attempted to clarify the mode of the photodegradation of 3-cephem derivatives. The present communication describes that irradiation of 3-cephem derivatives *in alcohols* (methanol or ethanol) causes a novel photorearrangement leading to thiazole derivatives, which involve incorporation of alcohols into an intermediate photoproduct. This type of photochemistry is general for 7-acylamido-3-cephem derivatives.

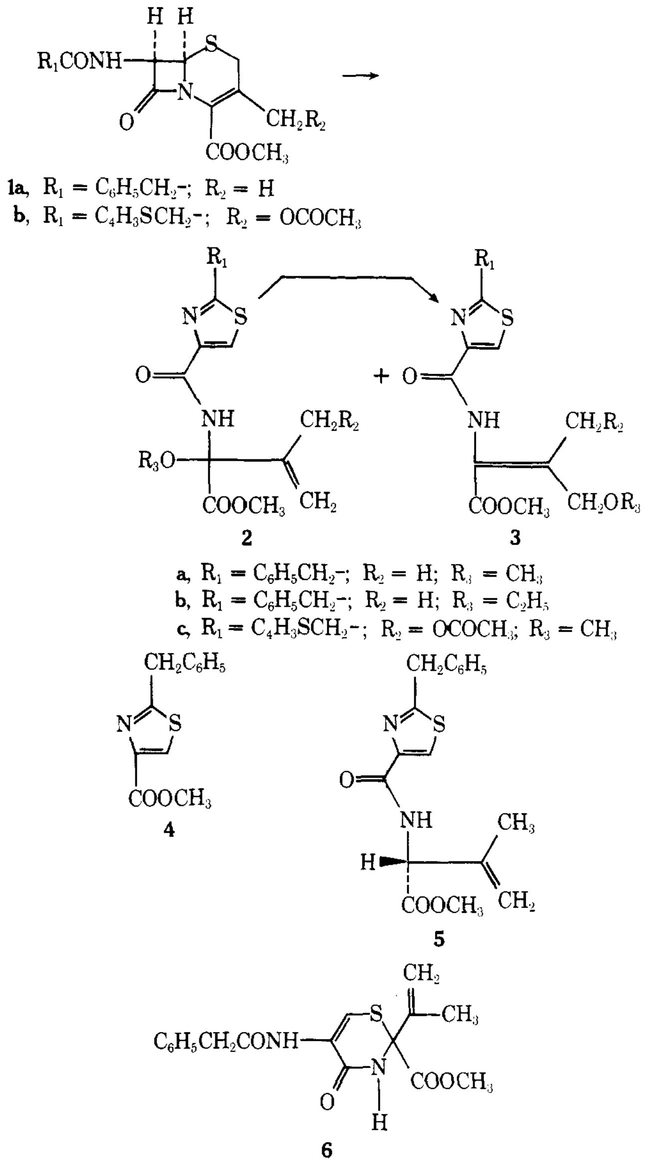
Methyl 7-phenylacetamido-3-methyl-3-cephem-4-carboxylate (**1a**) (0.01 *M*) in methanol[2] was irradiated by a 400-W high-pressure mercury arc lamp through Pyrex filter under nitrogen until disappearance of **1a** (monitored by TLC) was complete (about 8 hr). The solution was concentrated under reduced pressure to leave an oily residue which was subjected to chromatography on silica gel. Elution with $CHCl_3$-$(CH_3)_2CO$, evaporation of the initial elute, and recrystallization of the residue from ether-*n*-hexane gave 2-benzylthiazole-4-carboxamide derivative **2a** in 50% yield (mp 123-125°; ir (KBr) 3390 (NH), 1730 ($COOCH_3$), 1680 cm^{-1} (CONH); NMR ($CDCl_3$) δ 1.89 (3 H, broad s, CH_3—C=CH_2), 3.34 (3 H, s, -OCH_3), 3.87 (3 H, s, -$COOCH_3$), 4.37 (2 H, s, $C_6H_5CH_2$-), 5.27 and 5.53 (each 1 H, m, and broad s, isopropenyl vinyl protons), 7.40 (5 H, broad s, phenyl protons), 8.05 (1 H, s, thiazole-ring proton), 8.65 (1 H, broad NH, deuterium exchangeable)). Further elution afforded a small amount of an isomeric compound **3a** (vide infra) (mp 111-113°; ir (KBr) 3350 (NH), 1700 ($COOCH_3$), 1660 cm^{-1} (CONH); uvλ_{max}^{MeOH} nm (ϵ): 240 (8000); NMR ($CDCl_3$) δ 1.96 (3 H, broad s, =C—CH_3), 3.35 (3 H, s, -OCH_3), 3.80 (3 H, s, -$COOCH_3$), 4.34 (2 H, s, $C_6H_5CH_2$-), 4.40 (2 H, broad s, -CH_2OCH_3), 7.37 (5 H, broad s, phenyl protons), 8.06 (1 H, s, thiazole-ring proton), 8.67 (1 H, broad, NH)). Attempts to isolate other minor products from further eluates failed.

The isolated products, **2a** and **3a**, were insensitive to the irradiation under the analogous conditions. Microanalytical and mass spectral data of both the products established a molecular formula, $C_{18}H_{20}O_4N_2S$, respectively. These products were optically inactive.

Cooper et al.[3] have reported the transformation of penicillin V sulfoxide into the 2-phenoxymethylthiazole-4-carboxamide derivative. Analogously, penicillin G sulfoxide methyl ester was converted to optically active 2-benzylthiazole-4-carboxamide derivative **5**, mp 62-63°, ($[\alpha]^{15}$D −51(*c* 1.0, $CHCl_3$)) in 80% yield.

The NMR spectrum of **5** is similar to that of **2a**, except for the presence of a methine proton signal at 5.26 (1 H, d, *J* = 8 Hz, coalesced to a singlet by deuterium exchange) instead of a methoxy signal in **2a**. The uv spectrum of **2a** (λ_{max}^{MeOH} (ϵ) nm; 228 (sh 8000)) is superimposable on that of **5**.

Scheme I



1a, $R_1 = C_6H_5CH_2$–; R_2 = H
b, $R_1 = C_4H_3SCH_2$–; $R_2 = OCOCH_3$

a, $R_1 = C_6H_5CH_2$–; R_2 = H; $R_3 = CH_3$
b, $R_1 = C_6H_5CH_2$–; R_2 = H; $R_3 = C_2H_5$
c, $R_1 = C_4H_3SCH_2$–; $R_2 = OCOCH_3$; $R_3 = CH_3$

Further structural proof was obtained upon treatment of **2a** with methanolic hydrochloric acid at room temperature. Silica gel chromatography of the reaction mixture led to the isolation of the isomeric product **3a** and oily methyl 2-benzothiazole-4-carboxylate (**4**) in 96% and 2% yields, respectively.

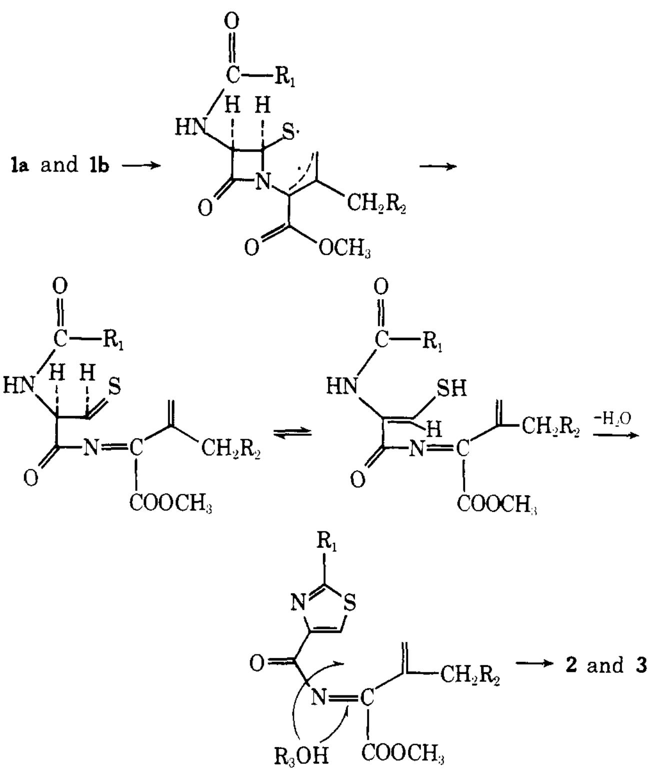
The major product **3a** thus obtained was identical in every respect with the compound isolated as a by-product upon irradiation of **1a** in methanol. The NMR spectral change going from **2a** to **3a** is consistent with isopropenyl-isopropylidene isomerization.[4]

Upon treatment of **2a** with aqueous dioxane containing hydrochloric acid, the corresponding α,β-unsaturated lactone (ir (film) 1760 cm^{-1} (lactone); NMR ($CDCl_3$) δ 2.30 (3 H, broad s, $=C-CH_3$), 4.83 (2H, s, $-OCH_2-C=$)) was obtained as an oily substance. Irradiation of **3a** in methanol caused photoisomerization to give a mixture of **3a** and its geometrical isomer. The newly formed isomer showed a vinylic methyl signal at δ 2.12 which is more deshielded than that of **3a** (δ 1.96). Thus, the cis orientation of an ester group to a methoxy-methyl group in **3a** was established.

The structure of the minor compound **4** was confirmed on the basis of spectral data and its independent synthesis.

When irradiation of **1a** was carried out in ethanol, ethoxy derivative **2b**, mp 118–121°, and its isomer **3b**, mp 93–95°, were obtained in 16% and 0.5% yields, respectively. The minor isomer **3b** was identical in every respect with the product obtained upon treatment of **2a** or **2b** with ethanolic hydrochloric acid.

Scheme II



On employing isopropyl alcohol as a solvent, irradiation of **1a** did not give detectable amounts of pure products.

In a similar manner, irradiation of methyl 7-(thiophene-2-acetamido)-3-acetoxymethyl-3-cephem-4-carboxylate (**1b**) resulted in the formation of thiazole derivative **2c** (26% yield, oil, mass (m/e) $M^+ = 424$; ir (film) 3380 (NH), 1730 ($COOCH_3$ and $OCOCH_3$), 1680 cm^{-1} ($CONH$); uv λ_{max}^{MeOH} nm (ϵ) 233 (9000); NMR ($CDCl_3$) δ 2.11 (3 H, s, $-OCOCH_3$), 3.35 (3 H, s, $-OCH_3$), 3.88 (3 H, s, $-COOCH_3$), 4.57 (2 H, s, $C_4H_3S-CH_2-$), 4.81 (2 H, broad s, $-CH_2-OCOCH_3$), 5.58 and 5.81 (each 1 H, m and broad s, vinyl protons), 7.00–7.50 (3 H, m, thiophene-ring protons), 8.09 (1 H, s, thiazole-ring proton), 8.87 (1 H, broad, $-CONH$)).

It is notable that 1,3-dihydrothiazine (**6**)[5] also rearranged to give **2a** and **2b** in moderate yields by irradiation in alcohols.

The present photorearrangement was not suppressed by addition of acetophenone in various concentrations and was almost completely quenched in the presence of piperylene. Accordingly, a triplet excited state of **1** may be involved in the initial stage of homolytic cleavage of an S–C_2 bond. Although some routes have been considered for the subsequent cyclization to thiazole,[6] we tentatively propose a cyclization process via an intermediate thioaldehyde or thiol formed after β-lactam cleavage[7] as shown in Scheme II. The final step presumably involves a thermal or light-induced 1,4-addition of the alcohols to the α,β-unsaturated acylimine moiety.

Acknowledgment. We are grateful to Dr. T. Watanabe, director of Research Laboratory of Toyo Jozo Co. Ltd., for his continuing interest and encouragement.

References and Notes

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(2) Irradiation of **1a** in acetonitrile or ether followed by chromatographic separation did not give any crystalline products.
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(4) Analogous isomerization has been observed in 3-methylene cepham derivative (cf. M. Ochiai, O. Aki, A. Morimoto, T. Okada, and T. Kaneko, *Tetrahedron Lett.*, 2345 (1972)).
(5) R. B. Morin, E. M. Gordon, T. Mcgrath, and R. Shuman, *Tetrahedron Lett.*, 2159 (1973), and references cited.
(6) Examples of thermal thiazole cyclization by attack of a ring sulfur to an 6-acylamido group in penicillins are precidented (cf. For a recent article, see R. Latree, *Justus Liebigs Ann. Chem.*, 1361 (1974); see also ref 3).
(7) A thiazolidine-azetidinone derivative independently prepared by Cooper's method (cf. ref 3) was stable under analogous irradiation. In the irradiated solution of **1a**, however, β-lactam compounds were not detected.

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Intermediacy of α,*p*-Dinitrocumene Anion Radical, *p*-Nitrocumyl Radical, and *p*-Nitrocumyl Anion in the Radiolytic Reduction of Deaerated Alkaline Methanolic α,*p*-Dinitrocumene

Sir:

Steady radiolysis of deaerated alkaline methanolic α,*p*-dinitrocumene (*p*-NC-NO_2) produces nitrite and mainly *p*-nitrocumene (*p*-NC-H). Pulse data, product yields, and results obtained with CH_3OD support a mechanism of reduction involving the intermediacy of the α,*p*-dinitrocumene anion radical (*p*-NC-$NO_2\cdot^-$), *p*-nitrocumyl radical (*p*-NC·), and *p*-nitrocumyl anion (*p*-NC$^-$). Radiolytically induced nucleophilic substitution of the α-nitro group by added azide was also observed. The anion radical *p*-NC-$NO_2\cdot^-$, proposed by Kornblum[1] as an intermediate in S_{RN} reactions of *p*-NC-NO_2 has been observed in methanol and in water by pulse radiolysis technique.

The mechanism proposed herein for the formation of *p*-NC-H is presented in eq 1–5:

$$p\text{-NC-NO}_2 + e_s^- \rightarrow p\text{-NC-NO}_2\cdot^- \quad (1)$$

$$p\text{-NC-NO}_2 + CH_2O\cdot^- \rightarrow p\text{-NC-NO}_2\cdot^- + CH_2O \quad (2)$$

$$p\text{-NC-NO}_2\cdot^- \rightarrow p\text{-NC}\cdot + NO_2^- \quad (3)$$

$$p\text{-NC}\cdot + p\text{-NC-NO}_2\cdot^- \rightleftarrows p\text{-NC}^- + p\text{-NC-NO}_2 \quad (4)$$

$$p\text{-NC}^- + CH_3OH(D) \rightarrow p\text{-NC-H(D)} + CH_3O^- \quad (5)$$

This mechanism differs significantly from that proposed by Burrows and Kosower for the radiolytic reduction of *p*-nitrobenzyl halides;[2] specifically, the key carbanion intermediate, *p*-NC$^-$, is formed by electron transfer from an anion radical, *p*-NC-$NO_2\cdot^-$, to a neutral radical, *p*-NC· (eq 4), rather than by dissociation of a dianion, as they postulate. The proposed mechanism also differs from the class of radiolytically induced reductions, of which there are a number of examples,[3] in which reduction product results from transfer of H· atoms.

Evidence for eq 1–3 was obtained by pulse radiolysis employing a Febetron 705[4,5] which supplied ~30-nsec pulses of 2.3 MeV electrons. Radiolysis of water produces the reactive transients e^-_{aq} (g = 2.8 ions/100 eV), H· (g = 0.6), and OH· (g = 2.8).[6] Pulsing of an argon-swept aqueous 0.10 m*M* *p*-NC-NO_2 solution, 16 m*M* in KOH, and 1.0 *M* in *tert*-butyl alcohol (to scavange ·OH) produced an absorbance with λ_{max} 305 ± 5 nm, Figure 1A. This absorbance did not develop when N_2O, a reagent which efficiently converts hydrated electrons to OH· radicals (eq 6, R = H) was used to deaerate the solution.

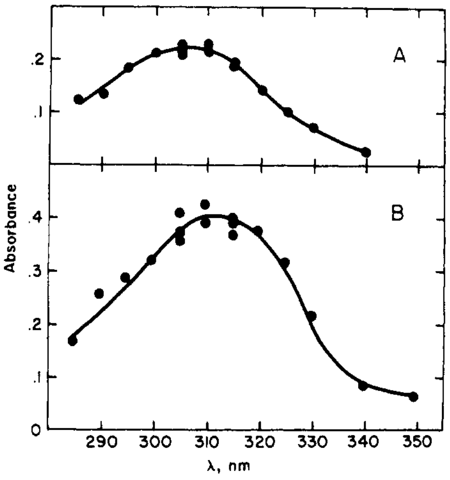

Figure 1. Absorption spectra of electron adduct produced by 1.5 × 10^{17} eV ml^{-1} dose per pulse to solutions 10^{-4} *M* in α,*p*-dinitrocumene and 1.5 × 10^{-2} *M* in KOH; 2.00-cm optical path length: (A) aqueous solutions, 1.0 *M* in *tert*-butyl alcohol; (B) methanol solutions.

$$e^-_{solv} + N_2O \xrightarrow{ROH} OH\cdot + RO^- + N_2 \quad (6)$$

$$k_6 = 8.7 \times 10^9 \text{ (aq)},^7\ 6.2 \times 10^9 \text{ (methanol)}^8$$

The observed λ_{max} is typical of electron adducts of nitroaromatics[2,9] and can be ascribed to *p*-NC-$NO_2\cdot^-$ anion radical. Ninety percent of the observed absorbance developed within 0.5 μsec while ~5 μsec was required for the remainder. The fast process can be attributed to reaction 1 involving solvated electrons formed during the pulse while the slower process is presumably due to the same reaction but involves electrons formed after the pulse by partial conversion of H· atoms, eq 7:

$$H\cdot + OH^- \rightarrow e_{aq}^- \quad (7)$$

$$k_7 = (1.4\text{–}2.3) \times 10^7\ M^{-1}\ sec^{-1}\ ^{10}$$

Assuming $G(p\text{-NC-NO}_2\cdot^-) = 1.1 \times g(e^-_{aq}) = 3.1$, ϵ_{max} of aqueous *p*-NC-$NO_2\cdot^-$ is 1.4 × 10^4 M^{-1} sec^{-1}. Radiolysis of methanol produces the reactive transients[8] e^-_s (g = 2.0), ·CH_2OH, H· (g = 2.0), $CH_3O\cdot$ (g = 2.0), and $CH_3\cdot$. e^-_s, ·CH_2OH (and its conjugate base $CH_2O\cdot^-$), and H· are one-electron reducing agents; H·, $CH_3O\cdot$, and $CH_3\cdot$ abstract hydrogen atoms from methanol to produce more ·CH_2OH. Pulsing of an argon-swept methanolic solution 0.10 m*M* in *p*-NC-NO_2 and 15 m*M* in KOH produced a spectrum, Figure 1B, λ_{max} 310 ± 5 nm, similar to the spectrum of the electron adduct in water. Based on the aqueous extinction coefficient, $G(p\text{-NC-NO}_2\cdot^-)$ = 8.0 ± 0.6 ions/100 eV in alkaline methanol. Development of this absorbance, which was complete in 20 μsec, took place in two steps, the observed first-order rates of which corresponded to second-order rate constants of 4 × 10^{10} and 2 × 10^9 M^{-1} sec^{-1}. Under N_2O, which converts solvated electrons to ·CH_2OH radicals via reactions 6 (R = CH_3) and 8, the same absorbance developed in a single step with k = 2 × 10^9 M^{-1} sec^{-1}. Thus, under pulse radiolytic conditions, alkaline methanolic *p*-NC-NO_2 reacts with both e^-_s and $CH_2O\cdot^-$ and/or ·CH_2OH under argon and with ·CH_2OH and/or $CH_2O\cdot^-$ under N_2O. In methanol, the absorbance ascribed to *p*-NC-$NO_2\cdot^-$ underwent first-order decay, k = 0.5 sec^{-1}. This decay can be ascribed to dissociation of *p*-NC-$NO_2\cdot^-$, eq 3, to nitrite and a resonance stabilized benzyl-type radical.