Condensation–Cyclization Reactions of Electron-Deficient Aromatics. VI. Isomeric Bridgehead and Nitronate Substituted Bicyclic Nitropropene Nitronates[1]

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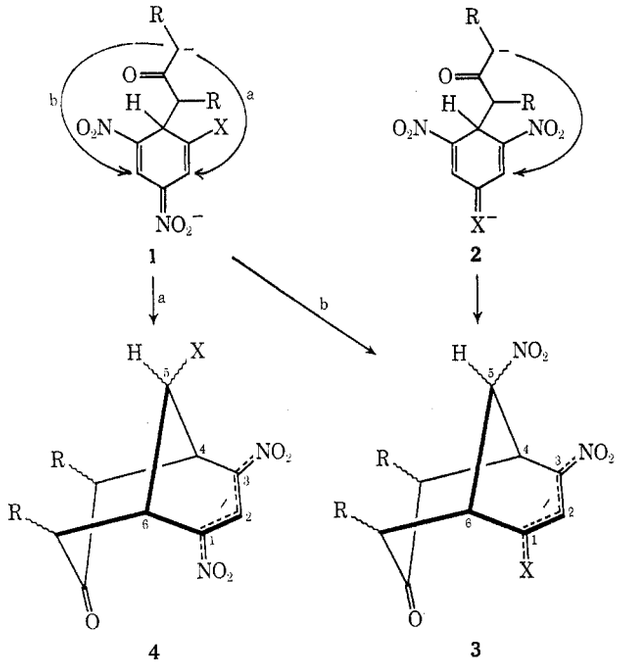
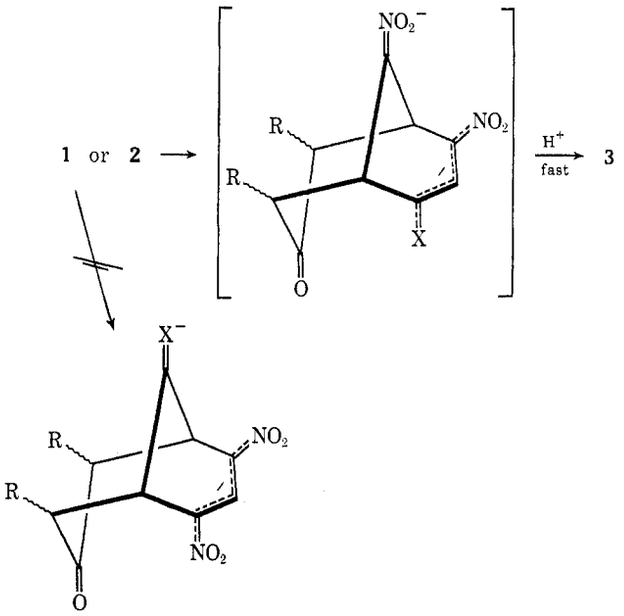
The reaction of 1-substituted 2,4,6-trinitrobenzenes with 1,3-dicarbomethoxyacetone has been shown to yield bridgehead-substituted and 2-substituted 3-nitropropene nitronates. The relationship of these isomeric products to the cyclohexadienate σ complexes formed from the reaction of simple nucleophiles with these aromatic precursors is discussed. Various mechanistic routes to products are considered, and the absence of isomers in certain cases is explained. Mechanistic aspects of the reactions of 1-substituted 3,5-dinitrobenzenes are also discussed.

Previous work on condensation–cyclization reactions of electron-deficient benzenes with ketones and keto esters has been concerned with systems in which three electron-withdrawing substituents on the aromatic ring are symmetrically disposed.[1] All those systems we have studied thus far have been 1-X-3,5-dinitrobenzenes where X = NO_2,[1] CN,[1] CO_2CH_3,[1] and COR.[2] Two possible products, **3** and **4**, could result from this type of aromatic, since the cyclization presumably could occur through either of the isomeric σ complexes **1** or **2**.[3] Only **3** was formed, however.[1,2] This result



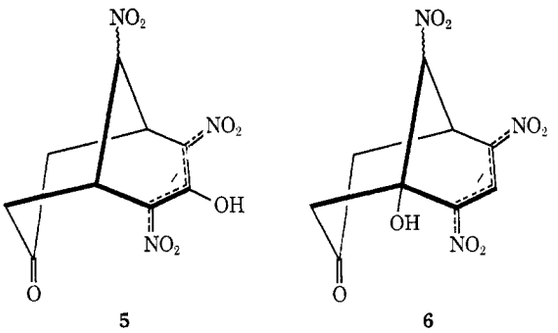
can be rationalized in two ways. The activated complex for the slow step in the cyclization process resembles that doubly charged conjugate base of the product produced by proton abstraction from C-5,[3] and the conjugate base of **3** should be much more stable than that of **4**. This stability could result in a lower energy path for cyclization leading to **3**, rather than **4** (X = CN, CO_2CH_3, or COR).

Alternately, it is possible that the only σ complex precursor to bicyclic product is **2**, which may be kinetically favored over **1**. Cyclization of **2** can only yield **3**. This latter possibility is supported by the recent



work of Crampton[4] and others,[5] which provides evidence for kinetically favored σ complexes formed by nucleophilic acetonate attack para to the X substituent (X = Cl[5] and CO_2CH_3[4]). It would require that cyclization be much more rapid than reversion of **2** to **1**, however.

We noted with interest the recent report of the bicyclic nitropropene nitronate **5**, prepared from picric acid and acetone,[6] which forms in preference to **6**.



With the objective of probing further the electronic structure of the nitropropene nitronate function,[7] and

(1) Previous papers: M. J. Strauss, T. C. Jensen, H. Schran, and K. O'Conner, *J. Org. Chem.*, **35**, 383 (1970); H. Schran and M. J. Strauss, *ibid.*, **36**, 856 (1971); M. J. Strauss and S. P. B. Taylor, *ibid.*, **36**, 3059 (1971); M. J. Strauss, S. P. B. Taylor, and H. Shindo, *ibid.*, **37**, 3658 (1972).

(2) M. J. Strauss and S. P. B. Taylor, unpublished work.

(3) M. J. Strauss and H. Schran, *Tetrahedron Lett.*, 2349 (1971).

(4) M. R. Crampton and H. A. Khan, *J. Chem. Soc., Perkin Trans. 2*, 733 (1972).

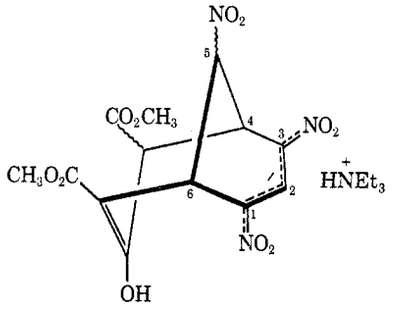
(5) M. Kimura, N. Obi, and M. Kawazoi, *Chem. Pharm. Bull.*, **20**, 452 (1972).

(6) T. Kabeya, K. Kohashi, Y. Ohkura, and T. Momose, *ibid.*, **19**, 645 (1971).

(7) M. J. Strauss and E. Weltin, *Tetrahedron Lett.*, 629 (1971).

in order to expand the scope of reactions of electron-deficient aromatics to yield both bridgehead- and nitronate-substituted bicyclics, we have investigated the reactions of 1-X-2,4,6-trinitro systems where X is inductively electron withdrawing and electron donating. It was anticipated that the inductive effect of X might influence the course of the reaction for preferential formation of bridgehead-substituted or nitronate-substituted products.

The bridging ketonic substrate used in the present study was 1,3-dicarbomethoxyacetone, which rapidly yields **7** when treated with 1,3,5-trinitrobenzene in the presence of triethylamine.[8] Three possible products, **8**, **9**, and **10**, might result from the reaction of 1-X-2,4,6-trinitrobenzenes with 1,3-dicarbomethoxyacetone. The reactions of 2,4,6-trinitrotoluene (TNT), methyl 2,4,6-trinitrobenzoate (MTNB), and *N*-(2-nitrophenyl)picramide (NPP) are now considered.



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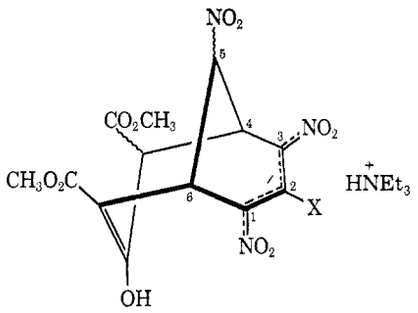
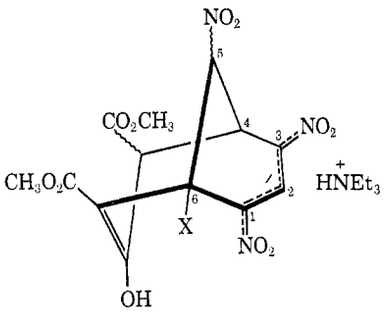
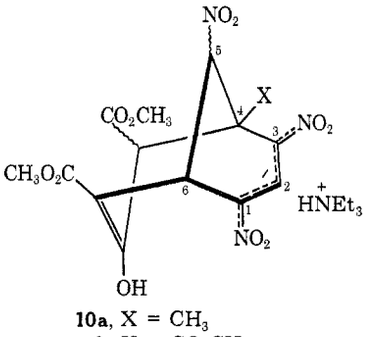


8a, X = CH_3
b, X = CO_2CH_3
c, X = $NHC_6H_4NO_2$

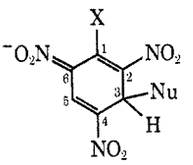


9a, X = CH_3
b, X = CO_2CH_3
c, X = $NHC_6H_4NO_2$



10a, X = CH_3
b, X = CO_2CH_3
c, X = $NHC_6H_4NO_2$

The reaction of TNT with nucleophiles has been the subject of extensive investigation by several research groups during the past 17 years.[9] It has become clear that a variety of different interactions can occur, including charge-transfer complexation, radical ion formation, proton abstraction, and σ complexation. With strongly basic nucleophiles such as hydroxide and alkoxide, the main processes occurring appear to be α-hydrogen abstraction and radical ion formation.[9a,b,d,g,h,k,l] With weaker bases such as cyanide, only σ complexation occurs to yield **11** (X = CH_3, Nu = CN).[9d,e] TNT σ complexes like **11** [Nu = C_2H_5O or 2,4,6-$(NO_2)_3C_6H_2CH_2$, X = CH_3] have been reported to form in small concentration in strongly basic solutions of TNT, however.[9k,l]



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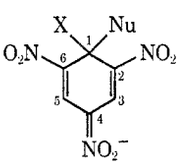

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Interestingly, with 2,4,6-trinitrobenzaldehyde addition occurs at C-1 to yield **12** (X = CHO, Nu = CN).[9d,e] This change in mode of addition with change in substrate structure is of considerable interest, since cyclization of carbanionic σ complexes (*vide supra*) like **12** (Nu = RCH_2COCH_2) can only yield bridgehead-substituted products analogous to **9** (and **10**). On the other hand, structures like **11** could yield products analogous to **8** or **9** (and **10**). The preference for **11** or **12** also bears directly on the much discussed problem of isomeric addition in 2,4,6-trinitroanisole and related electron-deficient aromatics.[10]

Since addition to C-1 of TNT has not yet been observed, whereas C-3 addition of both cyanide and TNT anion has been reported,[9] it is quite probable that the reaction of TNT with 1,3-dicarbomethoxyacetone in the presence of triethylamine will yield the C-3 adduct **11** [X = CH_3, Nu = $CH(CO_2CH_3)COCH_2CO_2CH_3$]. The cyclization step must then involve intramolecular attack at C-1 to yield **9a** or **10a**, or at C-5 to yield **8a**.

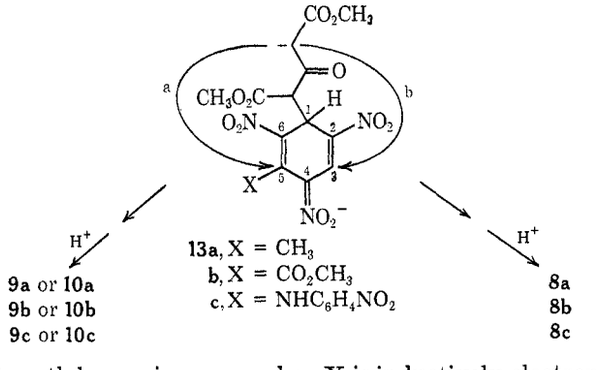
(8) M. J. Strauss and S. P. B. Taylor, *J. Org. Chem.*, **38**, 856 (1973).

(9) (a) E. F. Caldin and G. Long, *Proc. Roy. Soc., Ser. A*, **228**, 263 (1955); (b) J. A. Blake, M. J. B. Evans, and K. E. Russell, *Can. J. Chem.*, **44**, 119 (1966); (c) K. G. Shipp and L. A. Kaplan, *J. Org. Chem.*, **31**, 857 (1966); (d) E. Buncel, A. R. Norris, and W. Proudlock, *Can. J. Chem.*, **46**, 2759 (1968); (e) A. R. Norris, *ibid.*, **47**, 2895 (1969); (f) *ibid.*, **45**, 175 (1967); (g) R. E. Miller and W. F. K. Wynne Jones, *J. Chem. Soc.*, 2375 (1959); (h) K. Bowden and R. Stewart, *Tetrahedron*, **21**, 261 (1965); (i) S. S. Gitis and A. Ya. Kaminskii, *Zh. Org. Khim.*, **2**, 1811 (1966); (j) S. S. Gitis and T. Krosovskii, *J. Gen. Chem. USSR*, **29**, 2612 (1959); (k) E. Buncel, A. R. Norris, K. E. Russell, and R. Tucker, *J. Amer. Chem. Soc.*, **94**, 1646 (1972); (l) C. Bernasconi, *J. Org. Chem.*, **36**, 1671 (1971).

(10) (a) J. H. Fendler, E. J. Fendler, and C. E. Griffin, *J. Org. Chem.*, **34**, 689 (1969); (b) E. F. Fendler, J. H. Fendler, N. L. Arthur, and C. E. Griffin, *ibid.*, **37**, 812 (1972); (c) M. I. Foreman and R. Foster, *Can. J. Chem.*, **47**, 729 (1969); (d) F. Terrier and M. Simonnin, *Bull. Soc. Chim. Fr.*, **2**, 677 (1971); (e) F. Terrier, F. Millot, and P. Letellier, *ibid.*, **5**, 1743 (1970); (f) R. Schaal, F. Terrier, J. Halle, and A. Chatrousee, *Tetrahedron Lett.*, 1393 (1970); (g) F. Terrier, F. Millot, and M. Simonnin, *ibid.*, 2933 (1971); (h) C. Bernasconi, *J. Amer. Chem. Soc.*, **93**, 6975 (1971).

Addition of excess triethylamine to a saturated solution of TNT in 5 ml of 1,3-dicarbomethoxyacetone yields a dark red solution which turns dark orange on standing. Addition of anhydrous diethyl ether results in a brown-orange precipitate. After work-up and recrystallization from ethanol–ether solution, large orange crystals of product are obtained which analyze correctly for a 1:1:1 adduct of TNT, ketone, and amine. The pmr spectrum of this product (see Experimental Section) is similar to that reported previously for the analogous 1,3,5-trinitrobenzene adduct,[1] with one significant difference. The C-2 nitropropene nitronate proton which is expected to appear at $\sim\delta$ 8.5 is absent. This observation and the quartet observed for the C-5 proton are consistent only with structure **8a**. The methyl group appears at δ 2.46, 0.28 ppm upfield from that in the precursor TNT. The intermediacy of **12** [Nu = $CH(CO_2CH_3)COCH_2CO_2CH_3$, X = CH_3], at least on the reaction coordinate leading to product, is ruled out by the structure of **8a**.

Based on an analogy to tertiary and secondary carbanion stability, it might be supposed that **8a** would be less stable than **9a** or **10a**. This is not necessarily so, however, since most of the charge on **8**, **9**, or **10** resides on the oxygens of the nitro groups, and the carbon framework of the anion might in fact be slightly positive.[7,11] If this were the case, **8a** might be more stable than **9a** or **10a**. It is likely that the reaction pathway is not controlled by the thermodynamic stability of the possible products **8** or **9** and **10** in any case, but is kinetically controlled by the relative stability of the precursor intermediate **11** [X = CH_3, Nu = $CH(CO_2CH_3)COCH_2CO_2CH_3$] and the complexes for the alternate routes of cyclization of **11** through **13a**. The preference for cyclization of **13**



via path b remains, even when X is inductively electron withdrawing as in **13b**, although to a lesser extent (*vide infra*). The electronic effect of X does not cause a profound change in the course of the reaction. The preference for path b is thus likely to be steric in origin and probably results from noncoplanarity of the ring and nitro group ortho to both X and the side chain in **13**. Such noncoplanarity would favor attack by path b, where the nitro group developing additional charge is well conjugated with the site of anionic attack. Such an argument is in accord with that presented to explain why path b is favored over path a in the cyclization of **1** to **3**, rather than **4**. *It appears that the charge-stabilizing ability of the ring substituent developing charge in the cyclization step is most likely a major directive influence in intramolecular cyclizations of anionic σ complexes.*

The reaction of methyl 2,4,6-trinitrobenzoate (MTNB) with 1,3-dicarbomethoxyacetone in the presence of triethylamine gave two products, each analyzing correctly for a 1:1:1 adduct of amine, ketone, and MTNB. These were observed to crystallize separately from the reaction mixture during work-up (see Experimental Section). The product formed in larger quantity (*ca.* 80%) had a pmr spectrum characterizing **8b**; the nitronate proton resonance expected for **9b** or **10b** is absent. The other product isolated in smaller yield (*ca.* 20%) showed a singlet pmr absorption at δ 8.25, expected for a C-2 nitropropene nitronate proton,[1] and only *one* bridgehead proton, centered at δ 5.20 as a doublet ($J \cong 2.5$ cps). The latter proton is coupled to the C-5 bridging proton at δ 4.80, which also appears as a doublet ($J \cong 2.5$ cps). The proton α to CO_2CH_3 does *not* appear as a doublet, as in all the other 1,3-dicarbomethoxyacetone adducts studied, but as a singlet. This latter observation, as well as the above spectral results, provides substantial evidence for structure **10b**. The observation of this bridgehead-substituted product, even in minor amounts, would seem to support the idea that the greater electrophilic character of C-5 in **13b**, relative to **13a**, may moderate the preference for cyclization by path b in the former case.

It is interesting to note that, with *N*-(2-nitrophenyl)-picramide (NPP), the only product which could be detected and isolated was **8c**. This is not unexpected, since the *m*-nitrophenyl group is quite large, and should favor cyclization at C-3 in **13c**.

It is peculiar that the visible spectra of all the 2-substituted nitropropene nitronates prepared by us have visible maxima at about the same wavelength as unsubstituted compounds (from 446 to 499 nm in MeOH), whereas the only other previously reported 2-substituted structure, **5**, has a visible maximum at 398 nm.[6] This latter absorption is similar to that which we have previously found for nitropropene nitronic *acids*, and this suggests that the proposed structure for **5** may be incorrect. The pmr data reported by Momose, *et al.*, for **5** are completely consistent with **14**, a nitronic acid generated by hydroxylic proton

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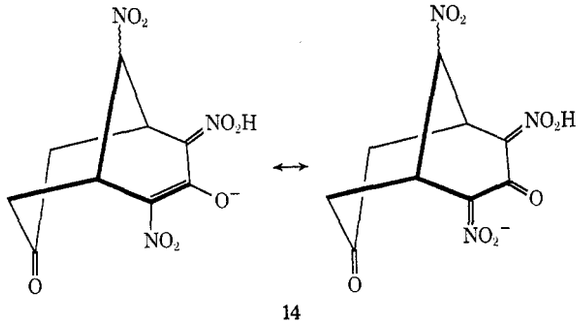

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transfer to an adjacent nitronate function of **5**, if proton transfer between nitronate and nitronic acid functions is rapid compared to the pmr time scale.

Experimental Section

All melting points are uncorrected. Ir and visible spectra were recorded with PE Models 21 and 402 spectrophotometers, re-

(11) H. Hosoya, S. Hosoya, and S. Nagakura, *Theor. Chim. Acta*, **12**, 117 (1968).

spectively. Pmr spectra were recorded on JEOL MH-100 and C-60 HL spectrometers, and chemical shifts are reported with respect to internal TMS. Elemental analyses were performed by G. I. Robertson Laboratory, Florham Park, N. J.

Preparation of 8a.—To a solution of 2.0 g (0.0093 mol) of TNT dissolved in a minimum amount of 1,3-dicarbomethoxyacetone at 25° was added about 3 ml of triethylamine. After standing at room temperature for 10 hr, the reaction mixture was washed with anhydrous ether to remove the unreacted ketone. After several 100-ml washings the oily residue finally solidified to an orange powder, which when recrystallized from a 1:4 ether–ethanol mixture yielded cubic crystals of **8a**: mp 116–117°; λ_{max} (MeOH) 446 nm; ir (KBr) 1730, 1662, 1610, 1555, 1490, 1450 cm^{-1}; pmr ($DCCl_3$) δ 1.36 [t, 9 H, $^+HN(CH_2CH_3)_3$], 2.46 (s, 3 H, CH_3), 3.18 [q, 6 H, $^+HN(CH_2CH_3)_3$], 3.75 and 3.85 (each a singlet, 3 H each, CO_2CH_3), 4.15 (d, 1 H, $CHCO_2CH_3$), 4.42 (q, 1 H, $CHNO_2$), 5.30 (d, 2 H, bridgehead protons), 11.08 [br, 2 H, $HN(CH_2CH_3)_3$ and OH]. A pmr spectrum of the crude product showed the absence of **9a**.

Anal. Calcd for $C_{20}H_{30}N_4O_{11}$: C, 47.81; H, 6.02; N, 11.15. Found: C, 48.04; H, 6.31; N, 11.09.

Preparation of 8b and 10b.—To a solution of 2.0 g (0.0074 mol) of methyl 2,4,6-trinitrobenzoate dissolved in a minimum amount of 1,3-dicarbomethoxyacetone at 50° was added 2 ml of tetrahydrofuran and 3 ml of triethylamine. After 4 hr at 25° the reaction mixture was washed with 75-ml portions of anhydrous ether. The resulting oil was dissolved in 35 ml of hot methanol and 90 ml of ether was added. After standing for 2 days at 25°, crystals were deposited on the bottom of the flask. Examination of these with a stereomicroscope showed two distinct crystalline forms. The crystals formed in larger quantity (*ca.* 80%) were a dull orange, while a smaller quantity of bright red-orange crystals were also formed (*ca.* 20%). These crystals were separated manually under the microscope, and each was recrystallized from ether–methanol solution. The product formed in the largest amount was **8b**, the remaining amount being **10b**. There was essentially no product left in the mother liquor.

8b had mp 142–143° and was hygroscopic; λ_{max} (MeOH) 499 nm; ir (KBr) 1742, 1725, 1665, 1610, 1555 cm^{-1}; pmr ($CDCl_3$) δ 1.35 [t, 9 H, $^+HN(CH_2CH_3)_3$], 3.15 [q, 6 H, $^+HN(CH_2CH_3)_3$], 3.80 (s, 3 H, CO_2CH_3), 3.85 (s, 6 H, two CO_2CH_3), 3.82 (d, 1 H, $CHCO_2CH_3$), 4.5 (q, 1 H, $CHNO_2$), 5.26 and 5.46 (two q, bridgehead protons), 12.1 [br, 2 H, $^+HN(CH_2CH_3)_3$ and OH].

Anal. Calcd for $C_{21}H_{30}N_4O_{13}$: C, 46.16; H, 5.53; N, 10.25. Found: C, 45.68; H, 5.76; N, 9.99.

10b had mp 142–143°; λ_{max} (MeOH) 497 nm; ir (KBr) 1755, 1740, 1650, 1610, 1555 cm^{-1}; pmr ($CDCl_3$) δ 1.35 [t, 9 H, $^+HN(CH_2CH_3)_3$], 3.15 [q, 6 H, $^+HN(CH_2CH_3)_3$], 3.70 (s, 3 H, CO_2CH_3), 3.85 (s, 6 H, two CO_2CH_3), 4.80 (s, 1 H, $CHCO_2CH_3$), 5.2 (d, 1 H, $CHNO_2$), 5.38 (br d, 1 H, bridgehead), 8.75 (s, 1 H, nitropropene nitronate), 12.1 [br, 2 H, $^+HN(CH_2CH_3)_3$ and OH].

Anal. Calcd for $C_{21}H_{30}N_4O_{13}$: C, 46.16; H, 5.53; N, 10.25. Found: C, 46.96; H, 6.19; N, 9.42

Preparation of 8c.—A solution of 2 g (0.008 mol) of *N*-(2-nitrophenyl)picramide and 3 ml of triethylamine in the minimum amount of 1,3-dicarbomethoxyacetone necessary for dissolution was allowed to stand at room temperature for 4 hr. After washing the resulting reaction mixture with two 125-ml portions of ether an oily residue was obtained, which when recrystallized from a methanol–ether solution yielded orange crystals of **8c**: mp 155°; λ_{max} (CH_3OH) 458 nm; ir (KBr) 1740, 1660, 1610, 1535 cm^{-1}; pmr ($CDCl_3$) δ 1.10 [t, 9 H, $^+HN(CH_2CH_3)_3$], 2.85 [q, 6 H, $^+HN(CH_2CH_3)_3$], 3.70 and 3.78 (two s, 3 H each, two CO_2CH_3), 4.1 (d, 1 H, $CHCO_2CH_3$), 4.3 (q, 1 H, $CHNO_2$), 5.15 and 5.50 (two q, 2 H, bridgehead), 7.2–7.8 (m, 4 H, *m*-$NO_2C_6H_4$), 12.4 [broad s, 2 H, $^+HN(CH_2CH_3)_3$ and OH].

Anal. Calcd for $C_{25}H_{32}N_6O_{13}$: C, 48.10; H, 5.18; N, 13.48. Found: C, 47.93; H, 5.31; N, 13.34.

Registry No.—**8a**, 38218-79-0; **8b**, 38355-40-7; **8c**, 38218-80-3; **10b**, 38413-80-8; TNT, 118-96-7; MTNB, 15012-38-1; NPP, 38229-29-7; 1,3-dicarbomethoxyacetone, 1830-54-2.

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Photochemical Transformations of Small Ring Heterocyclic Compounds. XLVIII. Further Studies on the Photocycloaddition and Photodimerization Reactions of Arylazirines[1]

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Further evidence for the mechanism of the photodimerization of arylazirines was obtained by irradiating a mixture of phenyl- and diphenylazirine. The formation of a mixture of *endo*- and *exo*-2,4,5-triphenyl-1,3-diazabicyclo[3.1.0]hex-3-ene is rationalized in terms of 1,3-dipolar addition of the nitrile ylide derived from diphenylazirine onto the C–N double bond of phenylazirine. Irradiation of methyl- and dimethylphenylazirine in an inert solvent gave 1,3-diazabicyclo[3.1.0]hex-3-enes as primary photoproducts. The initial photodimers undergo subsequent photoreaction. The products formed depend on the substituent groups, the time of irradiation, and the particular solvent employed. The photocycloaddition of arylazirines has been found to proceed with a wide variety of dipolarophiles and provides a synthetic route into systems otherwise difficult to prepare.

In earlier papers we have shown that arylazirines undergo photocycloaddition with electron-deficient olefins to give Δ^1-pyrroline derivatives.[1,5] The formation of the adducts was interpreted as proceeding by way of irreversible ring opening of the azirine ring to form a nitrile ylide intermediate, which was subsequently trapped by a suitable dipolarophile. Arylazirines are also known to undergo photodimerization to 1,3-diazabicyclo[3.1.0]hex-3-enes.[6,7] The formation of these dimers was rationalized in terms of 1,3-dipolar addition of the initially generated nitrile ylide onto a ground-state azirine molecule. This conclusion was reached by a study of the variation of the quantum

(1) Part XLVII: A. Padwa, M. Dharan, J. Smolanoff, and S. I. Wetmore, Jr., *J. Amer. Chem. Soc.*, **95**, 1954 (1973). Part XLVI: *ibid.*, **95**, 1945 (1973).

(2) Alfred P. Sloan Foundation Fellow, 1968–1972; National Institutes of Health Special Postdoctoral Fellow, 1972–1973.

(3) NDEA Title IV Fellow, 1969–1971.

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