α,β-Unsaturated Carboxylic Acid Derivatives. XV. The Reaction of Ethyl 3-Nitro-2-alkenoate with Bromine Azide or Bromine, and Transformations of the Products[1)]

Chung-gi SHIN,* Yasuchika YONEZAWA, Kaoru SUZUKI, and Juji YOSHIMURA**

Laboratory of Organic Chemistry, Faculty of Technology, Kanagawa University, Rokkakubashi, Kanagawa-ku, Yokohama 221

***Laboratory of Chemistry for Natural Products, Faculty of Science, Tokyo Institute of Technology, Nagatsuta, Midori-ku, Yokohama 227*

(Received November 4, 1977)

The reaction of ethyl (*Z*)-3-nitro-2-alkenoate (**1**) with one or two equivalents of bromine azide gave a one-to-one mixture of ethyl (*E*)-2-azido-3-nitro-2-alkenoate (**3**) and 4-ethoxycarbonyl-1,2,5-oxadiazole 2-oxide (**5**), or ethyl 3-bromo-2,2-diazido-3-nitroalkanoate (**6**), respectively, and the subsequent thermal and photochemical reactions of (*E*)-**3** gave 2-ethoxycarbonyl-3-nitro-1-azirine, together with a small amount of **5**. The addition of bromine to **1**, and the subsequent elimination of hydrogen bromide from the product, gave exclusively, the (*Z*)-2-bromo derivative (**9**). The reduction of **6** and **9** with diethyl phosphonate was examined, and the reaction mechanisms were discussed.

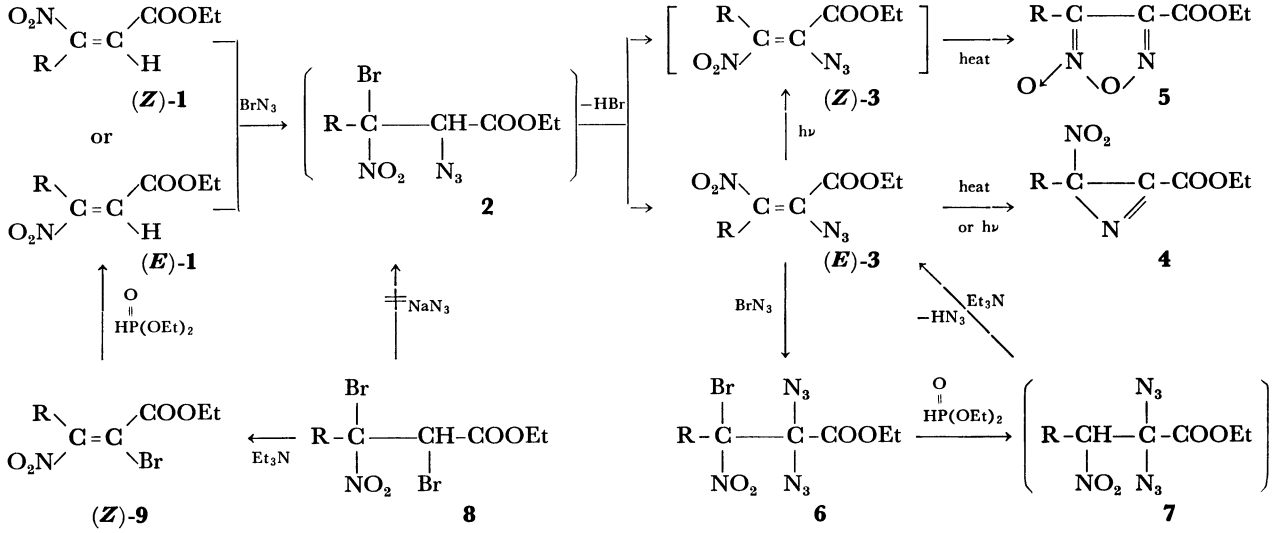
Although a few articles have been published on the properties of vicinal azido nitro olefins as intermediates, their isolation and their conversion into the corresponding nitroazirines have never been reported, except for the formation of 1,2,5-oxadiazole 2-oxides.[2-4)] Previously, however, we have ourselves reported the synthesis of stable α- and β-azido olefins[5,6)] and their conversion into the corresponding azirines[6)] and enamines.[7)]

In this paper, the reaction of bromine azide or bromine with ethyl 3-nitro-2-alkenoate[8)] and the subsequent elimination, substitution, and thermal and photochemical reactions of the products were examined, in order to isolate stably and convert the azido nitro olefins into the nitroazirine derivatives. Consequently, the expected several kinds of new vicinal azido nitro and bromo nitro compounds, nitroazirine, and 1,2,5-oxadiazole 2-oxide derivatives were obtained, as is shown in Scheme 1.

Results and Discussion

When an equimolar amount of ethyl (*E*)- or (*Z*)-3-nitro-2-alkenoate (**1**; **a**; R=CH_3, **b**; R=C_2H_5, **e**; R=C_6H_5) was treated with halo azide [formed from *N*-bromo- or *N*-chlorosuccinimide (NBS and NCS) and sodium azide in water][9)] in *N*,*N*-dimethylformamide (DMF), a syrup composed of two chemical species was obtained. In order to separate the mixture, it was carefully subjected to chromatography on a silica gel column, using benzene–petroleum ether (1:1 v/v), to give a pale yellow syrup (**3**) (1st fraction) and a colorless syrup (**5**) (2nd fraction) in a ratio of *ca.* 1:1. On the other hand, when the reaction was carried out in benzene under refluxing, **5** and a colorless syrup (**4**) were obtained in a ratio of *ca.* 1:1.

The structures of **3**, **4**, and **5** were assigned to ethyl 2-azido-3-nitro-2-alkenoate, 3-substituted 2-ethoxycarbonyl-3-nitro-1-azirine and 3-substituted 4-ethoxycarbonyl-1,2,5-oxadiazole 2-oxide respectively on the basis of their spectroscopic data as well as the results



a; R=CH_3, **b**; R=C_2H_5, **c**; R=*n*-C_3H_7, **d**; R=*i*-C_3H_7, **e**; R=C_6H_5

Scheme 1.

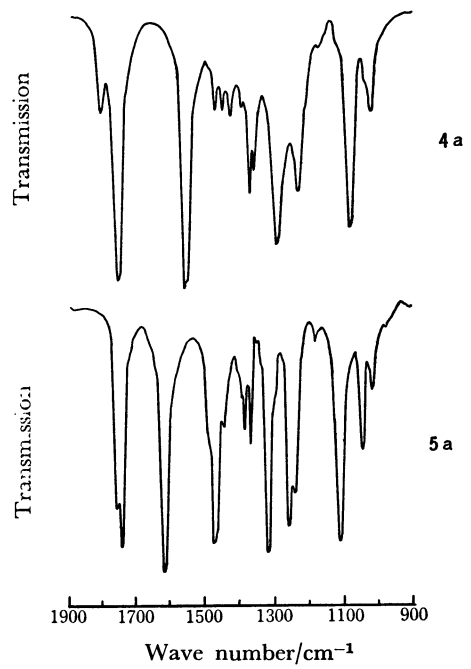


Fig. 1. IR spectrum of **4a** and **5a**.

of their elemental analyses. The difference between **4** and **5** can be characterized unambiguously by a comparison of their IR spectral data, shown in Fig. 1. The absorption bands at 1555—1560 and 1370 cm^{-1} assigned to the nitro group and the carbon-nitrogen double bond[6] of the azirine ring at 1790—1800 cm^{-1} indicate the formation of nitroazirine (**4**), whereas the disappearance of the nitro group in **5** supports the idea of ring formation between the oxygen in the nitro group and the nitrogen atom caused by the azido group.[2-4]

The configuration of a separated isomer of **3** could be determined as (*E*)-geometry by the formation of **4**, since the (*Z*)-isomer of vicinal azido nitro olefins is known to convert immediately at a higher temperature into the corresponding 1,2,5-oxadiazole 2-oxide.[2-4] It is noteworthy that (***E***)-**3** is the first example of an isolated azido nitro olefin.

Next, the thermal isomerization from (***E***)-**3** to (***Z***)-**3** was performed in benzene under reflux; however, only **4** was obtained in *ca.* a 60% yield. The irradiation of (***E***)-**3** in carbon tetrachloride externally with a high-pressure mercury lamp under a stream of nitrogen gas at room temperature also gave **4** in *ca.* a 35% yield, together with a small amount of **5**. This shows that (***E***)-**3** is slightly isomerized to (***Z***)-**3**, which is then immediately cyclized to **5**.

Moreover, the similar treatment of (***E***)-**1** or (***Z***)-**1** with two molar bromine azide gave the same compound as a colorless syrup in *ca.* a 70% yield. It was identified, by means of spectroscopic analyses, as ethyl 3-bromo-2,2-diazido-3-nitro-alkanoate (**6**). It is known that diethyl phosphonate does not react with both nitro[10] and azido[11] groups in the carboxylic acid ester and that it reduces the halogen atom.[12] Accordingly, when **6** was treated with diethyl phosphonate in benzene in the presence of triethylamine, (***E***)-**3** was obtained in a fairly good yield, along with **5** in a low ylied. This fact indicates that the bromide atom of **6** is reduced with phosphonate to form an unstable intermediate, ethyl 2,2-diazido-3-nitroalkanoate (**7**); the subsequent rapid elimination of hydrazoic acid[13] in the presence of the base from **7** gives (***E***)-**3** snd (***Z***)-**3**, the latter of which is further transformed into **5**.

From the above facts, the formation of **3** and **6** from **1** seems to be through successive the addition reaction of bromine azide to **1** and the elimination of hydrogen bromide to give (***E***)-**3** and (***Z***)-**3**, formed as a labile intermediate, which in turn reacts further with excess bromine azide to give **6**, as is shown in Scheme 1. The latter addition was substantiated unambiguously by the reaction of the isolated (***E***)-**3** with bromide azide.

The yields, physical constants, and spectral data of **3**—**6** are summarized in Tables 1 and 2.

On the other hand, the dehydrobromination of ethyl 2,3-dibromo-3-nitroalkanoate (**8**), prepared in a good yield from the reaction of (***E***)-**1** or (***Z***)-**1** with bromine in chloroform, with triethylamine gave 2-bromo-3-nitro-2-alkenoate (**9**) in *ca.* a 90% yield. Although the compound, **8**, derived from individual (***E***)-**1** and (***Z***)-**1** consisted of two stereoisomers in various ratios, listed in Table 3, according to the reaction, a single product, **9**, was formed stereospecifically. The configuration of **9** could be determined as the (*Z*)-geometry by conversion into (***E***)-**1** in *ca.* a 50% yield by reduction with diethyl phosphonate. From the above results, it was deduced that the base-catalyzed β-elimination of **8** composed of erythro- and threo-stereoisomers (see Table 3) proceeded by means of ElcB mechanism *via* the corresponding nitronate carbanion.[8] Attempts at the substitution of the bromo atom at the 2-position with the azido group in **8** and **9** by treatment with sodium azide was unsuccessful, forming an ambiguous mixture.

Table 1. The yields and spectral data of **3** and **6**

Compound[a] R		Yield[b] (%)	Yield[c] (%)	IR spectrum in KBr (cm^{-1}) N_3	ester	C=C	NO_2	NMR spectrum[d] 3-alkyl (J_{Hz}) (3-phenyl)
(***E***)-**3a**	CH_3	41.9	85.1	2100,	1730,	1640,	1515, 1320	2.20 s
(***E***)-**3b**	C_2H_5	38.8	81.2	2100,	1732,	1635,	1520, 1330	2.61 q (7.2 Hz)
(***E***)-**3e**	C_6H_5	36.5	75.8	2110,	1735,	1622,	1532, 1335	(7.30 s)
6a	CH_3	70.3		2100,	1750,		1562, 1332	2.48 s
6b	C_2H_5	74.2		2100,	1750,		1565, 1320	2.28—3.08m
6e	C_6H_5	75.2		2120,	1760,		1570, 1340	(7.45—7.76m)

a) **3**; pale yellow syrup, **6**; colorless syrup. b) From **1**. c) From **6**. d) δ value, measured in $CDCl_3$.

TABLE 2. THE YIELDS, PHYSICAL CONSTANTS, AND SPECTRAL DATA OF **4** AND **5**

Compound	R	Yield (%)[a]	Yield (%)[b]	Yield (%)[c]	Yield (%)[d]	(Mp °C) Bp °C/mmHg	Formula	Found (Calcd), % C	H	N	IR spectrum[f] (cm^{-1}) N→O C=N	Ester	NO_2	NMR spectrum[g] 3-alkyl (J_{Hz}) (3-phenyl)
4a	CH_3	32.5	62.5	36.7	—	69—72/0.5	$C_6H_8N_2O_4$	41.90 (41.86	4.70 4.68	16.19 16.28)	1800,	1750,	1555 1370	2.70 s
4b	C_2H_5	40.1	55.7	35.5	—	71—77/0.5	$C_7H_{10}N_2O_4$	45.12 (45.16	5.44 5.41	15.15 15.05)	1790,	1750,	1558 1370	3.06 q (7.6 Hz)
4e	C_6H_5	29.1	61.2	38.5	—	syrup	$C_{11}H_{10}N_2O_4$	56.40 (56.41	4.22 4.30	11.89 11.96)	1795,	1750,	1560 1370	(7.38—8.00m)
5a	CH_3	2.5	—	32.5	10.5	67—71/0.5	$C_6H_8N_2O_4$	41.91 (41.86	4.72 4.68	16.25 16.28)	1615,	1745		2.46 s
5b	C_2H_5	3.1	—	40.2	12.5	70—75/0.5	$C_7H_{10}N_2O_4$	45.11 (45.16	5.43 5.41	15.08 15.05)	1610,	1742		2.86 q (7.5 Hz)
5e	C_6H_5	3.2	—	35.6	17.2	(51—52)[e]	$C_{11}H_{10}N_2O_4$	56.44 (56.41	4.39 4.30	11.88 11.96)	1585,	1745		(7.48—7.77m)

a) From the photochemical reaction of **3**. b) From the thermal reaction of **3**. c) From **1**. d) From **6**. e) Colorless needles from ethanol. f) Recorded in KBr. g) δ value, measured in $CDCl_3$.

TABLE 3. THE YIELDS, PHYSICAL CONSTANTS, AND SPECTRAL DATA OF **8** AND **9**

Compound	R	Yield (%)	Bp °C/mmHg (Mp °C)	Formula	Found (Calcd), % C	H	N	IR spectrum in KBr (cm^{-1}) Ester	C=C	NO_2	MNR spectrum[a] 2-H	E[d] : T[e] ratio[c]
8a	CH_3	95.0	67—68/0.33	$C_6H_9NO_4Br_2$	22.52 (22.57	2.80 2.82	4.81 4.89)	1752,		1570, 1330	5.05 s, 5.03 s	6 : 1
8b	C_2H_5	92.3	88—90/0.13	$C_7H_{11}NO_4Br_2$	25.26 (25.22	3.34 3.30	4.25 4.20)	1745,		1560, 1325	5.29 s, 5.19 s	4 : 1
8c	n-C_3H_7	93.5	93—95/0.13	$C_8H_{13}NO_4Br_2$	27.39 (27.66	3.75 3.75	4.06 4.03)	1745,		1560, 1330	5.27 s, 5.14 s	3 : 1
8d	i-C_3H_7	61.5	84—85/0.18	$C_8H_{13}NO_4Br_2$	27.60 (27.66	3.72 3.75	4.05 4.03)	1760,		1580, 1325	5.28 s, 5.15 s	6 : 1
8e	C_6H_5	60.5	colorless syrup	$C_{11}H_{11}NO_4Br_2$	34.55 (34.65	2.97 2.87	3.62 3.67)	1750,		1570, 1330	5.72 s, 5.61 s	1 : 5
9b	C_2H_5	85.5	64—70/0.2	$C_7H_{10}NO_4Br$	33.40 (33.33	3.97 3.96	5.49 5.55)	1735,	1640,	1545, 1337		
9c	n-C_3H_7	87.7	75—79/0.4	$C_8H_{12}NO_4Br$	36.37 (36.09	4.35 4.51	5.33 5.26)	1730,	1635,	1535, 1330		
9d	i-C_3H_7	91.1	65—66/0.3	$C_8H_{12}NO_4Br$	36.12 (36.09	4.45 4.51	5.30 5.26)	1735,	1620,	1545, 1338		
9e	C_6H_5	90.2	(96.5—97.5)[b]	$C_{11}H_{10}NO_4Br$	44.05 (44.00	3.35 3.33	4.62 4.67)	1740,	1650,	1527, 1328		

a) δ value, measured in $CDCl_3$. b) Colorless needles crystallized from benzene-petroleum ether. c) Evaluated from the intensity of the methine proton in the 2-position. d) Erythro. e) Threo.

The yields, physical constants, and spectral data of **8** and **9** are listed in Table 3.

Experimental

All the boiling and melting points are uncorrected. The IR spectra were recorded with a Hitachi EPI-G3 Spectrometer. The NMR spectra were measured with a JNM-PS-100 Spectrometer (Japan Electron Optics Laboratory Co., Ltd.), using tetramethylsilane as the internal standard.

Preparation of ***3***, ***4***, *and* ***5***. Into a solution of NBS or NCS (0.06 mol) in DMF (100 ml) we stirred, drop by drop, a solution of sodium azide (0.06 mol) in water (18 ml) at −20 °C for 15 min. The resulting solution was added, drop by drop, to a solution of (***E***)-**1** or (***Z***)-**1** (0.06 mol) in DMF (20 ml) at −40——45 °C. After stirring at −30 °C for 45 min, the mixture was poured into ice-water (350 ml). After continuous stirring for 1 h, the aqueous solution was extracted three times with dichloromethane (130 ml). The extracts were collected, washed twice with water, and then dried over anhydrous magnesium sulfate. The dichloromethane layer was evaporated to give a residual syrup, which was chromatographed on a silica gel column, using benzene–petroleum ether (1:1 v/v) as an eluent below 5 °C. Mainly two fractions were obtained. After concentrating each fraction, the (***E***)-**3** compound as a pale yellow syrup from the first eluted fraction and **5** as a colorless syrup from the second eluted one were obtained.

On the other hand, the syrup obtained from the above dichloromethane solution was directly dissolved in dry benzene (60 ml), and then the benzene solution was refluxed for 1 h. The resulting solution was evaporated to give a residual syrup, which was distilled under reduced pressure to give a colorless syrup composed of a mixture of **4** and **5**. A similar separation gave **4** and **5** in *ca.* a 1:1 ratio.

Preparation of ***6***. *Procedure A*: Into a solution of (***E***)-**1** or (***Z***)-**1** (0.05 mol) and NBS (0.11 mol) in DMF (100 ml) we stirred drop by drop, a solution of sodium azide (0.11 mol) in DMF–water (1:1 v/v) (30 ml) below −10 °C. After continuous stirring for 40 min, the mixture was poured into ice water (400 ml). After stirring for 1 h, the aqueous solution was extracted three times with hexane (100 ml). The extracts were collected, washed twice with water, dried over sodium sulfate, and finally evaporated under reduced pressure to dryness. The residual syrup was placed in a silica gel column using benzene as the eluent. The fractions were collected and evaporated under reduced pressure to give **6** as a colorless syrup.

Procedure B: Into a solution of (***E***)-**3** (0.01 mol) in DMF (30 ml) we stirred drop by drop, a solution of NBS (0.01 mol) and sodium azide (0.01 mol) in water (10 ml) below −10 °C. After continuous stirring for 30 min, the mixture was worked up such as has been described in Procedure A.

Thermal Reaction of (**E**)-***3***. A solution of (***E***)-**3** (0.03 mol) in dry benzene (20 ml) was refluxed for 1 h. After the removal of the solvent under reduced pressure, the residual syrup was purified on a silica gel column, using benzene–ethyl acetate (20:1 v/v) as the eluent. The fraction was then collected and concentrated. The residue was distilled under reduced pressure to give **4**.

Photochemical Reaction of (**E**)-***3***. A solution of (***E***)-**3** (0.03 mol) in dry carbon tetrachloride (80 ml) was irradiated with a high-pressure mercury lamp (450 W) in a stream of nitrogen gas at 10 °C for *ca.* 7 h, at which time the azido group band at *ca.* 2100 cm^{-1} disappeared. The resultant solution was evaporated; the purification of the residual syrup thus obtained was worked up such as above to give **4** and **5** in *ca.* a 10:1 ratio.

Reaction of ***6*** *with Diethyl Phosphonate*. Into a mixture of **6** (0.01 mol) and diethyl phosphonate (0.01 mol) in dry benzene (30 ml) we stirred, drop by drop, triethylamine (0.01 mol) below 10 °C. After continuous stirring for 30 min, triethylammonium bromide was filtered off, and then the benzene layer was concentrated under reduced pressure. The residual syrup was chromatographed on a silica gel column, using benzene as the eluent; two fractions were thus obtained. After each fraction had been concentrated under reduced pressure, the first fraction gave (***E***)-**3** in *ca.* an 80% yield, while the second one gave **5** in *ca.* a 13% yield.

Preparation of ***8***. To a solution of (***E***)-**1** or (***Z***)-**1** (0.1 mol) in chloroform (70 ml) we added, drop by drop, a solution of bromine (0.1 mol) in chloroform (30 ml) with occasional shaking. The mixture was allowed to stand at room temperature for 24 h and then concentrated to dryness. The residual oil was distilled under reduced pressure to give **8** as a colorless oil.

Preparation of ***9***. Into a solution of **8** (0.1 mol) in dry benzene (80 ml) we stirred, drop by drop, triethylamine (0.12 mol) under cooling. After continuous stirring overnight at room temperature, triethylammonium bromide was precipitated. It was filtered off, and the filtrate was washed sucessively with 3 M-hydrochloric acid and water. The resulting benzene layer was dried over anhydrous magnesium sulfate and concentrated under reduced pressure to give a residual syrup. The residue was distilled under reduced pressure to give (***Z***)-**9** as a colorless oil.

Reaction of (***Z***)-***9*** *with Diethyl Phosphonate*. Into a solution of (***Z***)-**9** (0.1 mol) and diethyl phosphonate (0.1 mol) in dry benzene (70 ml) we stirred, drop by drop, triethylamine (0.12 mol) under cooling. After continuous stirring for 1 h at room temperature, triethylammonium bromide was filtered off and the filtrate was washed successively with 3 M-hydrochloric acid and water. The benzene layer was dried over anhydrous magnesium sulfate and concentrated under reduced pressure to give (***E***)-**1** as a colorless oil.

References

1) Part XIV: C. Shin, Y. Kosuge, M. Yamaura, and J. Yoshimura, *Bull. Chem. Soc. Jpn.*, **51**, 1134 (1978).
2) W. D. Emmons and J. P. Freeman, *J. Org. Chem.*, **40**, 456 (1975).
3) T. E. Stevens and W. D. Emmons, *J. Am. Chem. Soc.*, **80**, 338 (1958).
4) A. N. Thakeore, J. Buchshriber, and A. C. Oehleschlager, *Can. J. Chem.*, **51**, 2406 (1973).
5) C. Shin, Y. Yonezawa, and J. Yoshimura, *Tetrahedron Lett.*, **1974**, 7.
6) C. Shin, Y. Yonezawa, and J. Yoshimura, *Chem. Lett.*, **1976**, 1063.
7) C. Shin, Y. Yonezawa, and J. Yoshimura, *Chem. Lett.*, **1976**, 1095.
8) C. Shin, Y. Yonezawa, H. Narukawa, K. Nanjo, and J. Yoshimura, *Bull. Chem. Soc. Jpn.*, **45**, 3595 (1972); C. Shin, Y. Yonezawa, and J. Yoshimura, *Nippon Kagaku Kaishi*, **1974**, 718.
9) D. V. Ende and A. Krief, *Angew. Chem. Int. Ed. Engl.*, **13**, 279 (1974).
10) C. Shin, Y. Yonezawa, K. Katayama, and J. Yoshimura, *Bull. Chem. Soc. Jpn.*, **46**, 1727 (1973).
11) Unpublished data.
12) S. Dershowitz and S. Proskauer, *J. Org. Chem.*, **26**, 3595 (1961); A. J. Speziale and C. C. Tung, *ibid.*, **28**, 1353 (1963).
13) A. Hassner and F. W. Fowler, *J. Am. Chem. Soc.*, **90**, 2869 (1968).